New Research

American Psychiatric Association

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Addressing Patient Needs
Access, Parity and Humane Care

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San Diego, California, May 19-24, 2007
American Psychiatric Association

San Diego, CA May 19-24, 2007
NR1  Monday, May 21, 9:00 AM - 10:30 AM
Possible Criteria for Inpatient Psychiatric Admissions: Which Patients Are Transferred From Emergency Services to Inpatient Psychiatric Treatment?
Marc Ziegenbein, M.D., Hannover Medical School (MHH), Socialpsychiatry and Psychotherapy, Carl-Neuberg-Str.1, Hannover, 30623, 4280, Christoph Anreas, M.D., Bernhard Brueggen, Martin Ohimeier, M.D., Stefan Kropp, M.D.

Educational Objectives:

1. Understand the challenges of treating geriatric depression that include high rates of recurrence, chronicity, and limited efficacy of traditional antidepressants.
2. Identify the side effect profile of lamotrigine when used in geriatric patients.
3. Recognize the possible use of lamotrigine as a treatment for geriatric depression.

Summary:

Objective: To evaluate the safety and efficacy of lamotrigine (Lamictal®) in the treatment of unipolar late-life depression.

Method: Participants were nine older adults, aged 55 to 82 years, with recurrent Major Depressive Disorder. Exclusionary criteria included Bipolar Disorder and dementia. A physical examination, bloodwork, EKG, and MMSE were performed prior to study entry. Intervention consisted of a ten-week, open-label trial of lamotrigine titrated to a maximum dose of 200mg/day with flexible dosing. Participants were monitored every two weeks for mood symptoms and adverse events with the Montgomery Asberg Depression Rating Scale (MADRS) as the primary measure and the Geriatric Depression Scale (GDS) as secondary. All visits took place at Beth Israel Medical Center, New York.

Results: Six out of nine participants completed the trial. Of the three drop-outs, two could not tolerate 25mg/day (one with rash, one with GI distress) and the third could not tolerate 50mg/day (rash). We performed statistical analyses on six completers whose maximum doses ranged from 75mg-200mg/day. Five of 6 had previous exposure to antidepressants. Analyses revealed significant improvement in MADRS total scores from mean baseline of 33.0 (sd 7.8) to mean final score of 20.7 (sd 10.8; p=.001) and GDS total scores from mean baseline of 11.7 (sd 1.6) to mean final score of 7.8 (sd 4.7; p=.05). Adverse events included rash (none serious), GI complaints, weight gain, dizziness, headaches, unsteady gait, and nightmares. For most participants, adverse events resolved within the first month of treatment.

Conclusion: Lamotrigine was associated with statistically significant improvement in mood in six individuals who tolerated a 10-week exposure. Three other individuals started on medication terminated prematurely due to adverse effects. Given these results, a double-blind, placebo-controlled study is warranted to assess the safety and efficacy of lamotrigine in unipolar geriatric depression. This study was funded by GlaxoSmithKline.

References:

NR2  Monday, May 21, 9:00 AM - 10:30 AM
An Open-Label Trial of Lamotrigine (Lamictal®) for Unipolar Late-Life Depression
David Woo, M.D. Beth Israel Medical Center, Psychiatry, Beth Israel Medical Center, First Avenue at 16th Street, 2 Bernstein, New York, NY, 10003, 9000, David M. Roane, M.D., Jennifer A. Tucker, M.S., Igor I. Galynker, M.D., Melanie Akalal, M.D., Theresa E. Perlis, Ph.D.

Educational Objectives:

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

1. Understand the challenges of treating geriatric depression that include high rates of recurrence, chronicity, and limited efficacy of traditional antidepressants.
2. Identify the side effect profile of lamotrigine when used in geriatric patients.
3. Recognize the possible use of lamotrigine as a treatment for geriatric depression.

Summary:

Objective: To evaluate the safety and efficacy of lamotrigine (Lamictal®) in the treatment of unipolar late-life depression.

Method: Participants were nine older adults, aged 55 to 82 years, with recurrent Major Depressive Disorder. Exclusionary criteria included Bipolar Disorder and dementia. A physical examination, bloodwork, EKG, and MMSE were performed prior to study entry. Intervention consisted of a ten-week, open-label trial of lamotrigine titrated to a maximum dose of 200mg/day with flexible dosing. Participants were monitored every two weeks for mood symptoms and adverse events with the Montgomery Asberg Depression Rating Scale (MADRS) as the primary measure and the Geriatric Depression Scale (GDS) as secondary. All visits took place at Beth Israel Medical Center, New York.

Results: Six out of nine participants completed the trial. Of the three drop-outs, two could not tolerate 25mg/day (one with rash, one with GI distress) and the third could not tolerate 50mg/day (rash). We performed statistical analyses on six completers whose maximum doses ranged from 75mg-200mg/day. Five of 6 had previous exposure to antidepressants. Analyses revealed significant improvement in MADRS total scores from mean baseline of 33.0 (sd 7.8) to mean final score of 20.7 (sd 10.8; p=.001) and GDS total scores from mean baseline of 11.7 (sd 1.6) to mean final score of 7.8 (sd 4.7; p=.05). Adverse events included rash (none serious), GI complaints, weight gain, dizziness, headaches, unsteady gait, and nightmares. For most participants, adverse events resolved within the first month of treatment.

Conclusion: Lamotrigine was associated with statistically significant improvement in mood in six individuals who tolerated a 10-week exposure. Three other individuals started on medication terminated prematurely due to adverse effects. Given these results, a double-blind, placebo-controlled study is warranted to assess the safety and efficacy of lamotrigine in unipolar geriatric depression. This study was funded by GlaxoSmithKline.

References:

NR3  Monday, May 21, 9:00 AM - 10:30 AM
Atypical Antipsychotic Drug-Induced Acute Laryngeal Dystonia
Sandep Mellacheruvu, M.D. University Of Mississippi Medical Center, Psychiatry and Human Behavior, 2500 North State Street, Jackson, MS, 39216, 9000

Educational Objectives:

At the conclusion of this presentation, the participant should be able to: Identify the risk factors that can lead to antipsychotic induced acute laryngeal dystonia (LD); Identify the medications
that can cause LD: Promptly diagnose and understand the rationale behind prophylaxis and treatment of acute LD

Summary:

Acute laryngeal dystonia (LD) can be a life-threatening side-effect of antipsychotic medications, especially when administered parenterally. This condition requires rapid diagnosis and aggressive management with parenteral anticholinergics or benzodiazepines as well as careful monitoring. LD has primarily been reported in those receiving typical antipsychotics. We report two cases of LD in people who received intramuscular (IM) atypical antipsychotic, ziprasidone. In flexible dose trials, the most common adverse reactions to intramuscular ziprasidone mesylate were injection-site pain, nausea, somnolence, and dizziness. Given the risk of LD, risk-benefit ratio of administering parenteral antipsychotics should be considered in the treatment of acute agitation or psychosis to minimize the risk of complications such as laryngeal dystonia.

References:


NR4 Monday, May 21, 9:00 AM - 10:30 AM
Correlation Between Serum Estrogen and Spatial Memory in Peripartal Rats
Je-Min Park, Busan National Univ. Hospital, Psychiatry, Busan National Univ. Hospital, Amidong 1-ga, Seo-gu, Busan, 602-739, 5800, Sung-Hyun Shin

Educational Objectives:

This study was designed to find possible effect of pregnancy and parturition on spatial memory, especially in relation to levels of estrogen during the third trimester and postpartal period in rats.

At the conclusion of this presentation, it is suggested that decline in cognitive function might occur either by failure of rapid decrease of estrogen, immediately after parturition, or retarded restoration of estrogen in later postpartal period.

Summary:

Objectives: This study was designed to find possible effect of pregnancy and parturition on spatial memory, especially in relation to levels of estrogen during the third trimester and postpartal period in rats.

Methods: 25 female Sprague Dawley rats were divided into pregnant group (N=14) and control group (N=11). Changes in spatial memory during 6 weeks including third trimester and postpartal period were measured using Morris water maze. Time to reach the platform in the maze was indicator of spatial memory. Serum estrogen level was measured on 1 week before delivery, postpartal day 1, and day 14.

Results: Both groups showed gradual improvement in performance by trial days and weeks, but no significant difference was found between the two groups. However in the third trimester, pregnant group showed a trend of less achievement on 3 days of learning than control group. Serum estrogen levels did not differ significantly between groups over the 6 weeks of period. However there was positive correlation between serum estrogen level on postpartum day 1 and time to reach platform on postpartum week 2, and negative correlation between estrogen level on postpartum day 14 and latency to the platform on postpartum week 5.

Conclusion: These results imply that changes in the serum estrogen level may have dual effects on the spatial learning in peripartal period. It is suggested that decline in cognitive function might occur either by failure of rapid decrease of estrogen, immediately after parturition, or retarded restoration of estrogen in later postpartal period.

References:


NR5 Monday, May 21, 9:00 AM - 10:30 AM
Social Support and Geriatric Depression
Otema A. Adade, B.A. Duke University School of Medicine, Psychiatry, 115 Eriwood Way, Apt. 101, Durham, NC, 27704, 9000

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that social support variables are important diagnostic predictors of geriatric depression. Furthermore, social networks present a point of intervention to meet the needs of depressed elderly patients. The participant should learn that information about an older adult’s social context help predict mental health outcomes and can be used to guide appropriate interventions for the treatment of geriatric depression.

Summary:

Late life depression is embedded within a social context. Social networks present a point of intervention to meet the needs of depressed elderly individuals. Robust relationships are well established between social support and depression in late life. However, there is sparse and mixed evidence on the impact of social support on mental healthcare utilization. Based on previous research, we hypothesize the size of the social network, frequency of interaction, giving instrumental support, and perceived social support, will be related to increased use of mental health services and a decrease in depression at follow-up. Receiving instrumental support will be associated with use of less mental health services and an increase in depression. Data are from a representative sample of community-dwelling elders aged > 65 living in North Carolina (N=1436). Follow-up contact was made at six and ten years. The sample was approximately half Caucasian and half African-American. Social support was measured in four dimensions: network size, interaction frequency, instrumental assistance, and perceived support. Mental health service utilization was measured as visits to mental health professionals and use of antidepressants. Residualized change analysis was used to examine changes over time. Interaction terms tested for race differences. The results show perceived adequacy and availability of support, and receiving instrumental assistance are robust predictors of depression at six and ten year follow-up. Interestingly, mental health service utilization did not mediate the relationship between measures of social support and depression. The findings suggest social support is an important variable for addressing the mental health care needs of depressed elderly patients. The study indicates psychosocial variables should be used to assess risk, aid in treatment planning, and predict mental health outcomes in geriatric depression.

References:

Somnambulism Induced by Quetiapine

Zeba Hasan Hafeez, M.D. University of Nevada School of Medicine, Psychiatry, 3639 water song drive, las vegas, NV, 89147, 9000, Constance M. Kalinowski, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will be alerted to the risk of somnambulism as an untoward effect of quetiapine. At the conclusion of this presentation, the participant will learn that this effect may be dose dependent. Also, that quetiapine use in patients who have a coexistent attention deficit disorder may possibly increase their susceptibility to somnambulism.

Summary:

Objectives: Somnambulism, a previously unreported side effect of quetiapine, is described in two cases who had no prior history of this disorder.

Methods: We present two cases of somnambulism from the inpatient psychiatry unit at the VA hospital and the out patient clinic at Mojave counseling center, Las Vegas.

Results: Case 1: A 52 year old Caucasian male was undergoing treatment for panic disorder and schizoaffective disorder. He also had attention problems since childhood and restless leg syndrome for 35 years. He reported that somnambulism had begun 18 months previously, after quetiapine was increased to 200mg at bedtime. A polysomnogram done when the patient was taking 800 mg of quetiapine showed delayed sleep latency. EEG was normal. Leg EMG was significant for frequent leg jerks. Quetiapine was discontinued and methylphenidate and clonazepam were started. Somnambulism promptly remitted. Quetiapine 25 mg nightly was initiated later. No recurrence of somnambulism was reported at 8 month follow up.

Case 2: An 18 year old Caucasian male having diagnoses of attention deficit disorder and pervasive developmental disorder, sought consultation for episodes of somnambulism and nocturnal combativeness. He was receiving quetiapine 400mg nightly and dextroamphetamine sulfate 35mg daily in divided doses . EEG was normal. Dextroamphetamine was discontinued with no effect upon somnambulism. Quetiapine was then tapered. The symptoms resolved below a dose of 150mg nightly. Quetiapine was discontinued with no recurrence of somnambulism during one year of follow up.

Conclusion: Quetiapine may induce somnambulism in certain individuals, possibly due to its impact upon central serotonin activity. These cases suggest that this effect may be dose dependent. Both individuals described here had ADHD, which is interesting in view of recent evidence linking ADHD to polymorphism in the serotonin transporter gene and the genes for tryptophan hydroxylase and various serotonin receptors.

References:


NR8  Monday, May 21, 9:00 AM - 10:30 AM
Localized Cerebral Perfusion Abnormalities in Patients With Undifferentiated Somatoform Disorders

Kyung Bong Koh, Sr., M.D. Yonsei University College of Medicine, Department of Psychiatry, 134 Shinchon-dong, Seodaemun-gu, Seoul, 120-752, 5800, Jee In Kang, Jr., M.D., Youngjoon Lee, Jr., M.Psy., Jong Doo Lee, Sr., M.D.

Educational Objectives:

At the conclusion of this presentation, first, participants should be able to recognize that undifferentiated somatoform disorder may be associated with localized cerebral perfusion abnormalities. Second, they should be able to recognize that such localized cerebral perfusion abnormalities may occur in the right side of the brain. Therefore, this study will help participants understand and recognize the pathophysiology of undifferentiated somatoform disorder in terms of brain function, particularly, brain asymmetry.

Summary:

The objective of this study was to examine the differences of brain function in the resting state between patients with undifferentiated somatoform disorder and normal controls. Regional cerebral perfusion was measured by 99m-Tc-ECD (ethylcysteinate dismer) Single Photon Emission Computed Tomography (SPECT). Using statistical parametric mapping (SPM) analysis, the SPECT images were compared between sex and age-matched 16 patients with undifferentiated somatoform disorder and 10 healthy subjects on a voxel by voxel basis. Reduced cerebral blood flow in the right parahippocampal and right medial frontal areas were found in patients with undifferentiated somatoform disorder compared with normal controls. However, increased cerebral blood flow was found in the left inferior parietal, left middle occipital, left superior temporal, right middle frontal, and right superior frontal areas in these patients. In conclusion, undifferentiated somatoform disorder patients showed hypofunction in the right parahippocampal and right medial frontal areas. These results suggest that undifferentiated somatoform disorder may be associated with localized cerebral perfusion abnormalities in the right side.

References:


NR9  Monday, May 21, 9:00 AM - 10:30 AM
The Patients With Very High Serum Lithium Levels May Not Have a Poor Clinical Outcome

Nedim Havle, M.D. Bakirkoy Research and Training Hospital for Psychiatry, Psychiatry, Bakirkoy Research and Training Hospital, for Psychiatry, 7th psychiatry unit, Bakirkoy, Istanbul, 34147, 4890, Samuray Ozdemir, M.D.

Educational Objectives:

Lithium toxicity is a serious and sometimes deadly condition and the patients usually have central nervous system manifestations. It’s noteworthy that although the presented patient’s serum lithium concentration was in severe toxicity level, there were no features of neurotoxicity. At the conclusion of this presentation, the participant should be able to demonstrate that the patients with very high serum lithium levels may not have a poor clinical outcome.

Summary:

Objective: To report a case who was acutely intoxicated with very high dose lithium carbonate without any neurological side effects.

Methods: A 27 years-old female patient diagnosed with Bipolar Disorder Type I has been treating with lithium carbonate 900 mg/day and there was no use of concomitant medications. Following the ingestion of approximately 150x300 mg carbonate capsules, she was brought to the emergency psychiatry unit of our hospital.

Results: Her serum lithium level was 8.64 mEq/L 16 hours after ingestion. She had no complaints except nausea and diarrhea and the initial general physical and neurological examination was normal. All laboratory tests including complete blood cell count, serum electrolytes, BUN and creatinine, and thyroid function tests were within normal limits. No electrocardiogram changes were present. Following intravenous hydration, the patient was transferred to the hemodialysis unit. Her pre-dialysis serum lithium level was 8.40 mEq/L (22 hours after ingestion) and the hemodialysis treatment was discontinued when the serum lithium level was 0.50 mEq/L.

Conclusion: Lithium has a significant potential toxicity because of its narrow therapeutic index. Lithium toxicity may induce gastrointestinal, cardiovascular, renal, endocrine and mostly neurological manifestations. Due to the low permeability of the blood brain barrier for lithium, the distribution of it in the brain is approximately 24 hours. Therefore the patients with very high serum lithium levels may not show neurological symptoms in acute lithium intoxication. Although the presented patient’s serum lithium concentration was in severe toxicity level, there were no features of neurotoxicity or any other system manifestations except mild to moderate gastrointestinal symptoms.

References:


NR10  Monday, May 21, 9:00 AM - 10:30 AM
Biofeedback-assisted Autogenic Training for Chronic Tension-Type Headache: Efficacy and Its Relationship With Improvement of Anxiety and Depression

Eun-Ho Kang, M.D. Ingok Ja-Ae Hospital, Psychiatry, Ingok Ja-Ae Hospital, Eumseongk Kottongnae, Chungbuk Eumseong, 369-711, 5800, Joo-Yeon Ahn, M.D., Young Chul Kim, M.D., Bum-Hee Yu, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that biofeedback-assisted autogenic training is effective in treatment of chronic tension-type headache (CTTH), and that the efficacy of the treatment may be related to reduced anxiety levels rather than the changes of EMG activity in patients with CTTH.

Summary:

Objective: We aimed to evaluate the efficacy of biofeedback-assisted autogenic training for chronic tension-type headache (CTTH), and to determine the relationship among the changes in EMG activity, headache severity, and psychological states according to the biofeedback treatment.

Methods: Patients with CTTH were aged from 20 to 40 years (n = 35) and randomized to the record-only control group (n = 17) or the treatment group (n=18) receiving 8 sessions of biofeedback-assisted autogenic training.
Results: Both groups showed significant improvement of headache in the McGill Pain Questionnaire (MPQ) and Visual Analogue Scale (VAS). The treatment group showed greater improvement only in the VAS over time, compared with the control group. The treatment group showed lower scores on the Hamilton Rating Scales for Depression (HAM-D) than the control group at 4th session (F = 4.836, P = 0.035) and 8th session (F = 14.961, P < 0.01). The treatment group also showed lower scores on the Hamilton Rating Scales for Depression (HAM-D) than the control group at 4th session (F = 2.845, P = 0.016) and 8th session (F = 2.746, P = 0.019). Reductions in HAM-A scores tended to correlate with the decrease in MPQ-S scores (r = 0.447, P = 0.063), and VAS (r = 0.441, P = 0.067) only in the treatment group. There were no significant differences in EMG activities across the sessions between the treatment group and control group.

Conclusions: Our results suggest that the efficacy of biofeedback-assisted autogenic training may be related to reduced anxiety levels rather than the changes of EMG activity in patients with CTTT.

References:

NR11
Monday, May 21, 9:00 AM - 10:30 AM
Mirtazapine Versus Venlafaxine for the Treatment of Depressive and Physical Symptoms in Major Depressive Disorder
In-Soo Lee, M.D., Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Psychiatry, Ilwonbon-Dong 50, Gangnam-Gu, Seoul, 135-710, 5800, Sang-Keun Chung, M.D., Sang-Yeol Lee, M.D., Eui-Jung Kim, M.D., Jin-Pyo Hong, M.D., Kang-Seob Oh, M.D., Bum-Hee Yu, M.D.

Educational Objectives:
The authors want participants to learn serotonin-norepinephrine reuptake inhibitors (SNRIs) are effective in controlling somatic symptoms with depression and mirtazapine could be as effective as venlafaxine in depressive and physical symptoms in patients with major depressive disorder. In particular, compared with venlafaxine, mirtazapine appears to have a faster onset of therapeutic effect on physical and anxiety symptoms, and sleep disturbance in major depressive disorder.

Summary:
Objective: The aim of this study was to examine the efficacy of mirtazapine orally disintegrating tablet for the treatment of depressive and physical symptoms in major depressive disorder (MDD), compared with venlafaxine extended-release capsule.
Method: A total of 169 patients with MDD (HAM-D>18) were randomized to the mirtazapine treatment group (N=97) or the venlafaxine treatment group (N=72) for 8 weeks. Primary efficacy measures were the Hamilton Rating Scale for Depression (HAM-D), the Hamilton Rating Scale for Anxiety (HAMA), and Clinical Global Impression Scale (CGI). Secondary efficacy measures were the Patient Health Questionnaire 15-items: Somatic Sympolm Severity Scale (PHQ-15), the Somatic Subscale of Symptoms Check Lists-90-Revised (SCL-90-R), 19-items Pittsburgh Sleep Quality Index (PSQI), and 9-items of PHQ (PHQ-9).
Results: Both antidepressants were efficacious in improving depressed mood, anxiety, physical symptoms, sleep disturbance. Both treatment groups showed no differences both in primary and secondary efficacy measures at the endpoint. However, the mirtazapine group showed more favorable response at 1 week in the gastrointestinal symptoms (p=0.045), at 2 weeks in the HAMA (p=0.045) and CGI-I for physical symptoms (p=0.047), at 4 weeks in the HAMA (p=0.031), and the PSQI (sleep latency: p=0.008, quality of sleep: p=0.019), and at 8 Weeks in the SCL-90-R (p=0.048), and total sleep time (p=0.043). According to the Kaplan-Meier survival analysis of response (≥50% reduction in the HAMD), the mirtazapine group revealed faster onset of effect than the venlafaxine group (median of response time: 4±0.73 weeks vs. 8±1.20 weeks). The response rate and the remission rate (HAMD≤7) did not differ between the two groups at the end point.
Conclusion: These data suggest mirtazapine could be as effective as venlafaxine in treating depressive and physical symptoms in patients with MDD. Compared with venlafaxine, mirtazapine appears to have a faster therapeutic effect on physical and anxiety symptoms, and sleep disturbance in MDD.

References:

NR12
Monday, May 21, 9:00 AM - 10:30 AM
Use and Validation of PRIME-MD (Spanish Version) to Detect Generalized Anxiety Disorder in a Psychiatric Consultation in Venezuela
Gustavo D. Resler, M.D. Hospital Vargas de Caracas, Psychiatry, Av Río Caura, Residencias Parque Prado Torre 2B, Apto 111, Urb Parque Humboldt, Caracas, 1080, 3070, Mata Salvador, Ph.D., González Alfonso, Ph.D., Lavie Renéé, M.D.

Educational Objectives:
At the end of this presentation, the audience can experience the results of the first clinical study to detect the prevalence of Generalized Anxiety Disorder in a psychiatric consultation in Venezuela. Also we will show the results of the positive validation of the PRIME-MD questionnaire in Spanish.

Summary:
Background: The Generalized Anxiety Disorder (GAD) is a frequent diagnosis with a lifelong prevalence of 5-7%, being more frequent between females and is associated with a various kinds of anxiety and mood disorders. In Venezuela the prevalence is unknown and there are a limited number of clinical studies.

Objectives: To determine the frequency of the GAD in two types of psychiatric consultation settings and to validate the Primary Care Evaluation of Mental Disorders (PRIME-MD) as an instrument to identify GAD in psychiatric consultations.

Methods: We had been reviewed 1000 medical records of outpatients from the Psychiatry Department of the Hospital Vargas de Caracas to determine the frequency of GAD diagnosis. Then, the PRIME-MD was validated and used to detect the GAD diagnosis in 100 outpatients from the Hospital Vargas de Caracas and 200 outpatients from private hospitals, comparing the results with the Structured Clinical Interview for DSM-IV-TR (SCID-I).

Results: The frequency of GAD diagnosis was 2.8% in the medical records checked. The prevalence of GAD in the 300 patients evaluated was 3.7%. The PRIME-MD showed 90.9% of sensitivity and 88.9% of specificity for the diagnosis of GAD. The global comorbidity of GAD was 36.6%. In our study, the GAD had
a high frequency on patients between 40 and 49 years old, with a female/male rate of 2:1.

Conclusion: In our settings the GAD incidence was lower than other studies. The PRIME-MD proved to be a valid instrument to diagnose GAD in psychiatric outpatients.

References:

NR13  Monday, May 21, 9:00 AM - 10:30 AM
Meta-analysis of the P300 Wave Forms in Panic Disorder
Vincent De Luca University of Toronto, Psychiatry, 250 College Street, Toronto, ON, M5T1R8, 1220, Heather McNeeley, Giovanni Muscettola, James L. Kennedy, Andrea de Bartolomeis

Educational Objectives:
1. Be able to familiarize with meta-analysis technique applied to ERP studies.

Summary:
Using event-related potentials (ERPs), impairment in the components’ amplitude has been found in several psychiatric illnesses, leading to the suggestion that ERP abnormalities may represent a trait-marker. At the conclusion of this presentation, the participant should be able to be familiar with meta-analysis technique applied to ERP studies.

References:

NR14  Monday, May 21, 9:00 AM - 10:30 AM
The Impact of Comorbid Anxiety Disorders on Treatment Planning in Depressed Outpatients
Charissa F. Andreotti Brown University, Department of Psychology, Brown University, Box 5179, Providence, RI, 02912, 9000, Timothy J. Petersen, Ph.D., Mark Zimmerman, M.D.

Educational Objectives:
1. At the conclusion of the presentation, the participant should be able to recognize differences in community-based treatment approaches for depressed adult outpatients with and without comorbid anxiety disorders.
2. At the conclusion of the presentation, the participant should be able to recognize differences in community-based treatment approaches for depressed adult outpatients with and without comorbid anxiety disorders.

References:
Cycling Bipolar Disorder

A 6-Month, Pilot, Double-Blind, Maintenance Trial of 2. Bowden CL: A different depression; clinical distinctions between bipolar and unipolar depression who developed or not developed manic / hypomanic switch under antidepressant treatment

Summary:

Background: DSM-IV classifies antidepressant-induced mania/hypomania under “mood disorders due to medical conditions”. However, several investigators consider them as actual bipolar disorders.

Method: Seventy-six patients diagnosed as bipolar disorder-first episode depressive; 61 patients who developed manic switch due to antidepressant drug treatment or ECT, and 80 patients with major depressive disorder (unipolar depression) were evaluated. All the patients were diagnosed according to the criteria of DSM-IV, using SCID-I.

Results: The age of onset in bipolar disorder (27.2±9.4) was significantly lower than unipolar depression (35.4±13.29), but there was no difference with manic switch (31.9±12.8). Bipolar type I disorder (25.2±8.68) had an earlier age of onset than bipolar type 2 disorder (38.7±9.1). Compared to the bipolar and unipolar group, the manic switch group had more depressive episodes. The frequency of melancholic features was highest in the manic switch group (62.3%), followed by bipolar group (57.9%) and unipolar group (27.5%). Psychotic features were exhibited mostly in bipolar group (46.1%); 11.5% in manic switch and 1.3% in unipolar groups. Atypical features were exhibited by manic switch group (13.1%), bipolar group (10.5%) and the unipolar group (1.3%), respectively. Prevalence of attempted suicide was highest in the bipolar group (39.5%); manic switch group (23%) and the unipolar group (15%) followed, respectively.

Conclusions: Bipolar disorder-first episode depressive patients had similar clinical features and DSM-IV specifiers compared to unipolar depressive patients who switched to mania with antidepressant. Manic switch due to antidepressant treatment may reflect a transition between unipolar and bipolar disorder. These findings support that manic/hypomanic episodes triggered by antidepressant treatment should be classified under bipolar disorders in the future.

References:

Educational Objectives:

To understand the differences between clinical characteristics of the patients regarding DSM-IV specifiers, diagnosed first episode depressive bipolar disorder and unipolar depression who developed or not developed manic / hypomanic switch under antidepressant treatment

Summary:

Background: DSM-IV classifies antidepressant-induced mania/hypomania under “mood disorders due to medical conditions”. However, several investigators consider them as actual bipolar disorders.

Method: Seventy-six patients diagnosed as bipolar disorder-first episode depressive; 61 patients who developed manic switch due to antidepressant drug treatment or ECT, and 80 patients with major depressive disorder (unipolar depression) were evaluated. All the patients were diagnosed according to the criteria of DSM-IV, using SCID-I.

Results: The age of onset in bipolar disorder (27.2±9.4) was significantly lower than unipolar depression (35.4±13.29), but there was no difference with manic switch (31.9±12.8). Bipolar type I disorder (25.2±8.68) had an earlier age of onset than bipolar type 2 disorder (38.7±9.1). Compared to the bipolar and unipolar group, the manic switch group had more depressive episodes. The frequency of melancholic features was highest in the manic switch group (62.3%), followed by bipolar group (57.9%) and unipolar group (27.5%). Psychotic features were exhibited mostly in bipolar group (46.1%); 11.5% in manic switch and 1.3% in unipolar groups. Atypical features were exhibited by manic switch group (13.1%), bipolar group (10.5%) and the unipolar group (1.3%), respectively. Prevalence of attempted suicide was highest in the bipolar group (39.5%); manic switch group (23%) and the unipolar group (15%) followed, respectively.

Conclusions: Bipolar disorder-first episode depressive patients had similar clinical features and DSM-IV specifiers compared to unipolar depressive patients who switched to mania with antidepressant. Manic switch due to antidepressant treatment may reflect a transition between unipolar and bipolar disorder. These findings support that manic/hypomanic episodes triggered by antidepressant treatment should be classified under bipolar disorders in the future.

References:

NR16

Monday, May 21, 9:00 AM - 10:30 AM
A 6-Month, Pilot, Double-Blind, Maintenance Trial of Lithium Monotherapy Versus the Combination of Lithium and Divalproex for Dual Diagnosis Rapid Cycling Bipolar Disorder

David E. Kemp, M.D. Case Western Reserve University, Department of Psychiatry, 4893 Highland Place Court, Richmond Heights, OH, 44143, 9000, Stephen J. Garoczy, Ph.D., Kerning Gao, M.D., Omar Elhaj, M.D., Daniel Rapport, M.D., Sarah Bilali, M.S., Joseph R. Calabrese, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the differences in maintenance efficacy between lithium monotherapy and the combination of lithium plus divalproex when used in the treatment of dual diagnosis rapid-cycling bipolar disorder.

Summary:

Objective: This prospective, maintenance trial comparing lithium (Li) monotherapy to the combination of Li and divalproex (DVX) in rapid-cycling bipolar I or II disorder (RCBD) comorbid with substance use disorders (SUDs) was conducted to estimate the difference in overall survival for use in designing a future large-scale maintenance study.

Methods: Outpatients with RCBD who experienced an episode of mania, hypomania, or mixed state (M/H/M) within 3 months of entry and met DSM-IV criteria for substance abuse/dependence within 6 months of entry were enrolled. Participants were initially treated with open Li + DVX for up to 6 months, and subjects who achieved stabilization were randomized (stratified for type I or II) to double-blind Li vs. Li + DVX. The study randomized subjects who tolerated Li + DVX and achieved stabilization for > 4 consecutive weeks: 1) HAM-D17 ≤ 20; 2) YMRSS≤ 12.5; 3) GAS ≥ 51; 4) blood levels of Li ≥ 0.8 meq/L and DVX ≥ 50 ug/ml. Kaplan-Meier methodology was used to plot survival data.

Results: Of 149 subjects receiving open Li + DVX, 42% were non-adherent and 10% experienced adverse events leading to discontinuation. Li + DVX was ineffective at improving mood for 25%; 19 had refractory depression and 18 refractory M/H/M. Stabilization was achieved in 21%, who were subsequently randomized to Li (N=16) or Li + DVX (N=15). Time to intervention until a mood episode and overall survival time until discontinuation for any reason was not different between Li and Li + DVX. Subjects were more likely to relapse into M/H/M (N=13) than into depression (N=4; p=0.029).

Conclusion: The difference in survival between Li and Li + DVX was small to moderate, suggesting a future study would require 77 - 151 patients per arm to have an 80% chance of detecting a significant advantage for combination therapy.

References:

NR17

Monday, May 21, 9:00 AM - 10:30 AM
Polypharmacy and Clinical Outcome of Patients With Dementia Treated in a Geriatric Psychiatry Inpatient Unit

Virginia T. Chan UCSD, Senior Behavioral Unit, 7878 Camino Tranquilo, San Diego, CA, 92122, 9000, Benjamin K.P. Woo, John W. Daly, Valerie Rice, Edward C. Allen, Daniel D. Sewell

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:
1) recognize how commonly both polypharmacy and potentially inappropriate medication use impact older patients with dementia;
2) understand how an acute geriatric psychiatric inpatient unit may optimally treat older patients with dementia;
3) identify factors that may improve functioning in older patients with dementia.

Summary:

Objective: The purpose of this analysis was to compare the prevalence of polypharmacy and potentially inappropriate medication use in older demented patients before and after admission to a geriatric psychiatry inpatient unit.
Methods: We collected demographic and clinical data on a cohort of 118 patients consecutively admitted to a senior behavioral inpatient unit (SBU) who met DSM-IV-TR criteria for dementia. All subjects completed the Mini-Mental State Examination (MMSE), the Mattis Dementia Rating Scale (DRS), and the Scale of Functioning (SOF).

Results: The patients (n=118) had the following demographic characteristics: mean age (SD) = 82 (6), mean LOS = 14 (7) days, ethnicity = 86% Caucasian, gender = 78% female, education = 89% high school graduate. The MMSE and DRS scores were 22 (6) and 117 (19), respectively. SOF score at admission versus discharge was 31.6 (7.7) versus 37.5 (8.5). The number of medications used at admission versus discharge was 7.7 (3.5) versus 7.9 (3.3). The total numbers of psychiatric medications and non-psychiatric medications at admission versus discharge were 207 versus 284 and 760 versus 710, respectively. In the category of psychiatric medications, anti-dementia agents accounted for 22 of the 77 additional medications prescribed at discharge. In the category of non-psychiatric medications, there were 24 cases of constipation. The total number of non-psychiatric medications at admission versus discharge was decreased by 6.6%.

Conclusions: Our findings demonstrated that demented patients experienced an improvement in functioning as measured by a comparison of SOF score on admission versus discharge. In addition, demented patients were likely to be started on anti-dementia agents, to receive pharmacological treatment for behavioral and psychological symptoms of dementia, to benefit from a decrease in potentially inappropriate medication use, and to obtain appropriate treatment for previously unrecognized medical illnesses such as constipation.

References:

NR18 Monday, May 21, 9:00 AM - 10:30 AM
Suicide and Psychiatric Diagnoses in Stockholm County
Johan Reutfors, M.D. Karolinska Institute, Clinical Epidemiology Unit, Karolinska University Hospital M9:01, Stockholm, SE-17176, 4010, Lena Brandt, B.S.C., Par Sparen, Ph.D., Anders Ekborn, M.D., Urban P. Osby, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the increased suicide risk among individuals in psychiatric treatment, especially young patients treated for psychosis.

Summary:
Introduction: Suicide causes the death of around 1,500 Swedes per year out of a 9 million population (1). Since psychiatric disorder is the most important marker for suicide risk, increased knowledge about the association between suicide and psychiatric admission is important for suicide prevention (2).

Methods: All suicides in Stockholm County, Sweden, from 1985 - 1995, age 15 - 69 years (n=2599) were linked to the Patient Database. Psychiatric diagnoses within 5 years prior to the suicide were classified into three diagnostic groups: 'All mental disorders', 'Non-affective psychosis' and 'Affective psychosis.' Standardized mortality ratio (SMR) for suicide was calculated relative to the population. Population attributable risk (PAR) was calculated to estimate what proportion of suicides may be ascribed to the different mental disorders.

Results: Among the 2599 suicides, 46 - 55% in different age groups had been psychiatric inpatients within 5 years prior to the suicide. A 0 - 20 % were admitted for a non-affective psychosis, and 7 - 12 % for an affective psychosis. SMR for suicide was 16 - 25 for patients admitted for a mental disorder. The increased risk was most evident in the 15 - 34 year age group, with an SMR of 43 for non-affective psychosis and 55 for affective psychosis. PAR showed that 30 - 34 % of all suicides in the population were attributable to a mental disorder that had required inpatient treatment; 7 - 16 % of the suicides were attributable to non-affective psychosis and 6 - 10 % to affective psychosis.

Conclusion: A large proportion of persons who died by suicide had recently been admitted for psychiatric treatment. Suicide preventive strategies may be most effective if directed to individuals in psychiatric treatment, especially young patients treated for psychosis, since the evidence shows their highly increased risk.

References:
1. http://www.ki.se/suicide/
patient's granulocytopenia persisted for 7 days when HCTZ was continuously administered. Suspecting that other factors might explain the delay in return of ANC to normal values, HCTZ was then also discontinued. ANC and WBC then normalized two days after the discontinuation of HCTZ.

In conclusion, one case of possible HCTZ Prolongation of Clozapine-induced Granulocytopenia is reported.

References:

NR20 Monday, May 21, 9:00 AM - 10:30 AM
Aerobic Exercise in the Treatment of Psychiatric Disorders: How Can Compliance Be Improved?
Andreas Broocks, M.D., Hans Jürgen Rumpf, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to establish an endurance training program in a psychiatric setting, know about common obstacles and difficulties and how to overcome these difficulties using specific motivational interventions.

Summary:
Therapeutic effects of aerobic exercise have been demonstrated for depressive and other psychiatric disorders. However, many patients have difficulties in developing regular exercise habits and to persist for a longer period of time. 223 patients who had to be treated in a psychiatric hospital because of various psychiatric conditions were offered to participate in a three month running/walking program, which could be completed on an outpatient basis. 82 patients decided to participate and attended the weekly meetings which included exercise-related psychoeducation, stretching and 40-50 min of aerobic exercise. In addition, the experimental group received brief interventions according to the principles of motivational interviewing. In comparison to the control group the completer rate in the experimental group was significantly higher (78% vs 33%, p<0.001). The patients initial self assessments concerning the importance and efficacy of regular exercise for their individual recovery did not predict compliance. In conclusion, specific motivational interventions are highly effective in improving adherence to regular exercise.

References:

NR21 Monday, May 21, 9:00 AM - 10:30 AM
PHIL WHANG, M.D. UMDNJ, psychiatry, 183 SOUTH ORANGE AVE, NEWARK, NJ, 07103, 9000, Michael Y. Hwang

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the need for more multidimensional assessment of pain, distress, and suffering in patients who may not have full capacity to self report how much they are suffering.

Summary:
Background: While limited existing evidence suggest that psychosis blunts an individual's pain perception and subjective distress. Implication of this perception (finding) is that the presence of such impairment renders an increased pain tolerance and less distress. However, pain and distress is not only sensory experience but also affective, cognitive and evaluative experience. Measures of multidimensional domains of distress measurements have been largely lacking in this population.

Study Design/Measurements: Subjects were recruited from a cohort who had schizophrenia spectrum disorders at Veteran Administration System(n = 57). The McGill Pain Questionnaire-SF was used to assess multidimensional pain experience while associated psychotic symptoms were measured using PANSS scales. And depressive symptoms were measured using HAMD scales. The data was analyzed by Mann Whitney test.

Results: 57 subjects rated distress using the McGill Pain Questionnaire. The subjects were divided into low and high pain groups to examine the relationship between severity of psychosis and subjective pain perceptions. The study subjects were divided into low and high pain groups. The Mean Affective and Cognitive Pain Rating Index scores were 6.52 in low pain group and 12.1 in high(p 0.001). The mean PANSS rating scores were 60.8 for low pain group and 71.2 for the high group(p 0.01). The severity of psychotic symptoms did not correlate with impairment in overall pain perception and depressive symptom scores on both groups were not significant to serve as a confounder.

Discussion: The affective and cognitive capacities to perceive pain and distress did not appear to be impaired in patients with psychotic disorders. In contrast to existing data, our study suggests that presence of psychotic symptoms may not indicate impairment in patient's capacity for pain perception. These findings suggest a need for multidimensional assessment tool to adequately assess the pain and distress in patients with psychotic disorders.

References:

NR22 Monday, May 21, 9:00 AM - 10:30 AM
Seasonal pattern assessment questionnaire in relation to the temperament and character inventory of personality in Korean high-school students
Jun-Keun Hong Korea University Guro Hospital, Psychiatry, Korea Univ. Guro Hospital 10th floor, Psychiatry Depart, Seoul, S.Korea, Seoul, 152-703, 5800, Moon-Soo Lee, In-Kwa Jung

Educational Objectives:
Research in personality disorder suggests that personality traits are likely influenced by several genetic and environmental factors. If we could find out the correlations between the seasonality and personality dimensions, these would be attributable to common genetic factors. In this study, we investigated the personality structure in subjects from high-school students in relation to different degrees of seasonal variations in mood and behavioral dimensions and how these are experienced by the subject, as measured by SPAQ. At the conclusion of this presentation, the participant should be able to recognize relationship between SPAQ and TCI in Korean high-school students.

Summary:
In this study, we investigated the personality structure in subjects from high-school students in relation to different degrees of seasonal variations in mood and behavioral dimensions and how these are experienced by the subject, as measured by SPAQ. The data was analyzed by Mann Whitney test.

600 high-school students who are living in Seoul, Korea participated in this study. Subjects were surveyed with Korean translation of the SPAQ and Korean version of Temperament and Character Inventory.
Women showed significantly higher scores on harm avoidance and men showed higher scores on self-directedness. GSS showed positive correlation with self-transcendence and negative correlation with cooperativeness.

In case of SAD, regression coefficients were significantly negative in CO, and positive in ST. S-SAD regression coefficients were significantly negative in CO, and positive in ST. Those with GSS the serotonergic system or by an interaction between the dopaminergic system or by the dopaminergic system or by the serotonergic system or by an interaction between the dopamine and serotonin neurotransmitter systems.

Although there have been many reports on seasonal variations in mood and behavior in foreign countries, there has been very limited report from Korea before. Different personality scales are believed to be modulated by different neurotransmitters and thereby by different genetic configurations. Correlations between the seasonality and personality dimensions were attributable to common genetic factors.

References:

NR23 Monday, May 21, 9:00 AM - 10:30 AM
A New Data-Based Motor Subtype Scheme For Delirium
Maeve Leonard, M.B.B.S. Regional Hospital, Psychiatry, Dooradoyle, Limerick, xx; 4190, David J. Meagher, M.D., Paula T. Trzepacz, M.D.

Educational Objectives:
- To highlight the means by which greater clarity and consistency can be brought to the study of clinical subtypes of delirium
- To introduce a new subtyping scheme based on objective motor monitoring and derived from key components of existing methods

Summary:
- Background: Ascertaining clinically meaningful motor subtypes in delirium is hampered by inadequate standardization and validation of instruments, contributing to inconsistent reports of subtype frequencies and outcomes
- Aim: We sought to validate a new approach to motor subtyping based on analysis of data from a controlled comparison of items from three existing psychomotor schema to identify items that correlated substantially with an independent severity rating of motor presentation and were relatively specific for delirium
- Methods: Consecutive cases (n=100) of DSM IV delirium were assessed by a research physician using the Delirium Rating Scale-Revised-98 (DRS-R98) and the Cognitive Test for Delirium (CTD). Motor symptoms were rated by nurses using the Delirium Motor Checklist (DMC). The DMC consists of 30 nonredundant items from among three previously published psychomotor subtyping schema. Nondelirious controls (n=52) were compared on DMC ratings.
- Results: Principal components analysis of the DMC identified nine factors. Only two factors correlated significantly with either the DRS-R98 motor agitation (#7) or retardation (#8) items. Symptoms loading at > 0.65 were extracted to form subtype criteria composed of 4 hyperactive items and 7 hypoactive items. Application of these criteria to the delirious population suggested a cutoff of 2 items for subtypes with 30 hypoactive, 28 hyperactive, 27 mixed, and 15 no motor subtype patients. Patients who did not meet criteria for a motor subtype had less severe delirium as measured by the DRS-R98 and CTD.
- Conclusions: We validated a new scale for rating motor subtypes in delirium that, while derived from existing approaches, is more concise, focused on motor disturbances, and validated against nondelirious controls and an independent rating of pure motor disturbance. Future work will validate this scale against objective motor activity monitoring in delirious and control patients to determine whether motor symptoms are indicative of clinically meaningful delirium subtypes.

References:

NR24 Monday, May 21, 9:00 AM - 10:30 AM
Case report of Neuroleptic Malignant Syndrome in a Patient With a combination of Aripiprazole and Multiple Other Medications
Abid Malik, M.D. Albany Medical Center, Psychiatry, 434 Hudson Ave, Albany, NY, 12203, 9000, Nashwa Hasabou, M.D., Victoria Balkoski, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participants will be able to 1) Recognize symptoms of neuroleptic malignant syndrome in a patient on aripiprazole and other medications; 2) Demonstrate knowledge about neuroleptic malignant syndrome associated with aripiprazole from previously published case reports.

Summary:
Neuroleptic Malignant Syndrome (NMS) is a rare but life threatening syndrome commonly associated with antipsychotic agents. NMS occurring with atypical antipsychotics may have a lower mortality rate than that seen with conventional antipsychotic drugs, although this may be a reflection of enhanced physicians' awareness and ensuing earlier treatment (1). We describe a case of 26 year old white female who developed NMS after her standing dose of aripiprazole was increased. She may have started taking excess amounts of topiramate around that time. She was also on bupropion, alprazolam and pregabalin.

References:

NR25 Monday, May 21, 9:00 AM - 10:30 AM
The Functioning Assessment Short Test (FAST) in Bipolar Disorder
Adriane R. Rosa, Pharm.D. Hospital Clinic of Barcelona, Program of Bipolar Disorder, Rosellon, 140, Barcelona, 08036, 4700
Educational Objectives:

Development of a brief instrument to assess the main functioning problems experienced by bipolar patients, particularly, bipolar patients.

Summary:

Background: High rates of functional impairment among bipolar patients, even during remission, have been documented in numerous studies. However, the majority of instruments available to date have been focused on global or limited measures of functional recovery, rather than specific domains of psychosocial activity. In this context, the Functioning Assessment Short Test (FAST) was designed as a brief instrument assessing the main functioning problems experienced by psychiatric patients, and particularly bipolar patients. It comprises 24 items that assess impairment or disability in six specific areas of functioning such as autonomy, occupational functioning, cognitive functioning, financial issues, interpersonal relationships and leisure time.

Methods: 103 patients with DSM-IV TR bipolar disorder and 61 healthy controls were assessed by the Bipolar Disorder Program, at the Hospital Clinic of Barcelona. The feasibility, internal consistency, concurrent validity, discriminant validity between euthymic and acute patients, factorial analyses, and test-retest reliability were analysed.

Results: The internal consistency obtained was high, Cronbach's alpha being 0.909. Concurrent validity showed highly significant negative correlation with GAF (r=0.903; p<0.00). The test-retest reliability analysis showed a strong correlation between the two measures (r=0.953; p<0.00). The total mean FAST scores were lower in euthymic (18.55; p<0.001) patients, as compared with manic (38.50), depressed (42.36) and mixed patients (43.21). Conclusion: The FAST showed strong psychometrics properties and was able to detect differences between euthymic and acute patients. In addition, it is a short (6 minutes) simple interview-administered instrument, which is easy to apply, only requires short period of time for implementation, and it is now available for use in both clinical practice and research settings.

References:


NR26 Monday, May 21, 9:00 AM - 10:30 AM
Psychogeriatric Unit Within a General Hospital: Descriptive Analysis of Outpatient Assessment, Diagnosis and Treatment

Martin Ruiz hospital italiano, Psiquiatria, Florida 336, Buenos Aires, 1005, 3570, Daniel Matusevich, Carolina Vairo, Hugo Pisa, Alfredo Job, Carlos Finkelstein

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize some epidemiological issues about outpatients over 65 years old.

Summary:

Objective: To assess the frequency of some epidemiological variables in 200 patients over 65 years old that came to admission as outpatients in the psychogeriatric area in the psychiatric unit at the Hospital Italiano in Buenos Aires, Argentina.
NR28  Monday, May 21, 9:00 AM - 10:30 AM
A Pilot Study of Clonazepam Versus Psychodynamic Group Treatment Plus Clonazepam in the Treatment of Generalized Social Anxiety Disorder

Daniela Z. Knijnik, M.D.  
Federal University of Rio Grande do Sul, Psychiatry, Rua Hilário Ribeiro 202 sala 503, Porto Alegre, 90610040, 3510, Carlos Blanco-Jerez, Ph.D., Giovanni Sallum, Carolina Moraes, M.D., Gisele Manfro, Ph.D., Claudio Eizirik, Ph.D.

Educational Objectives:
At the end of this presentation, the participant should be able to consider a combined treatment strategy (medication plus a psychodynamic group therapy) for generalized social anxiety disorder as an alternative to its treatment.

Summary:
Objective: Psychodynamic Group Therapy (PGT) and clonazepam have proven efficacious in reducing symptoms of generalized social anxiety disorder (GSAD). Despite their efficacy, many individuals remain symptomatic after treatment with PGT or clonazepam as monotherapy. The goal of this study was to compare the efficacy of PGT plus clonazepam administered concurrently versus clonazepam alone for the treatment of GSAD.

Method: Fifty-eight adult outpatients with a diagnosis of GSAD according to DSM-IV criteria, participated in a 12-week randomized clinical trial: 29 underwent a combined treatment (PGT plus clonazepam) and 20 took clonazepam alone. The Clinical Global Impression-Improvement (CGI-I) scale was the primary efficacy measure. Secondary efficacy measures included the Liebowitz Social Anxiety Scale (LSAS) total score, the World Health Organization Instrument to Assess Quality of Life-Brief (WHOQOL-bref) scale, and the Beck Depression Inventory (BDI). The trial was conducted between March and November 2005.

Results: CGI-I data from 57 patients (intent-to-treat population) showed that the PGT plus clonazepam group presented significantly greater improvement than clonazepam alone (p=0.043). Using a CGI-I of 1 or 2 as the criterion for response, the difference in the response rate of PGT plus clonazepam versus clonazepam alone approached significance (79.3% vs. 53.6%, respectively; p=0.052).

Conclusion: This study is the first to compare combined PGT and medication versus medication alone in the treatment of GSAD. Our study suggests that addition of PGT may be a promising augmentation strategy for clonazepam treatment of GSAD.

References:


NR29  Monday, May 21, 9:00 AM - 10:30 AM
Changes of Platelet [3H]5-HT Uptake After Pharmacotherapy in Panic Disorder

Hyun-Bo Sim, M.D. Samsung Medical Center, Sungkyunkwan University School of Medicine, Department of Psychiatry, Ilwonbon-Dong 50, Gangnam-Gu, Seoul, 135-710, 5800, Insoo Lee, M.D., Kyung-Jeong Kim, B.S.C., Joo-Eon Park, M.D., Hyun-Wook Cho, M.D., Jong-Min Woo, M.D., Bum-Hee Yu, M.D.

Educational Objectives:
The authors want participants to learn serotonin dysfunction in panic disorder and changes of serotonin function after pharmacotherapy. Patients with panic disorder showed decreased serotonin function measured by maximum [3H]5-HT uptake rate (Vmax) and affinity (Km) before the treatment, and the affinity was normalized after 12-weeks of paroxetine treatment. The [3H]5-HT uptake affinity could be a good predictor of improvement in panic symptoms after pharmacotherapy of panic disorder.

Summary:
Objective: The purpose of this study is to examine changes of serotonin function in panic disorder patients after short-term pharmacotherapy with paroxetine.

Method: Twenty patients with panic disorder and 20 age and sex-matched healthy control subjects were recruited for this study. Platelet [3H]5-HT maximum uptake rate (Vmax) and affinity (Km) were measured both in the control subjects and panic patients at baseline. After 12-weeks of treatment with paroxetine, platelet [3H]5-HT uptake measures were measured again in the patients. Psychological symptoms were measured using the Hamilton rating scale for anxiety (HAM-A), Hamilton rating scale for depression (HAM-D), Spielberger state-trait anxiety inventory-State (STAI-S) and Trait (STAI-T), anxiety sensitivity index (ASI), and acute panic inventory (API).

Results: Before the treatment, the panic patients showed significantly lower Vmax (3.41±2.81 nmol/109 platelets/min vs. 5.69±5.15, p=0.016) and Km (726.84±588.77 nM vs. 1357.10±784.44, p=0.005) values than the control subjects. They also showed higher scores on all psychological measures than the control subjects, which were significantly decreased after the treatment. The Km value was significantly increased after the treatment (726.84±588.77 vs. 1396.17±1177.40, p=0.027), whereas the Vmax value was not significantly increased (3.41±2.81 vs. 5.29±5.04, p=0.141). The change of Km was significantly correlated with the changes of STAI-T (r=0.573, p=0.007), and API (r=-0.604, p=0.004). Using a linear regression model, the Km value was found to be a good predictor of the API (adjusted R2=0.331, p=0.004) scores after the treatment.

Conclusion: Panic disorder patients showed decreased serotonin function measured by maximum [3H]5-HT uptake rate and affinity before the treatment, and the affinity was normalized after the treatment with paroxetine. The [3H]5-HT uptake affinity could be a good predictor of clinical improvement after pharmacotherapy in panic disorder.

References:

NR30
Monday, May 21, 9:00 AM - 10:30 AM
Panic Disorder Respiratory Subtype: A Comparison Between Responses to Hyperventilation and CO2 Challenge Tests
Rafael C. Freire, M.D. Inst of Psychiatry - Fed Univ of Rio de Janeiro, Laboratory of Panic & Respiration, Av Visconde de Albuquerque 694 302, Rio de Janeiro, 22450-000, 3510, Fabiana L. Lopes, M.D., Alexandre M. Valenca, M.D., Isabella Nascimento, M.D., Andre B. Veras, M.D., Walter A. Zin, M.D., Antonio E. Nardi, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will be able to recognize the differences between the respiratory and the non-respiratory panic disorder subtypes. Participants will be able to identify the clinical and laboratorial characteristics of these subtypes.

Summary:
Objectives: Several provocative tests have been used in panic disorder (PD) research. The 35% carbon dioxide challenge test induces panic attacks (PA) in most PD patients, and the hyperventilation test also induces PAs in some of these patients. The objective of this study is to find correlations between these two tests, and correlate them to the PD respiratory subtype, which is characterized by intense respiratory symptoms.

Methods: We examined 117 panic disorder patients in the Laboratory of Panic and Respiration at the Institute of Psychiatry of the Federal University of Rio de Janeiro. The diagnoses were made using the SCID-I for DSM-IV. The criterion for the respiratory subtype was the presence of 4 or more respiratory symptoms (choking, smothering sensations; shortness of breath; chest pain/discomfort; numbness/tingling sensations; fear of dying) during the panic attacks. The CO2 challenge test and the hyperventilation test were conducted in all patients. The t-test and the chi-square were used in the statistical analysis.

Results: Respiratory subtype represented 56.4% (n = 66) of our sample. Previous studies indicated a higher familial history of PD in patients with the respiratory subtype, which was confirmed in our data (P= 0.004) and we also found a lower age of onset in the respiratory subtype group (P= 0.011). Patients with the respiratory subtype had a higher prevalence of previous alcohol use (P= 0.003), which is a new finding. Both respiratory tests were correlated with the PD respiratory subtype (P< 0.001). Patients who had a positive response to the carbon dioxide test had more respiratory symptoms than the hyperventilation responsive patients.

Conclusion: The hyperventilation and the carbon dioxide tests were correlated to the respiratory subtype; however, it seems that the carbon dioxide test has a stronger association with this subtype.

References:

NR31
Monday, May 21, 9:00 AM - 10:30 AM
Plasma Concentrations of Clozapine and Its Metabolites and FMO3 Variations in Korean Schizophrenic Patients
Young Kyung Sunwoo, M.D. INHA university hospital, psychiatry, 7-206 3Ga, Shinheung-dong, Jung-gu, Incheon, 400-711, 5800, Jei Young Kim, M.D., Kyung Hoon Lee, M.D., Chul Eung Kim, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to demonstrate the effect of Glu158Lys and Glu308Gly variation in FMO3 gene on clozapine metabolism could not be shown.

Summary:
Object: The relationship between the total daily dose of clozapine given and the plasma concentrations of clozapine and its metabolites(N-desmethylclozapine and clozapine N-oxide) and the effect of Glu158Lys(wide-type:Glu,'H';variant:Lys,'h') and Glu308Gly(wide-type:Glu,'D';variant:Lys,'d') variation in FMO3 gene on plasma concentrations of clozapine and its metabolites was studied in schizophrenic patients.

Methods: Trough plasma concentrations of clozapine and its metabolites were measured in 34 schizophrenic patients receiving clozapine. The genetic variation of 'h' and 'd' in FMO3 were analyzed in 21 among 34 patients.

Results: A linear relationship between the total daily dose of clozapine given(mg/kg body weight per day) and the plasma concentrations(nM) of clozapine was revealed by regression analysis(p<0.001) in the 23 patients receiving a constant daily dose of clozapine for 8 days. The plasma molar concentration ratios of clozapine N-oxide/clozapine in 8 subjects with 'hh' or 'Hh' alleles were not different from those in 8 subjects with 'HH' alleles and the plasma molar concentration ratios in 6 subjects with 'dd' or 'Dd' alleles were not different form those in 8 subjects with 'DD' alleles.

Conclusion: The effect of Glu158Lys and Glu308Gly variation in FMO3 gene on clozapine metabolism could not be shown.

References:

NR32
Monday, May 21, 9:00 AM - 10:30 AM
Detection of functional impairments in euthymic bipolar patients using the International Classification of Functioning, Disability and Health (ICF)
Jose Sanchez-Moreno, Psy.D. Clinical Institute of Neuroscience. Hospital Clinic of Barcelona, Psychiatry, c/ Rosellon, 140, bajos, Barcelona, 08036, 4700, Anabel Martinez-Aran, Ph.D., Marta Nieto-Moreno, Psy.D., Carla Torrent, Psy.D., Eduard Vieta, M.D., Herminio Martinez, M.D., Jose Luis Ayuso-Mateos, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to identify the most common problems by patients with bipolar disorder using the ICF framework, to recognize the importance of assessing the different health related domains involved in patient's functioning, and the utility of the ICF model and its related instruments to provide a comprehensive functional profile both in the clinical and the research field.
Summary:

Background: Recent studies have suggested a low functioning even when bipolar patients are euthymic. However, the extent to which functional recovery is related to clinical remission has not been studied systematically. In this context, the International Classification of Functioning, Disability and Health (ICF; WHO, 2001) provides the framework to describe individual’s functioning and allows the study of the interaction between patient’s health status and the environmental factors involved. The ICF classifies functioning and health by a number of categories divided into three main domains: Body functions and structures, Activities and Participation, and Environmental factors.

Objectives: To use the ICF model to explore the functional profile of euthymic bipolar patients.

Methods: Fifty euthymic patients with a diagnosis of bipolar disorder (ICD-10) were included. Data on clinical and socio-demographic information were recorded. The ICF-checklist, which includes a selection of 165 ICF categories, was used to describe participant’s functioning.

Results: Functioning was impaired in at least 35 ICF categories in more than 75% of participants. Body functions was the ICF component in which patients referred less impairment. In spite of the absence of manic or depressive symptoms, more than two-third of the patients referred limitations in Activities and restrictions in Participation. Finally, within the Environmental Factors component, “health professional”, “support of family members and friends” were the main facilitators, while “attitudes of immediate family members and friends”, “social norms”, “practices and ideologies”, and “health services, systems and policies” were the main barriers identified by participants.

Conclusions: Around 75% ICF-checklist categories represent functioning in euthymic bipolar patients from the patients’ perspective. These results show the utility of using the ICF model in providing a comprehensive functional profile of bipolar patients, emphasize the relevance of functioning beyond symptoms and, give clinicians a clearer idea of the areas requiring intervention.

References:

NR34 Monday, May 21, 9:00 AM - 10:30 AM
Attachment and Well-Being in the Elderly
Mudhasir Bashir, M.D. University of Virginia, Psychiatric Medicine & Neurobehavioral Sciences, 1414 Teawood Cv, Charlottesville, VA, 22911-8289, 9000, Adrienne Keller, Ph.D.

Educational Objectives:
1) identify the primary attachment styles;
2) describe the relevance of attachment research to understanding the needs of elderly patients;
3) understand the relationship between attachment style and trust in physician;
4) understand the relationship between attachment style and coping style; and
5) discuss the implications of these findings for care for the elderly and for further research

Summary:
Objective: This pilot study tests the hypothesis that, for elderly patients, health-related quality of life, style of coping with illness, and trust in physician will vary significantly among the three primary attachment classifications (secure, dismissing, enmeshed).

Method: Participants aged sixty-five and above were recruited from patients attending a university hospital clinic. Each participant completed an anonymous standardized questionnaire including a...
10-item instrument to assess attachment styles in the elderly, the SF-12 to assess health-related quality of life, a 27-item coping with illness scale, the 11-item Trust in Physician scale, and 10 demographic questions.

Results: The sample included 27 females and 12 males; 49% of participants were 65-74 years old; 51% were over 74; 54% were Caucasian; 41% were African-American. Forty-one percent of women and 33% of men reported that their activities were limited by physical and/or emotional problems; 41% of women and 17% of men endorsed at least 2 of 3 indicators of depression. There were no significant differences between males and females in prevalence of attachment styles: 28% were secure, 59% avoidant and 13% enmeshed. This is a higher prevalence of avoidant attachment, particularly in a predominantly female sample, than is typically found in younger populations. Endorsement of at least 2 indicators of depression was highest among those with secure attachment (46%) and lowest among those with avoidant attachment (28%). Those with secure attachment also had the lowest score for trust in physician (mean=14.7, s.d.=7.1 compared to mean=17.6, s.d.=7.8). Those with secure attachment are significantly more likely to use objects of attachment for coping (F=5.3, df=2/38, p=.01).

Conclusions: Avoidant attachment may be a more common attachment pattern among the elderly than among younger populations. Further, understanding attachment style could be very helpful in understanding both reactions to health care providers and preferred coping styles.

References:

NR35  Monday, May 21, 9:00 AM - 10:30 AM Does smoking increase the gravity of panic disorder?
Rafael C. Freire, M.D. Inst of Psychiatry - Fed Univ of Rio de Janeiro, Laboratory of Panic & Respiration, Av Visconde de Albuquerque 694 / 302, Rio de Janeiro, 22450-000, 3510. Marco A.U Mezzasalma, M.D., Alexandre M. Valenca, M.D., Valfrido L. de-Melo-Neto, M.D., Fabiana L. Lopes, M.D., Isabella Nascimento, M.D., Antonio Egidio Nardi, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will be able to identify the risks of smoking and its consequences in panic disorder.

Summary:
Objectives: Several studies indicate that smoking is associated with anxiety disorders, especially with the panic disorder (PD), and possibly, smokers have a more intense form of panic disorder. Our aim is to find correlations between smoking and gravity of the PD and prevalence of comorbidities.
Methods: We examined 61 panic disorder patients in the Laboratory of Panic and Respiration at the Institute of Psychiatry of the Federal University of Rio de Janeiro. The diagnoses of panic disorder and its comorbidities were made using the SCID-I for DSM-IV. Expert psychiatrists evaluated the patients and gave a Clinical Global Impression (CGI) score for each one. Patients were also questioned about the age of beginning of the symptoms and if they had familial history of PD. Those who stopped smoking within the last 12 months were considered along the smokers group. The t-test and the chi-square were used in the statistical analysis.
Results: Regarding familial history and age of beginning, the two groups were similar. There was a significantly higher proportion of smokers with comorbid depression (P = 0.006), and there were no significant differences regarding agoraphobia prevalence. Also, the gravity scores were very similar between smokers and non-smokers.
Conclusions: Panic disorder in smokers and non-smokers is very similar, with the exception of a higher prevalence of major depression in the smokers.

References:

NR36 Monday, May 21, 9:00 AM - 10:30 AM Off-Label Use of Quetiapine in Psychiatric Inpatients
Noah S. Phillip, M.D. Brown University, Psychiatry and Human Behavior, 345 Blackstone Blvd, Providence, RI, 02906, 9000, Kerry S. Mello, Pharm.D., Audrey R. Tyrka, M.D., Linda L. Carpenter, M.D., Lawrence H. Price, M.D.

Educational Objectives:
At the conclusion of this poster presentation, the participants should be able to demonstrate an understanding of indications, frequency and diagnoses treated with off-label quetiapine, and be able to recognize the need for further research into the safety and efficacy of low-dose quetiapine.

Summary:
Background: There is emerging recognition that off-label use of atypical antipsychotics is widespread, but there is little data concerning the patterns of such use. After observing high-volume use of quetiapine (seroquel), an atypical neuroleptic approved for the treatment of schizophrenia and mania, we conducted a retrospective utilization review of prescribing practices of this drug at our acute-care psychiatric hospital.
Methods: Inpatient orders for quetiapine were obtained from October 2004 to March 2006 and divided into standing or prn dose regimens. For patients receiving standing dose regimens, diagnosis, total daily dose, and dosing adequacy were ascertained. For patients receiving prn dosing, diagnosis, behavioral indication, dose, and frequency were determined.
Results: The most common diagnoses in patients receiving standing dose quetiapine were depressive disorders, followed by substance-related, bipolar, and psychotic disorders. Mean standing dose was 169 +/- 154 mg/day (median = 200 mg/day), with 29.8% of patients receiving at least 300 mg/day. Only 28.5% of patients had one of the diagnoses for which quetiapine is approved; in these patients, 46.4% received at least 300 mg/day. Patients receiving prn dosing had a similar distribution of diagnoses. The most common prn dose was 50 mg, given every 1-2 hours for agitation or at evening/bedtime.
Conclusions: We found extensive off-label use of quetiapine. Further research is needed on the safety and range of efficacy of quetiapine in non-approved doses and diagnoses.

References:
2. Lehman AF et al. Practice guidelines for the treatment of patients with schizophrenia. In: APA Practice Guidelines for The
NR37  Monday, May 21, 9:00 AM - 10:30 AM
How Are Adverse Effects Assessed and Reported In Antidepressant Clinical Trials?

Educational Objectives:
At the conclusion of this presentation, participants should be able to identify possible consequences of not using a standardized rating scale to assess adverse effects in clinical research of antidepressants. Participants should also be able to recognize reasons to use standardized means of evaluating adverse effects in treating their own patients.

Summary:
Background: Adverse effects are the main reason for choosing between antidepressants and the greatest single reason for non-adherence. The methodology of adverse effect assessment, however, is being neglected, particularly in the US. Clinical decisions also require that the severity and persistence of adverse effects be reported. However, little attention has been paid to methods of identifying and characterizing adverse effects of antidepressants.

Methods: Data extraction from clinical trials of antidepressants published between July 2006 to June 2007 (n=73).

Results: Only 15% of trials used a specific rating scale for adverse effects; 16% specified lab tests for adverse effects; 18% reported severity of adverse effects; and 12% reported assessing their persistence.

In multivariable logistic regression, studies done outside the US were 4.8 times more likely to report using a rating scale for adverse effects (p=0.045), even while controlling for source of funding.

Unexpectedly, use of an adverse effect rating scale was associated with a higher attrition rate due to adverse effects (p=0.048), and with a lower likelihood that the study medication was effective (p=0.02). In a regression model, use of an adverse effect rating scale showed marginal significance for predicting a lower likelihood for finding the medication effective (OR 4.96, p=0.07) even while controlling for percentage of dropouts due to adverse effects.

Discussion: Greater efforts to appropriately identify and characterize adverse effects are needed. However, use of a rating scale without aggressive management of the adverse effects identified may lead to more dropouts. Rating scales may sensitize patients to their adverse effects leading to increased dropouts and therefore to the medication appearing to be ineffective. Our findings highlight the tension between patients and patient advocates who emphasize increased awareness of adverse effects, and sponsor and investigators who may be concerned about its impact on attrition and drug effectiveness.

References:

NR38  Monday, May 21, 9:00 AM - 10:30 AM
Selective Serotonin Reuptake Inhibitor Use in Pregnancy and Fetal Outcomes
Christina L. Wichman, D.O. Mayo Clinic, Department of Psychiatry and Psychology, 200 First Street SW, Rochester, MN, 55905, 9000, Katherine M. Moore, M.D., Tara R. Lang, M.D.; Robert H. Heise, Jr., M.D., William J. Watson, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to discuss recent data and concerns regarding the safety profile of serotonin specific reuptake inhibitors in pregnancy.

Summary:
Objective: To study the effects of selective serotonin reuptake inhibitors (SSRIs) in pregnancy on fetal outcome.

Background: Recent data indicates that approximately 10% of women will have depression at any point during pregnancy or the post-partum period. Selective serotonin reuptake inhibitors (SSRIs) are the first line pharmacotherapy to treat depression. SSRi use in pregnancy has been well documented. Inconsistent data has been reported regarding the safety of SSRIs in pregnancy. Many studies have indicated no major fetal malformations with use of SSRIs in pregnancy. More recently, reports of ventricular septal defects associated with use of first-trimester use of paroxetine and persistent pulmonary hypertension of the newborn associated with late-pregnancy exposure of SSRIs have been published. In this project, we examined the medical records of pregnant women who had SSRI exposure during pregnancy, and correlated this to fetal outcome, specifically assessing for cardiac malformations and pulmonary hypertension.

Methods: We received IRB approval to conduct a retrospective chart review of all pregnant women presenting at our medical center, from the year 1993 to 2005. We identified 25,214 total deliveries during that time period. 745 mothers were treated with SSRIs during their pregnancy. We also reviewed the medical charts of the babies exposed to SSRIs during pregnancy to review fetal outcomes.

Results: 208 babies had congenital heart disease, however only 2 had been exposed to SSRIs. We did not identify any statistical association with SSRI use and congenital heart disease. Of the 745 SSRI-treated mothers, 153 had exposure to paroxetine (Paxil®). None of the paroxetine-exposed babies had ventricular septal defects. Additionally, 16 babies were diagnosed with persistent pulmonary hypertension, however none had been exposed to SSRIs.

Conclusion: Our data supports the safety of SSRIs during pregnancy in regards to cardiac malformations, including ventricular septal defects, and persistent pulmonary hypertension.

References:

NR39  Monday, May 21, 9:00 AM - 10:30 AM
Depression in Adults with Type 2 Diabetes at a Military Medical Center
Sheryl A. Bedno, M.D. Walter Reed Army Medical Center, National Capital Consortium Psychiatry Residency, 1215 East West Highway, Apt 417, Silver Spring, MD, 20910, 9000, Susan D. Fracisco, M.D., Anthony D. Puopolo II, M.D.
Alcoholism Indicators and Quality of Life

symptomatology to alcoholism indicators and to quality of life in
able to demonstrate the relation among findings about depressive

Educational Objectives:

Hilgert, Jeanette Farina, Patricia Lemos
clauhilg@terra.com.br, Porto Alegre, 90630090, 3510,
Claudia
Moinhos de Vento Hospital, Psiquiatria,


visits in the depression group, with or without type 2 DM, were


current health care utilization was also significantly elevated in the

type 2 DM group as measured by health care contacts (23 vs.

Health care utilization was also significantly elevated in the
type 2 DM group as measured by health care contacts (23 vs.

Comparison of depression in type 2 diabetes in this

To determine the impact of depression on type 2 DM in primary care
patients at a US military medical center, we conducted a pilot
case-control study consisting of a one year period of health care,
from May 2001 to April 2002. Outpatient records of adults over
age 45 with type 2 DM were randomly selected and compared to
age and sex matched controls. We found that 22.8% of patients
(n=13) with type 2 DM had the diagnosis of depression as com-
pared to 8.8% of controls (n=5) (p=0.07). Independent of depres-
sion, hypertension (96% vs. 63%, p<.0005), hyperlipidemia (77%
vs. 56%, p=.028), and body mass index (29 vs. 27, p=.028) were
significantly elevated in type 2 DM compared to controls, respec-
tively. Health care utilization was also significantly elevated in the
type 2 DM group as measured by health care contacts (23 vs.

patients

Type 2 Diabetes Mellitus (Type 2 DM) and depression are major
public health problems affecting all segments of the population.
Depression is a serious, co-morbid illness of type 2 DM. To deter-
mine the impact of depression on type 2 DM in primary care
patients, a case-control study was performed. We included one
case and one control for each patient with type 2 DM. Controls
were matched for age, sex, and diabetes status. We found that
22.8% of patients with type 2 DM had the diagnosis of depres-
sion compared to 8.8% of controls (p=0.07). Independent of depres-
sion, hypertension (96% vs. 63%), hyperlipidemia (77% vs.

Health care utilization was also significantly elevated in the
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pared to 8.8% of controls (n=5) (p=0.07). Independent of depres-
sion, hypertension (96% vs. 63%, p<.0005), hyperlipidemia (77% vs.

visits in the depression group, with or without type 2 DM, were

and with or without diabetes in a primary care military population; (2)
compare the prevalence of depression in type 2 diabetes in this
study to data in similar literature; (3) evaluate other illnesses com-
orbid to both depression and diabetes; and (4) assess the impact of
comorbid depression and diabetes on health care utilization.

Summary:

Type 2 Diabetes Mellitus (Type 2 DM) and depression are major
public health problems affecting all segments of the population.
Depression is a serious, co-morbid illness of type 2 DM. To deter-
mine the impact of depression on type 2 DM in primary care
patients at a US military medical center, we conducted a pilot
case-control study consisting of a one year period of health care,
from May 2001 to April 2002. Outpatient records of adults over
age 45 with type 2 DM were randomly selected and compared to
age and sex matched controls. We found that 22.8% of patients
(n=13) with type 2 DM had the diagnosis of depression as com-
pared to 8.8% of controls (n=5) (p=0.07). Independent of depres-
sion, hypertension (96% vs. 63%, p<.0005), hyperlipidemia (77% vs.

Summary:

Type 2 Diabetes Mellitus (Type 2 DM) and depression are major
public health problems affecting all segments of the population.
Depression is a serious, co-morbid illness of type 2 DM. To deter-
mine the impact of depression on type 2 DM in primary care
patients at a US military medical center, we conducted a pilot
case-control study consisting of a one year period of health care,
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age 45 with type 2 DM were randomly selected and compared to
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sion, hypertension (96% vs. 63%, p<.0005), hyperlipidemia (77% vs.

visits in the depression group, with or without type 2 DM, were

Appendix A

The prevalence of depression in type 2 diabetes was not a prevalent comorbidity in depressive patients eval-
uated.

NR41    Monday, May 21, 9:00 AM - 10:30 AM
Prevalence of Serotonin Specific Reuptake Inhibitor (SSRI) Use in Pregnant Women
Christina L. Wichman, D.O. Mayo Clinic, Department of Psychiatry and Psychology, 200 First Street SW, Rochester,
MN, 55905, 9000, Katherine M. Moore, Tara R. Lang, M.D.,
Robert H. Heise, Jr., M.D., William J. Watson, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be
able to discuss recent trends of serotonin specific reuptake inhibi-
tor (SSRI) use in pregnant women.

Summary:

At the conclusion of this presentation, the participant should be
able to: (1) summarize the prevalence of depression in adults with
and without diabetes in a primary care military population; (2)
compare the prevalence of depression in type 2 diabetes in this
study to data in similar literature; (3) evaluate other illnesses com-
orbid to both depression and diabetes; and (4) assess the impact
of comorbid depression and diabetes on health care utilization.

Summary:

Type 2 Diabetes Mellitus (Type 2 DM) and depression are major
public health problems affecting all segments of the population.
Depression is a serious, co-morbid illness of type 2 DM. To deter-
mine the impact of depression on type 2 DM in primary care
patients at a US military medical center, we conducted a pilot
case-control study consisting of a one year period of health care,
from May 2001 to April 2002. Outpatient records of adults over
age 45 with type 2 DM were randomly selected and compared to
age and sex matched controls. We found that 22.8% of patients
(n=13) with type 2 DM had the diagnosis of depression as com-
pared to 8.8% of controls (n=5) (p=0.07). Independent of depres-
sion, hypertension (96% vs. 63%, p<.0005), hyperlipidemia (77% vs.

Summary:

Approximately 40% of patients with neurological diseases present
some kind of depressive disorder, besides the existence of 2-4 times
increase in the prevalence of a major depression if the disorders related to alcohol are associated.

This is a cross-sectional study. For three months in 2006, 70
persons between male and female that consulted at the neurol-
yogy ambulatory of the Independência Hospital were evaluated. A ques-
tionnaire was applied to collect personal, demographical and clini-
cal data; besides of the BDI, AUDIT and WHOOQOL-Bref. The
statistical analysis was done through ANOVA, Pearson, T of Stu-
dent and Spearman tests.

Thirty per cent of the patients did not have depressive symp-
toms, 28.6% had mild symptoms, 21.4% with moderate symptom-
tology and 20% with severe symptoms. Only 5.7% of the inter-
viewed presented alcohol abuse. All domains evaluated by
WHOOQOL-bref had significant statistic data when correlated to
BDI.

The prevalence of depression is high in neurological outpatients
of the Independência Hospital, especially in moderate to severe
forms and it was highly associated to a worst quality of life. Alcohol-
ism was not a prevalent comorbidity in depressive patients evalu-
ated.

References:

Psychiatry 2003; 74: 893 ’ 96.

NR40    Monday, May 21, 9:00 AM - 10:30 AM
Prevalence of Depressives Symptoms Evaluated in Neurological Outpatients and Its Relationship with
Alcoholism Indicators and Quality of Life
Nora Jane Thomann Moinhos de Vento Hospital, Psiquiatria,
clauhilg@terra.com.br, Porto Alegre, 90630090, 3510, Claudia
Hilgert, Jeanette Farina, Patricia Lemos

Educational Objectives:

At the conclusion of this presentation, the participant should be
able to demonstrate the relation among findings about depressive
symptomatology to alcoholism indicators and to quality of life in
patients that have consultation in a general neurology ambulatory
at Independência University Hospital in Porto Alegre, Rio Grande
do Sul, Brazil.

Summary:

At the conclusion of this presentation, the participant should be
able to discuss recent trends of serotonin specific reuptake inhibi-
tor (SSRI) use in pregnant women.

Summary:

Background: Recent data indicates that approximately 10% of
women will have depression at any point during pregnancy or
the post-partum period. Selective serotonin reuptake inhibitors
(SSRIs) are the first line pharmacotherapy to treat depression and
SSRI use in pregnancy has been well documented. There have
not been any epidemiologic studies specifically evaluating the use
of SSRIs in pregnant women, but approximately 2-3% of pregnant
women in the United States 1 have been reported to use anti-
depressants in general. In this project, we examined the medical
records of pregnant women who had SSRI exposure during preg-
nancy compared to the total number of deliveries in order to deter-
mine prevalence of SSRI use in pregnancy over the past several
years.

Methods: We received IRB approval to conduct a retrospective
chart review of all pregnant women presenting at our medical
center, from the years 1993 to 2005. Data was obtained from a
database that has been prospectively maintained since 1993 by
the Department of Obstetrics at Mayo Clinic. Data was confirmed
by individual chart review. We identified 25,214 total deliveries
during that time period. 745 mothers were treated with SSRIs
during their pregnancy.
Conclusion: SSRI use in pregnancy has been increasing in the past several years and is currently averaging approximately 5% of all pregnancies in our practice. Use may be on the rise secondary to physician and patient perception of safety with SSRIs in pregnancy, however recent reports outlining potential adverse fetal effects indicate the need for ongoing research in this area.

References:

NR42 Monday, May 21, 9:00 AM - 10:30 AM
Profile of Suicidal Attempters Admitted in an Emergency Unit at Puerto Rico
Claudia I. Lopez, M.D. University of Puerto Rico, Psychiatry, 256 Calle Rosario, Apt 704, San Juan, PR, 00912, 9000, Dinorah Quiles, M.D., Adalis Maria Millan, M.D.

Educational Objectives:
At the conclusion of this presentation the participant should be able to recognize the profile of suicidal attempters that present to a general emergency room at a general hospital in Puerto Rico. The participants will also be able to recognize how this specific population compares with the Puerto Rico general population and the part of the population in the United States.

Summary:

Introduction: The suicide attempts represent a public health problem. The individual attempting suicide is similar in many aspects, but differ from those who commit suicide. In Latinos the data about suicide attempts is limited.

Method: This is an explorative and retrospective study. The data were obtained from the medical consultants of the patients evaluated at a General Emergency Room in Puerto Rico by the psychiatry service due to suicidal attempt. The consults reviewed were from January 2005 to December 2005. A total of 294 consults were reviewed, 44 were excluded and 250 consults (8 to 74 years of age) were used for analysis.

Results: In this study the higher number of suicidal attempts was during July, August and October. In the sociodemographic aspect most were females (male/female ratio of 1:1.6); most of the population was in the 15-24 years age group, was unemployed, without a partner, with high school education and had at least one son. In the psychiatric aspect most reported a mood disorder, denied active psychiatric treatment, denied the use of psychotropic medications, and reported a family history of psychiatric illness and at least one previous suicidal attempt. The most common precipitant identified was interpersonal problems. The male population was more likely to report unemployment, toxic habits and identify other stressors like medical/psychiatric problems and legal problems. In the female population the percent of unemployment was very close to the percent of employed woman's, this differs from male population. In the population taking psychotropic medications the antidepressants and benzodiazepines were the most commonly reported.

Conclusions: The suicide attempters under study were in many aspects similar to suicide attempters studied in populations other than Latino. The toxic habits and unemployment were more significant for male than female population. Further studies with larger populations are needed to replicate the results.

References:

NR43 Monday, May 21, 9:00 AM - 10:30 AM
Treating Obsessive Compulsive Disorders: An Examination of Group Cognitive Behavioral Therapy (CBT) vs. Group CBT plus Motivational Interviewing and Thought Mapping
elisabeth M. Silva, M.S. Federal University of Rio Grande do Sul, Psychiatry, to_bethmeyer@hotmail.com, Porto Alegre, 91340390, 3510, Carl Leukefeld, Ph.D., Daniela Benzano, B.A., Fernanda Souza, M.S.C., Katia Niederauer, M.S.C., paulo knapp, M.S., Aristides Cordioli, Ph.D.

Educational Objectives:
At the end of this poster presentation, the participant should be able to examines the impact of adding 4-individual sessions of motivational interviewing and Thought Mapping to a 12 week Group Cognitive Behavior Therapy OCD outpatient treatment. Attending this conference would provide me with an opportunity to meet and collaborate with U.S. researchers and clinicians to discuss ways that advances in the field can be adapted and applied in the Brazilian setting.

Summary:
Obsessive-Compulsive Disorder (OCD) is characterized by repeated and persistent attempts to control thoughts and actions using rituals to prevent feared or personally distressing outcomes. Group Cognitive Behavioral Therapy (GCBT) involving Exposure and Ritual Prevention (ERP) has been shown to be effective for OCD. This study targets patients who refuse ERP, drop out prematurely, or do not benefit from GCBT. The present behavioral trial examines the impact of adding 4-individual sessions of motivational interviewing (MI) and Thought Mapping to a 12 week GCBT outpatient treatment. 96 subjects with OCD will be randomly assigned from January 2006 to December 2007 to one of two conditions: (1) GCBT or (2) GCBT plus MI and Thought Mapping in a general hospital in the South of Brazil. Differences between groups are presented for the initial 48 subjects.

References:

NR44 Monday, May 21, 9:00 AM - 10:30 AM
Reliability of Sensory Gating of Mid-Latency Auditory Evoked Responses in Relation to Endophenotypes of Schizophrenia.
Andrei B. Vedeniapin, M.D. Penn State University, Psychiatry, 97 Townhouse, Hershey, PA, 17033, 9000, Andrei P. Anokhin, Ph.D., Nash Boutros, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand impaired central mechanisms of sensory filtering and information processing in schizophrenia spectrum disorders, and that a study of mid-latency auditory evoked brain responses in conditioning-testing paradigm may be helpful for establishing endophenotypes for genetic studies of schizophrenia. The participant should be able to recognize the importance of test-retest reliability assessments in studies of endophenotypes of psychiatric disorders.
Summary:

A deficit in sensory gating measured by suppression of mid-latency auditory brain evoked response P50 to the second of a pair of clicks has been associated with risk for schizophrenia spectrum disorders and proposed as an endophenotype for genetic studies of schizophrenia. However, there are mixed reports regarding test-retest reliability of the P50 gating parameters that questions their use as endophenotypic markers. The deficit of suppression of a longer latency auditory evoked response, the N1/P2 complex, has been shown to be also associated with schizophrenia. While test-retest studies have revealed a moderate reliability of the N1 potential suppression, little is known about the reliability of the P2 sensory gating. In this study we examined test-retest reliability of P50, N1, and P2 potentials and the corresponding sensory gating measures. The two clicks paradigm was administered to 52 non-deprived smokers (mean age 25.3 y.o., 31 female) twice within the same session with a one-hour interval, and 45 participants also completed another session with an average inter-session interval of 18 days. The data from a monopolar recording from a midline Cz EEG electrode were used. Within- and between-session reliability of P50, N1 and P2 components and their gating parameters was estimated using intraclass correlations. The amplitudes of all three mid-latency components showed high and significant test-retest reliability. P50 gating showed significant but weak within-session reliability (r = 0.24), however, long-term (between-session) reliability was non-significant (r = 0.04, n.s.). On the contrary, both N1 and P2 suppression were short and long-term reliable (r = 0.48 and 0.28 for N1, and r = 0.61 and 0.37 for P2, respectively). The data revealed that auditory N1-P2 suppression in the sensory gating paradigm is a more reliable measure than P50 suppression, and may be more suitable as an endophenotypic marker for schizophrenia spectrum disorders.

References:

NR45 Monday, May 21, 9:00 AM - 10:30 AM
The Metabolic Syndrome: Identification and Monitoring in a Community Mental Health Center
Sosunmolu O. Shoyinka Maimonides Medical Center, Psychiatry, 974 47th Street # 1D, Brooklyn, New York, NY, 11219, 9000

Educational Objectives:

The educational objective of this report is to increase awareness of the need to monitor patients on second generation antipsychotic medications for the metabolic syndrome by psychiatrists. Current compliance rates with existing screening guidelines are very low (in this study - less than 20%).

Summary:

Screening guidelines for the Metabolic Syndrome in severely mentally ill patients on Second Generation Antipsychotics (SGAs) have been available since 2003 (1). Rates of compliance with current guidelines are unknown. This study examined compliance rates with established guidelines in a community mental health center. A review of the charts of sixty patients currently receiving treatment in the Continuing Day Treatment Service at the Maimonides Mental Health Center was done spanning the time period from February 2004-August 2006. Patients included in the study had been in long-term treatment (>2.5yrs), were on at least one SGA and were being seen for medications on a monthly basis. Patients were excluded from the study if their treatment was discontinued for any reason during the period over which the study was carried out. Screening practices were compared against the protocol developed by the Consensus Development Conference on Antipsychotic Drugs, Obesity and Diabetes in 2003(1). This study was approved by the Institutional Review Board.

Compliance rates with the ATP protocol were less than 20% overall. Rates were lower (10%) for checking personal histories of hypercholesterolemia, Diabetes Mellitus, and weight at 1 year. Not a single patient was fully screened or monitored according to these guidelines.

Fewer than 20% of patients at Maimonides-CMHC are being monitored in compliance with current guidelines for screening for the Metabolic Syndrome.

References:

NR46 Monday, May 21, 9:00 AM - 10:30 AM
Feasibility of Humor as a Treatment Modality in Patients with Depression
Anna Bokarius Cedars-Sinai Medical Center, Psychiatry and Mental Health, 8730 Alten Dr Rm E123, Los Angeles, CA, 90048, 9000, Waguih W. Ishak, M.D., Vladimir Bokarius, MD, Ph.D., Mark H. Rapaport, M.D., Russell Poland, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be familiar with the trends in recent humor and depression research as well as the methodology used to carry out the present investigation. The participant should also gain an understanding of the importance of the discovery of no correlation between sense of humor and level of depression and possibly develop an interest in using humor as a potential intervention in treating depression.

Summary:

Humor as a method of treatment has stirred up much interest in various fields, including psychiatry. Despite an abundance of relevant publications, the majority of existing studies are of low evidence. While some literature suggests positive clinical use of humor in reducing stress and anxiety, the results of studies on depression are largely inconclusive.

While seems logical to investigate the effects of humor on depression in a well-designed study, it is first wise to consider how suitable such research would be for the patients. We investigated the dispositions toward humor of the depressed patients, rather than the effects. This study sheds light on the actual wishes of our patients. By finding out their preferences we can decide whether an extensive research on the clinical use of humor in treating depression is worthwhile.

This study was carried out at the outpatient psychiatric department of Cedars-Sinai Medical Center. Patients were asked to complete a short questionnaire comprised of regular depression scale and a modified Svebak’s Sense-of-Humor Questionnaire. A correlation between the disposition toward humor and the level of depression was measured.

When we began this study over a year ago we expected that welcoming humor as part of treatment will depend largely on the level of depression and the inherent sense of humor of the individual patient. After conducting an interim efficacy analysis, we discovered that there was no correlation between the disposition toward humor and level of depression. After presenting these
initial findings last year, we have expanded and concluded this study. Our final findings confirm of the lack of such a relationship as well as a general acceptance of humor as an intervention among most patients.

With these promising findings, we propose further research on the new and exciting intervention of humor in depressed patients.

References:

NR48 Monday, May 21, 9:00 AM - 10:30 AM
Clinical Characteristics of Early Onset Bipolar Disorder

Min Hyeon Park, Catholic University of Korea, Psychiatry, Seochogu Banpodong 505 Kangnam Saint Mary Hospital, Seoul, Korea, 137-040, 5800, Young Sup woo, M.D., Ho-Jun seo, Jeong-Ho chae, Tae-Youn Jun, Won-Myong Bahk

Educational Objectives:

The results of this study will help understand the mechanism of the onset of complex bipolar disorder and estimate the prognosis.

Summary:

Objective: Bipolar disorder is a disease that has diverse clinical profiles and outcomes. In recent years, it is suggested that if bipolar disorder occurs early in one's life, functional and symptomatologic prognoses are poor. The prognoses include severe symptoms, frequent psychotic symptoms, comorbidity of mental illnesses, slow improvement of the symptoms, and high suicide rate. So we investigated clinical characteristics of early onset bipolar inpatients.

Method: The subjects of this study were selected from the patients who were discharged after hospitalization between January 1, 2001 and May 31, 2005 and diagnosed as having bipolar disorder according to DSM-IV criteria. These patients were examined for the following data: the type of bipolar disorder, comorbid Axis I disorder, the age at onset of the illness, the acuteness of the disorder, and the duration of the disorder. Also examined was the existence of four major clinical psychopathology: rapid cycling, psychotic symptoms, comorbid psychiatric disorders, and suicide attempt. The patients for whom the onset of the disorder was before the age of 19 were classified as early onset group. Data on demographics, family histories, four major clinical psychopathology and other clinical variables were compared between early onset group and late onset group.

Results: Of the 53 patients, 19 patients were belonged to the early onset group. There were higher incidences of psychotic symptoms in the early onset group. The incidence of comorbid psychiatric disorders was higher in the early onset group.

But there was no statistically significant difference between the groups regarding the incidence of rapid cycling and suicide attempt. The result of logistics regression showed that there were correlations between the early onset group and psychotic symptoms, and comorbid psychiatric disorders.

Conclusions: Early onset of bipolar disorder is related to the manifestation of psychotic symptoms and it frequently accompanies comorbid psychiatric disorders.

References:
NR49  Monday, May 21, 9:00 AM - 10:30 AM

Age Associated Tolerability in the Treatment of Bipolar Depression with Aripiprazole

Vanessa Stan, B.A. Cambridge Health Alliance, Psychiatry, 1493 Cambridge St., Cambridge, MA, 02139, 9000, Lyvia Chriki, B.A., Robert T. Dunn, M.D.

Educational Objectives:

- Participants should understand the association between tolerability of short-term aripiprazole treatment and age.

Summary:

Objective: Tolerability is an important issue in patient medication compliance (1). A previous study indicated that aripiprazole is effective for mania (2). In this first prospective study of the safety and efficacy of aripiprazole in bipolar depression, we examined the association between age and tolerability.

Method: An open label, prospective, non-randomized, 6-week study was conducted in depressed bipolar outpatients (type I, type II, or NOS). Previous treatments were continued unchanged. Patients began treatment at 2.5 mg and were titrated up to an effective, well-tolerated dose. Changes in depression were monitored using the Montgomery-Asberg Depression Rating Scale (MADRS). Potential extrapyramidal symptoms were monitored using the Barnes Akathisia Scale (BAS) and Simpson-Angus Scale (SAS). Preliminary analysis of 18 patients was conducted; full data will be presented.

Results: Patients were 13 males, 5 females (8 BPI, 7 BP II, 3 BP NOS) with a mean age of 38.7 years ± 10.0 years (ranging 24-53 years) and a mean endpoint dose of 14.4 mg ± 10.3 mg. Average duration of treatment was 4.7 weeks ± 2.1 weeks. An overall correlation of 0.5675 (p=0.0175) was observed between final dose and age. Regression analysis confirmed this observation regardless of endpoint MADRS, BAS or SAS scores. Patients below the median age were more likely to withdraw from the study prior to completion (4 of 5 drop-outs below median age), with all due to side effects (2 for nausea, 1 for insomnia, 1 for extrapyramidal symptoms, and 1 for akathisia).

Conclusion: A significant positive correlation was seen between final dose and age. This was likely due to reported side effects. These side effects were seen even at low doses in many young patients, indicating a need for cautious titration in the treatment of young patients with aripiprazole.

Funding Source: Bristol-Myers Squibb Company

References:

NR50  Monday, May 21, 9:00 AM - 10:30 AM

Predictors of Completers vs Noncompleters of a VA PTSD Residential Rehabilitation Program (PTSD-RRP)

Ramsey Pevsner, D.O., JMH, Psychiatry, 301 Desoto Street, Hollywood, FL, 33016, 9000, Saiqa Ismail, M.D., Daniella David, M.D.

Educational Objectives:

- At the conclusion of this presentation the participant should be able to recognize characteristics of veterans who are at risk of not completing the residential program for PTSD.

Summary:

Educational Objectives: At the conclusion of this presentation, the participant should be able to: 1) recognize the prevalence of polypharmacy in the treatment of major depression, and 2) understand that increased numbers of psychotropic medications does not correlate with better outcomes, and thereby become more cognizant of their own prescribing practices.

Summary: Background: Recent studies of soldiers returning from deployment to Iraq and Afghanistan have documented significant rates of PTSD and other mental health conditions (15-17.1% after service in Iraq and 11.2% after service in Afghanistan). Specialized PTSD residential rehabilitation programs are one of the interventions used in the VA system to address this growing problem, and there is a perception that early intervention is essential. The goal of this retrospective study is to identify characteristics of veterans who are at risk of not completing a PTSD-RRP. Early identification of patients at risk for dropping out of the program can then lead to implementing interventions in order to decrease the likelihood of leaving treatment prematurely.

Methods and Procedures: Male veteran patients (n=132, mean age=53.9±9.2, range=23-78, 34.8% White, 34.1% Black, 31.1% Hispanic) with a primary diagnosis of PTSD (per DSM-IV TR based clinical interview), who were exposed to military related trauma (non-sexual) and were consecutively admitted to the PTSD-RRP at the Miami VAMC between October 2004-September 2006, were grouped into completers (n=109, 82.6%) and non-completers (n=23, 17.4%) of the program. Military-related trauma exposure was verified by review of patients’ DD-214. A retrospective chart review of demographic variables (age, ethnicity, marital status, education level, employment status), period of abstinence from substance abuse, number of comorbid psychiatric diagnoses, family psychiatric history, and self report questionnaire results of the Beck Anxiety Depression Inventory, PTSD Symptom Checklist and the Mississippi scale for Combat Related PTSD is being conducted. A logistic regression analysis will be performed.

Results: Logistic regression found four variables, (age, the Beck Anxiety Inventory scores, whether the patient lived alone or had a support person, and family psychiatric history) to be significant in determining whether patients stayed in treatment and was able to predict overall group membership 78.45%. Prediction of completion of treatment was 80.61% and prediction of non-completion was 66.67% based on the four variables.

Conclusions: Patients were less likely to complete PTSD treatment if they scored less anxiety on the Beck Anxiety Scale, were younger, did not have a support person and had a family history of mental illness.

References:

NR51  Monday, May 21, 9:00 AM - 10:30 AM

Prevalence Rates of Polypharmacy in Depressed Patients in an Outpatient Clinic

Anna Glezer University of Massachusetts Medical School, Psychiatry, 7D Goldthwarte Road Apt9, Worcester, MA, 01605, 9000, Nancy Byatt, Richard W. Cook Jr, Anthony J. Rothschild

Educational Objectives:

- At the conclusion of this presentation, the participant should be able to: 1) recognize the prevalence of polypharmacy in the treatment of major depression, and 2) understand that increased numbers of psychotropic medications does not correlate with better outcomes, and thereby become more cognizant of their own prescribing practices.

Summary: Background: Recent studies of soldiers returning from deployment to Iraq and Afghanistan have documented significant rates of PTSD and other mental health conditions (15-17.1% after service in Iraq and 11.2% after service in Afghanistan). Specialized PTSD residential rehabilitation programs are one of the interventions used in the VA system to address this growing problem, and there is a perception that early intervention is essential. The goal of this retrospective study is to identify characteristics of veterans who are at risk of not completing a PTSD-RRP. Early identification of patients at risk for dropping out of the program can then lead to implementing interventions in order to decrease the likelihood of leaving treatment prematurely.

Methods and Procedures: Male veteran patients (n=132, mean age=53.9±9.2, range=23-78, 34.8% White, 34.1% Black, 31.1% Hispanic) with a primary diagnosis of PTSD (per DSM-IV TR based clinical interview), who were exposed to military related trauma (non-sexual) and were consecutively admitted to the PTSD-RRP at the Miami VAMC between October 2004-September 2006, were grouped into completers (n=109, 82.6%) and non-completers (n=23, 17.4%) of the program. Military-related trauma exposure was verified by review of patients’ DD-214. A retrospective chart review of demographic variables (age, ethnicity, marital status, education level, employment status), period of abstinence from substance abuse, number of comorbid psychiatric diagnoses, family psychiatric history, and self report questionnaire results of the Beck Anxiety Depression Inventory, PTSD Symptom Checklist and the Mississippi scale for Combat Related PTSD is being conducted. A logistic regression analysis will be performed.

Results: Logistic regression found four variables, (age, the Beck Anxiety Inventory scores, whether the patient lived alone or had a support person, and family psychiatric history) to be significant in determining whether patients stayed in treatment and was able to predict overall group membership 78.45%. Prediction of completion of treatment was 80.61% and prediction of non-completion was 66.67% based on the four variables.

Conclusions: Patients were less likely to complete PTSD treatment if they scored less anxiety on the Beck Anxiety Scale, were younger, did not have a support person and had a family history of mental illness.

References:
increasing polypharmacy is not without its complications, such as higher incidence of side-effects or drug-drug interactions, as well as increasing costs as medical care and pharmacotherapies become more expensive. Furthermore, there is little evidence of efficacy for most of the polypharmacy regimens used. Therefore, it is important to know whether patients are being placed on polypharmacy regimens only after previous trials with single medications have failed, or if these treatment guidelines are being bypassed, and if the use of polypharmacy actually increases the efficacy of treatment. This study attempts to answer these questions.

Methods: Names of patients being treated for depression were provided by psychiatry residents in the UMass program. By obtaining subjects through resident physicians, the teaching methods of the institution can also be assessed. The charts of these patients were analyzed to collect data regarding names, types, duration of medication use and to access efficacy using the CGI. These data were then statistically analyzed using SPSS software.

Results: Of 160 reviewed charts, 135 subjects were included in the final analyses (others excluded due to incomplete data or no depression diagnosis). Mean age of patients was 45 ± 14 years old. Patients were on average on 2.0 medications (SD=0.5) with 2.1 past trials. There was no statistically significant correlation between the number of antidepressant medications taken and clinical response as measured by CGI. The relationship of medication side-effects, numbers of past antidepressant trials, and contribution of substance abuse and trauma history were also examined as contributing factors to improvement in depressive symptomatology as measured by a change in the CGI.

Conclusions: The use of polypharmacy does not appear to improve treatment efficacy in depressed patients.

References:

NR52 Monday, May 21, 9:00 AM - 10:30 AM
Reliability and Validity of the Para-Psychotic Symptoms Scale
Samantha Yard, B.A. Beth Israel Medical Center, Psychiatry, First Avenue & 16th Street, 6th Floor, Karpas Pavilion, New York, NY, 10003, 9000, Lucia Tecuta, B.A., Adare Blumenfeld, B.A., Jacqueline Shaffer, B.A., Ramin Mojtabai, M.D., M.P.H., Lisa J. Cohen, Ph.D., Igor I. Galynker, M.D.

Educational Objectives:
At the end of this presentation participants should understand the construct of para-psychotic symptoms in affective disorders and be familiar with the psychometric properties of a novel measure of these symptoms.

Summary:
Objectives: Considering the possibility of suicidal and violent behavior during panic attacks with psychotic features, it is important to develop a scale that assesses the symptoms of this potentially dangerous psychiatric condition. In this context, the purpose of the study was to establish the reliability and validity of a revised Para-Psychotic Symptoms Scale (PPSS) administered to psychiatric patients.

Method: Initial reliability and validity data for the (PPSS) is presented. The current 39-item scale is a revised version of an earlier scale. The PPSS was administered to 40 psychiatric patients of varying diagnoses along with the SCL-90. Results: Reliability for our scale was assessed by Chronbach’s Alpha (.95) and Spearman-Brown split-half correlation (.94). Concurrent validity was ascertained by examining correlations with SCL-90 total and subscale scores. PPSS correlated strongly with total score on SCL-90 (r=0.87) and with specific SCL-90 subscales (r=0.61 to 0.88). The highest correlations were with SCL-90 anxiety (r=0.88) and psychotism (r=0.77) subscales.

Conclusion: The PPSS appears to be a reliable scale with good concurrent validity. Further research is needed to fully delineate the construct of a para-psychotic affective state and explore the relationship between psychotic panic and violence to self and others.

References:
NR54 Monday, May 21, 9:00 AM - 10:30 AM
A Survey of Journal Clubs in Psychiatry Residency Programs

Sejal Shah, B.A. Thomas Jefferson University, Jefferson Medical College, Psychiatry, 1000 Walnut Street, Apt 1700, Philadelphia, PA, 19107, 8000, Rajnish Mago, Constantine Daskalakis, S.Sc.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
1. recognize how journal clubs are structured in psychiatry residency programs.
2. recognize various deficiencies within psychiatry journal clubs.
3. demonstrate various methods by which journal clubs in psychiatry residency programs can be improved.

Summary:
Introduction: To better understand the organization and effectiveness of journal clubs in psychiatry residency training programs.
Methods: Residency training directors, or their designees, completed an online survey about the format, content, and perceived effectiveness of journal clubs in their programs.
Results: 94% of residency programs reported having a journal club for their residents. 89% of programs hold their journal club meetings relatively regularly. And food is provided in 48% journal clubs. 53% of programs have greater than a quarter of participants attending the meetings. While 48% of programs perceived their journal club to be helpful for the residents’ knowledge of critical appraisal of the literature, the majority found it somewhat, minimal, or not at all helpful. Only 27% of programs found the journal club to be helpful for the residents’ knowledge of research methodology. And only 10% of respondents believed the meetings to be helpful for the residents’ knowledge of biostatistics.
Greater overall satisfaction with their journal clubs was reported by respondents from university programs than non-university programs (p < 0.001) and by respondents who reported greater perceived importance of journal clubs in residency education (p < 0.001). Higher attendance at the journal clubs was associated with university programs (p = 0.046) and with programs where it is mandatory for residents to attend the meetings (p = 0.002).
Discussion: A few programs continue to not have journal clubs or hold them irregularly. Limited attendance by the residents is common. Journal clubs are perceived to be of limited benefit, especially for knowledge of research methodology or biostatistics. Greater efforts are needed to make journal clubs regular and well-attended, especially in non-university programs.

References:
5. Linzer M: The journal club and medical education: over one university programs (p = 0.046) and with programs where it is mandatory for residents to attend the meetings (p = 0.002).
ces at baseline to predict subsequent treatment response to anti-depressants in patients with major depression.

Summary:

Introduction: The delayed onset of therapeutic response to anti-depressants remains a major problem in the treatment of depression. Triiodothyronine (T3) has been shown to be an effective acceleration strategy to decrease response time to antidepressants, mostly TCAs. The primary aim of this pilot trial was to further study the relationship between baseline thyroid indices and subsequent response to citapram with either pindolol or T3 acceleration in patients with major depression. Secondary goal is to compare directly T3 and pindolol as accelerating agents to the SSRI treatment of depression.

Method: 23 subjects (9 males and 14 females) received citapram 20mg/day in a 6-week open trial and randomized simultaneously to either Liothyronine 50 mg (n=7), Pindolol 10 mg (n=8), or placebo (n=8). All subjects were diagnosed with the SCID and their mood was rated with the MADRS, CGI, and BDI. Blood samples for thyroid indices, TSH, FT4, FT3, and TT3, were collected at baseline and endpoint. The primary outcome measure was the time to a 50% decrease in baseline MADRS score.

Results: 65% (15/23) of subjects achieved remission. Baseline TSH (n=23, mean ± SD: 1.54 ± 0.7, for males (n=9, mean ± SD: 1.71 ± 0.7), for females (n=14, mean ± SD: 1.27 ± 0.5) df=21, t=1.57, p=0.13) correlated with time to reach 50% response as measured by change in MADRS scores. K-M remit by accelerated failure time \( \chi^2 = 4.53 \), df = 1 and p = 0.03. Low TSH values correlated with better chance to reach 50% reduction in baseline MADRS scores faster.

Conclusion: Baseline thyroid function, as measured by serum TSH, may predict a patient's response time to antidepressant treatment with Citalopram. Although this finding requires replication, it is consistent with other reports of the usefulness of thyroid-axis indices measured at baseline to predict subsequent treatment response.

References:
The patients' mean age was 36.92 years (SD=11.597, range=19-67). The mean dose of Ziprasidone prescribed was 127.96 mg/day (SD=56.271, range=20-300), consideration on diagnostic categories was made. A personality disorder was diagnosed in 39 patients (47.94%) receiving a mean dose of 120 mg/day of Ziprasidone. Axis III diagnosis was made in 45 inpatients (48.39%) with a mean dose of 135.11 mg/day (SD=61.961). Mean number of days hospitalized was 18.72 (SD=14.978). Other antipsychotic in addition to Ziprasidone were prescribed at discharge for 18 (19.35%) of the patients.

Conclusions: These findings suggest that risperidone is as effective as paroxetine in the treatment of panic attacks.

References:

NR59 Monday, May 21, 9:00 AM - 10:30 AM Ziprasidone Prescribing Practices for Inpatients in Psychiatric Short-Term Hospitalization Unit Juan Jose De Frutos Guijarro Hospital Universitario La Paz, Servicio de Psiquiatría, Hospital La Paz. Servicio de Psiquiatría, Pso de la Castellana 261, Madrid, 28046, 4700, Maria Belden Bardon Rivera, Maria Benitez Alonso, Estibaliz Lauzurica Martinez, Alejandro Ana Garcia Rosales

Educational Objectives:
Describe Ziprasidone prescribing practices and tolerability for inpatients in La Paz University Hospital psychiatric short-term hospitalization unit (reference center of the area) in Madrid.

Summary:
Objective: Ziprasidone was commercialized in Spain in March 2003. The objective of this study is to describe Ziprasidone prescribing practices and tolerability for inpatients in La Paz University Hospital psychiatric short-term hospitalization unit (reference center of the area) in Madrid.

Methods: The authors reviewed the clinical records of all the patients from March 2003 to November 2006 to determine the patient's sex, age, number of days hospitalized, doses of all medications given at discharge and DSM-IV diagnosis (including presence of diagnosis in axes II and III and score in the Global Assessment of Functioning Scale).

Results: Of patients considered, 6.57% (N=93) received Ziprasidone as treatment at discharge. These inpatients comprise the present study group of 40 women (51.61%) and 45 men (48.39%). The patients' mean age was 36.92 years (SD=11.597, range=19-67). The mean dose of Ziprasidone prescribed was 127.96 mg/day (SD=56.271, range=20-300), consideration on diagnostic categories was made. A personality disorder was diagnosed in 39 of these patients (47.94%) receiving a mean dose of 120 mg/day of Ziprasidone (SD=64.563). Axis III diagnosis was made in 45 inpatients (48.39%) with a mean dose of 135.11 mg/day (SD=61.961). Mean number of days hospitalized was 18.72 (SD=14.978). Other antipsychotic in addition to Ziprasidone were prescribed at discharge for 18 (19.35%) of the patients.

Conclusions: Mean dose of Ziprasidone used depends of DSM-IV-TR multiaxial diagnose and patient characteristics, creating a profile for the use of the drug. No sedation side effects and simple outpatient manage of the treatment could be decisive factors sustaining it as first line treatment. Intramuscular formulation at doses of 20 mg / 8 hours had been used during stay when oral formulation taking was not possible. More studies are needed to evaluate other therapeutic indications.

References:
The Relationship Of Depression, Psychoses and Functioning in Older Schizophrenic Adults

Pia Natalya Reyes, M.D. SUNY Downstate Medical Center, Psychiatry, 862 East 17th Apt C1, Brooklyn, NY, 11230, 9000, Ipsit Vahia, M.D., Shilpa P. Diwan, M.D., Azziza O. Bankole, M.D., Nikhil Palekar, M.D., Paul M. Ramirez, Ph.D., Carl I. Cohen, M.D.

Educational Objectives:
To more fully understand the interaction between co-morbid depression and symptoms of psychosis in older persons with schizophrenia, and to greater appreciate the clinical significance of psychopathology and its impact on functioning.

Summary:
Background: Studies show varying relationships of positive symptoms, negative symptoms, and depression on cognitive functioning. Older adults with schizophrenia in this study were categorized based on the presence or absence of psychoses and depression. We examined the association between these categories and measures of functioning.

Methods: The sample consisted of a stratified convenience sample of 188 community-dwelling schizophrenic (S) persons aged 55 in residential and non-residential settings. 113 persons comprised a matched comparison group (C). The independent variable consisted of 4 categories of depression/positive symptoms based on cut-off scores on the PANSS and the CESD. The dependent variables consisted of the 5 subscales and the total score on the Dementia Rating Scale, the Instrumental Activities of Daily Living scale, and the number of confidants.

Results: The S subgroups scored significantly worse than the C group on the IADL scale, number of confidants, and all scales of the DRS. In the subcategories of the S group, there were significant group differences on the DRS Conceptualization, DRS total and number of confidants. Groups without positive symptoms scored higher than the groups with positive symptoms, regardless of the presence of depression. When the group was dichotomized (with and without positive symptoms), those with positive symptoms had significantly lower scores in the DRS scales for Memory, Initiation/Perseveration, DRS Conceptualization, total DRS score and number of confidants. After controlling for negative symptoms (because of a significant correlation between the PANSS positive and PANSS negative symptom scales), only 2 retained significance: DRS Conceptualization Subscale and DRS total.

Conclusion: All S groups were more impaired when compared to the general community and those persons with positive symptoms had the greatest impairment. Being depressed without psychoses was not associated with any additional functional impairment. These findings suggest that positive symptoms may have more impact on functional status.

References:

NR62
Monday, May 21, 9:00 AM - 10:30 AM
The Interplay of Depression and Psychosis in Older Adults with Schizophrenia
Shilpa P. Diwan, M.D., M.P.H. State University of New York, Psychiatry, 415 100 Street, Brooklyn, NY, 11209, 9000, Carl I. Cohen, M.D., Paul M. Ramirez, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to: 1. To examine factors affecting the interplay of depression and psychosis in older adults with schizophrenia; 2. To examine the implications of the findings for treatment strategies and future research involving older schizophrenic persons with depression and psychoses.

Summary:
Objective: The literature suggests that there is a core group of schizophrenic persons who suffer from psychosis with concomitant depression. Older schizophrenic persons provide an opportunity to examine this issue because the disorder has attained its most developed and complex forms.

Methods: We used a stratified sample, drawn from residential programs and clinics in NYC that consisted of 198 schizophrenic persons aged 55 who developed the disorder prior to age 45. We examined 2 levels of depression: “syndromal” and “subsyndromal/syndromal” that were defined as > 16 and > 8 on the CESD scale, respectively. “Psychosis” was based on scoring > 3 on any of the PANSS items for hallucinations, delusions, or conceptual disorganization. Using 17 independent variables, we contrasted 4 categories: (1) no depression/no psychosis, (2) depression/no psychosis, (3) no depression/psychosis, (4) depression/psychosis. The groups were compared using bivariate analyses, and then multinomial regression analyses.

Results: With syndromal depression, the percentages in categories 1, 2, 3, 4, were 53, 19, 14, and 14, respectively. With subsyndromal/syndromal depression, the percentages in categories 1, 2, 3, 4, were 33, 39, 6, and 22, respectively. In multinomial regression analysis, for syndromal depression, 11 variables were found to significantly differentiate categories 1, 2, and 3 from category 4, and for subsyndromal/syndromal depression, 9 variables were significant. Significant variables included cognitive functioning, education, family history of depression, number of lifetime hospitalizations, number of physical disorders, acute stressors, and proportion of confidants, PANSS negative scale, use of spiritualists, psychiatric services, and number of psychotropic medications.

Conclusions: Although longitudinal studies are needed to examine causal directionality, our findings suggest that because a variety of clinical and psychosocial variables are associated with differences among the various categories, the notion of a core group of psychotic/depressed persons may not be warranted. The implications for research and treatment will be discussed.

References:
NR63  Monday, May 21, 9:00 AM - 10:30 AM
Olanzapine Prescribing Practices for Inpatients in Psychiatric Short-Term Hospitalization Unit
Juan Jose De Frutos Guijarro, Hospital Universitario La Paz, Servicio de Psiquiatria, Hospital La Paz, Servicio de Psiquiatria., Pso de la Castellana 261, Madrid, 28046, 4700, Alejandro Ana Garcia Rosales, Maria Beilen Bardon Rivera, Maria Benitez Alonso, Estibaliz Lauzurica Martinez

Educational Objectives:
- Describe Olanzapine prescribing practices and tolerability for inpatients in La Paz University Hospital psychiatric short-term hospitalization unit (reference center of the area) in Madrid.

Summary:
Objective: The objective of this study is to describe Olanzapine prescribing practices and tolerability for inpatients in La Paz University Hospital psychiatric short-term hospitalization unit (reference center of the area) in Madrid.

Methods: The authors reviewed clinical records of all the inpatients from December 2002 to November 2006 to determine patient's sex, age, number of days hospitalized, doses of all medications given at discharge and DSM-IV diagnosis (considering also presence of diagnosis in axes II and III and score in the Global Assessment of Functioning Scale).

Results: Of patients considered, 26.7% (N=410) received Olanzapine as treatment at discharge. These inpatients comprise the present study group of 194 women (47.3%) and 216 men (52.7%). The patients' mean age was 36.97 years (SD=12.085, range=18-81). The mean dose of Olanzapine prescribed was 20.4 mg/day (SD=9.92, range=2.5-60), consideration on diagnostic categories was made. A personality disorder was diagnosed in 126 of these patients (30.7%). Axis III diagnosis was made in 150 inpatients (36.8%). Mean number of days hospitalized was 14.9 (SD=8.536). Other antipsychotic in addition to Olanzapine were prescribed at discharge for 119 (29.02%) of the patients.

Conclusions: Doses of Olanzapine higher than label were used for inpatients at discharge. Olanzapine-Fluoxetine combination capsule is not available in Spain. Sedative effects and rapid onset of antipsychotic action could be a factor to choose Olanzapine instead of another first line antipsychotic. Metabolic side effects are usually considered. Mores studies are needed to assess tolerability of higher than label doses.

References:

NR64  Monday, May 21, 9:00 AM - 10:30 AM
Use of ECT in Treatment Resistant Agitation in Alzheimer's Disease
Asad - Mehdi Penn State University, Psychiatry, 1905 Wexford Road, Palmyra, PA, 17033, 9000

Educational Objectives:
- At the end of this poster presentation the audience will be able to recognize ECT as a treatment option for Agitation in Alzheimer's Disease

Summary:
Introduction: Agitation in Alzheimer's Disease is a difficult management problem. Electroconvulsive therapy (ECT) may be effective in treatment.

Method: A retrospective chart review of three women (average age =77) suffering from Alzheimer's Disease with severe verbal agitation, self harm, and decreased PO intake was performed. Psychiatric history (including depression) was negative before the onset of dementia in all three. All patients failed treatment with divalproex sodium, SSRIIs, benzodiazepines, and atypical antipsychotics for 15 to 20 days. They then received 7 or 8 ECT treatments over 16 to 22 days for treatment of agitation. Improvement was measured by Global Assessment of Functioning (GAF) Scales. Clinical Global Impression Scale (CGI) was performed by a blinded rater. Use of pm meds was assessed before and after ECT.

Results: ECT was associated with a clinically meaningful reduction in agitation and mood stabilization in all 3 patients. GAF improved by an average of 10 points, and CGI showed very much improved by 100%. FRN medication use decreased by 40% in these patients.

Conclusion: ECT was associated with a reduction in agitation in these resistant patients. ECT was well tolerated. ECT can be helpful in treating agitation in Alzheimer's Disease.

References:

NR65  Monday, May 21, 9:00 AM - 10:30 AM
Serum Homocysteine Levels Are Not Elevated In Euthymic Bipolar Type I Patients With Neurocognitive Deficits: Preliminary Results
Vasco V. Dias, Psy.D. Autonomous University of Lisbon, Psychology, Rua Ilha Amores Lote 4.12 Bloco C 1 Esq, Lisbon, 1190-122, 4710, Sofia Brissos, M.D., Carlos Cardoso, M.D., Ana I. Carita, Ph.D., Florência Castro, Ph.D., Anabel Martinez-Aran, Ph.D.

Educational Objectives:
- At the conclusion of this presentation, the participants should gain knowledge that homocysteine serum levels have been implicated as a possible risk factor in several psychiatric disorders, but that in young, physically healthy, euthymic patients, homocysteine levels do not seem to play a major role in the pathophysiology of bipolar disorder, and do not seem to be responsible for the neurocognitive deficits associated with this disorder.

Summary:
Background: Previous studies have found elevated plasma homocysteine levels in patients with schizophrenia and bipolar disorder (BD) in euthymia.

Objectives: To investigate serum homocysteine levels in euthymic BD type I patients and healthy controls, and its relationship with neurocognitive function.

Methods: Thirty BD euthymic patients, and 30 healthy controls performed a neuropsychological test battery to assess attention and mental control, perceptual-motor skills, executive functions, verbal fluency and abstraction, visuo-spatial attention, and memory. Homocysteine levels were measured by using a HPLC method with fluorescence detection.

Results: Bipolar patients differed significantly from controls on measures of perceptual motor skills, executive functions, attention, and memory. We found no significant differences regarding homocysteine values between bipolar patients and controls. Spearman's correlation coefficient revealed no significant associations between homocysteine levels and all sociodemographic, clinical and neurocognitive variables in patients.

Female patients showed significantly lower homocysteine levels than male patients (p = 0.010). To explore the effect of age with homocysteine levels, we divided patients in two categories: younger (age < 35), and older patients (age ≥ 35), and found no statistically significant differences between the groups (p = 0.729).
We further separated patients according to gender, older female patients showed significantly lower homocysteine levels than their younger counterparts ($p = 0.039$), but we did not observe this effect in male patients ($p = 0.084$).

Bipolar patients with cognitive deficits had a significantly longer disease duration ($p = 0.043$) and worse psychosocial functioning as measured through the GAP ($t = -2.005, p = 0.055; Z = -2.012, p = 0.044$), but homocysteine levels did not differ between patients with or without cognitive deficits ($p = 0.915$).

**Conclusion**

Our results suggest that euthymic bipolar type I patients with or without cognitive deficits do not have an elevation of serum homocysteine levels as compared with controls.

**References:**


**NR66**

**Monday, May 21, 9:00 AM - 10:30 AM**

**Quetiapine Prescribing Practices for Inpatients in Psychiatric Short-Term Hospitalization Unit**

Estibaliz Lauzurica Martinez, Hospital Universitario La Paz, Servicio de Psiquiatria, Hospital La Paz, Servicio de Psiquiatría, Pso de la Castellana 261, Madrid, 28046, 4700, Juan Jose De Frutos Guiljarro, Maria Belen Bardon Rivera, Maria Benitez Alonso, Alejandro Ana Garcia Rosales

**Educational Objectives:**

The objective of this study is to describe Quetiapine prescribing practices and tolerability for inpatients in La Paz University Hospital psychiatric short-term hospitalization unit (reference center of the area) in Madrid.

**Summary:**

**Objective:** The objective of this study is to describe Quetiapine prescribing practices and tolerability for inpatients in La Paz University Hospital psychiatric short-term hospitalization unit (reference center of the area) in Madrid.

**Methods:** The authors reviewed clinical records of all the inpatients considered, 22.34% (N=343) received conventional antipsychotics as treatment as discharge. These inpatients comprise the present study group of 171 women (49.9%) and 172 men (50.1%). The patients’ mean age was 39.03 years (SD=13.882, range=16-82). The mean dose of Conventional antipsychotics prescribed is distributed as follows: Haloperidol 10.98 mg/day (N=228, SD=7.605, range=0.5-30), Chlorpromazine 106.74 mg/day (N=23, SD=85.727, range=10-300), Fluphenazine 24.68 mg each two weeks (N=79, SD=1.976, range=12.5-25), Levomepromazine 59.54 mg/day (N=57, SD=31.796, range=24-200), consideration on diagnostic categories was made. Personality disorder was diagnosed in 102 inpatients (29.7%). An Axis III diagnosis was made in 137 inpatients (39.9%). Mean number of days hospitalized was 16.99 (SD=11.061). Atypical antipsychotic in addition to conventional antipsychotics were prescribed at discharge for 185 (53.9%) of the patients.

**Conclusions:** Combination of antipsychotics is used when only partial response is shown. More studies are needed to evaluate these combinations. A longer clinical experience in the use of the conventional antipsychotics could be a decisive factor in the prescribing pattern. Levomepromazine at low doses is usually administered as hypnotic.

**References:**


**NR67**

**Monday, May 21, 9:00 AM - 10:30 AM**

**Conventional Antipsychotics Prescribing Practices for Inpatients in Psychiatric Short-Term Hospitalization Unit**

Juan Jose De Frutos Guizarro Hospital Universitario La Paz, Servicio de Psiquiatria, Hospital La Paz, Servicio de Psiquiatría, Pso de la Castellana 261, Madrid, 28046, 4700, Maria Benitez Alonso, Estibaliz Lauzurica Martinez, Maria Belen Bardon Rivera, Alejandro Ana Garcia Rosales

**Educational Objectives:**

The objective of this study is to describe conventional antipsychotics prescribing practices and tolerance for inpatients in La Paz University Hospital psychiatric short-term hospitalization unit (reference center of the area) in Madrid.

**Summary:**

**Objective:** The objective of this study is to describe conventional antipsychotics prescribing practices and tolerance for inpatients in La Paz University Hospital psychiatric short-term hospitalization unit (reference center of the area) in Madrid.

**Methods:** The authors reviewed clinical records of all the inpatients from December 2002 to November 2006 to determine patient’s sex, age, number of days hospitalized, doses of all medications given at discharge and DSM-IV diagnosis (considering diagnosis in Axis I, diagnostic category of the disease, diagnosis in Axis II, presence of diagnose in Axis III and score in the Global Assessment of Functioning Scale).

**Results:** The conventional antipsychotics contemplated were Haloperidol, Chlorpromazine, Fluphenazine and Levopromazine. Of patients considered, 22.34% (N=343) received conventional antipsychotics as treatment as discharge. These inpatients comprise the present study group of 171 women (49.9%) and 172 men (50.1%). The patients’ mean age was 39.03 years (SD=13.882, range=18-82). The mean dose of Conventional antipsychotics prescribed is distributed as follows: Haloperidol 10.98 mg/day (N=228, SD=7.605, range=0.5-30), Chlorpromazine 106.74 mg/day (N=23, SD=85.727, range=10-300), Fluphenazine 24.68 mg each two weeks (N=79, SD=1.976, range=12.5-25), Levopromazine 59.54 mg/day (N=57, SD=31.796, range=24-200), consideration on diagnostic categories was made. Personality disorder was diagnosed in 102 inpatients (29.7%). An Axis III diagnosis was made in 137 inpatients (39.9%). Mean number of days hospitalized was 16.99 (SD=11.061). Atypical antipsychotic in addition to conventional antipsychotics were prescribed at discharge for 185 (53.9%) of the patients.

**Conclusions:** Combination of antipsychotics is used when only partial response is shown. More studies are needed to evaluate these combinations. A longer clinical experience in the use of the conventional antipsychotics could be a decisive factor in the prescribing pattern. Levomepromazine at low doses is usually administered as hypnotic.

**References:**


NR68  Monday, May 21, 9:00 AM - 10:30 AM
Plasma Brain-Derived Neurotrophic Factor Levels And Its Relationship With Neurocognitive Function In Euthymic Bipolar Type I Patients: Preliminary Results
Vasco V. Dias, Psy.D. Autonomous University of Lisbon, Psychology, Rua Ilha Amores lote 4.12 bloco C 1 Esq, Lisbon, 1190-122, 4710, Sofia Briseso, M.D., Carlos Cardoso, M.D., Ana I. Carita, Ph.D., Anabel Martinez-Aran, Ph.D., Florêncio Castro, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participants should gain knowledge on the possible relationship between BDNF plasma levels and neurocognitive function in bipolar disorder, and the implications this may have for diagnosis in the future, since BDNF plasma levels seem to be a state-related biological marker of bipolar disorder.

Summary:
Background: Genetic and pharmacological studies have suggested that brain-derived neurotrophic factor (BDNF), one of the most common neurotrophic factors in the brain, may be associated with the pathophysiology of bipolar disorder (BD). BDNF has been associated with both poorer and better neurocognitive test performance on tests measuring prefrontal cortex functions in BD.

Objectives: To investigate plasma BDNF levels in euthymic BD type I patients and in healthy controls, and its relationship with neurocognitive function.

Methods: Twenty-eight BD euthymic patients and 25 healthy controls performed a battery of neuropsychological tests to assess attention and mental control, perceptual-motor skills, executive functions, verbal fluency and abstraction, visuo-spatial attention, and memory. BDNF levels were assessed using a BDNF Emax Immunoassay System kit.

Results: BDNF plasma levels did not differ between BD patients and healthy controls (p = 0.971), even after controlling for mood symptoms. Sixteen (57%) patients had prior psychotic symptoms, but these patients' BDNF levels did not differ from those of BD patients without prior psychotic symptoms (p = 0.797). There were no significant correlations between BDNF plasma levels and both clinical and neuropsychological variables, except for a positive correlation between BDNF level and the Comprehension sub-test of the Revised Wechsler Intelligence Scale for Adults in the BD group (r = 0.400, p = 0.039).

Conclusion: Our sample of BD euthymic patients presented attentional and executive dysfunction. Plasma BDNF levels in euthymic BD patients were similar to those of healthy controls, and were only positively associated with a test of memory function in BD patients. Attention and executive dysfunction may be a trait-marker of BD, whereas BDNF plasma levels may be a possible state-related biological marker in BD.

The mechanisms involved in structural and neuropsychological changes caused by BDNF need clarification, warranting further investigation in this area.

References:

NR69  Monday, May 21, 9:00 AM - 10:30 AM
Clozapine Prescribing Practices for Inpatients in Psychiatric Short-Term Hospitalization Unit
Maria Benitez Alonso Hospital Universitario La Paz, Servicio de Psiquiatria, Hospital La Paz. Servicio de Psiquiatría., Pso de la Castellana 261, Madrid, 28046, 4700, Juan Jose De Frutos Guijarro, Estibaliz Lauzurica Martinez, Maria Belen Bardon Rivera, Alejandra Ana Garcia Rosales

Educational Objectives:
The objective of this study is to describe Clozapine prescribing practices and tolerability for inpatients in La Paz University Hospital psychiatric short-term hospitalization unit (reference center of the area) in Madrid.

Summary:
Objective: The objective of this study is to describe Clozapine prescribing practices and tolerability for inpatients in La Paz University Hospital psychiatric short-term hospitalization unit (reference center of the area) in Madrid.

Methods: The authors reviewed clinical records of all the inpatients from December 2002 to November 2006 to determine patient's sex, age, number of days hospitalized, doses of all medications given at discharge and DSM-IV diagnosis (including diagnosis in Axis I, diagnostic category of the disease, diagnosis in Axis II, presence of diagnose in Axis III and score in the Global Assessment of Functioning Scale).

Results: Of the patients considered, 2.47% (N=38) received Clozapine as treatment at discharge. These inpatients comprise the present study group of 13 women (34.2%) and 25 men (65.8%). The patients' mean age was 32.68 years (SD=9.427, range=18-65). The mean dose of Clozapine prescribed was 266.45 mg/day (SD=104.34, range=100-600); with respect to diagnostic categories, schizophrenia and other psychotic disorders received the highest dose. A personality disorder was diagnosed in 9 of these patients (23.7%). Axis III diagnosis was made in 15 inpatients (39.5%). Mean number of days hospitalized was 26.68 (SD=17.518). Other antipsychotic in addition to Clozapine were prescribed at discharge for 9 (23.68%) of the patients.

Conclusions: Clozapine remains as a second line antipsychotic because the potential side effects. No life threatening or dangerous side effects appeared but sedation and salorrhea could make patient leave the treatment. In this group mainly used in treatment-refractory schizophrenia and sometimes used for treatment-resistant bipolar disorder. Due to possible metabolic syndrome, Clozapine is less used in patients with other organic pathologies or older patients. Clozapine use depends of DSM-IV-TR multiaxial diagnosis and patient characteristics, creating a profile for the use of the drug.

References:

NR70  Monday, May 21, 9:00 AM - 10:30 AM
Dosing Frequency and Adherence to Antipsychotic Medications
Paul N. Pfeiffer, M.D. University of Michigan, Psychiatry, 1500 E. Medical Center Dr., Ann Arbor, MI, 48108, 5000, Mara Ganoczy, M.P.H., Marcia Valenstein, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the relationship between dosing frequency of
antipsychotic medications and medication adherence in VA patients with schizophrenia.

**Summary:**

**Introduction:** Antipsychotic medications are effective in the treatment of schizophrenia. However, partial adherence is common and is associated with increased hospitalization. Medication dosing schedule may influence adherence rates and is an inexpensive and modifiable target for intervention. This study utilized a large dataset of Veterans Affairs (VA) pharmacy information to determine whether dosing schedule has a significant impact on antipsychotic adherence among patients with schizophrenia.

**Methods:** Patients with a diagnosis of schizophrenia were identified from the VA National Psychosis Registry. The VA pharmacy database was used to identify those that had been on haloperidol or an atypical antipsychotic (excluding clozapine) for all of fiscal year 2005 with no change in dosing schedule. Based on dosing schedule, subjects were divided into “once daily” and “more than once daily” dosing groups. Adherence was determined by calculating the Medication Possession Ratio (MPR), which is the ratio of the supply of medication that was filled from the pharmacy to the supply needed for continuous use. Mean MPR for each group was compared using the Mann-Whitney-Wilcoxon test and multivariate linear regression analyses.

**Results:** 32,556 subjects were eligible for the MPR calculation. In bivariate analyses, there was no significant difference in mean MPR between groups. Both groups had a mean MPR of .80. In multivariate analyses, adjusting for patient and clinical factors, patients with once-a-day dosing were more likely to have higher MPRs but the difference was small. For individual antipsychotic medications there were no statistically significant differences between dosing groups with the exception of haloperidol and quetiapine (Seroquel®). Once daily dosing was associated with higher MPRs among patients receiving haloperidol but lower MPRs among patients receiving quetiapine.

**Conclusion:** This study suggests that the difference between once daily dosing and more than once daily dosing may not be an important factor in adherence to antipsychotic medications.

**References:**


**NR71**  
**Monday, May 21, 9:00 AM - 10:30 AM**  
**After Acute Electroconvulsive Therapy: A 6 Month Multicenter Follow Up Study**

Jan Di Pauli  
Regional Hospital Rankweil, Department I, Valdnasstrae 16, Rankweil, 6900, 4330, Gerhard Eschweiler, Reinhard Vonthin, Michael Hüll, Mathias Bartels, Andreas Conca

**Educational Objectives:**

At the conclusion of this presentation, the participant should be aware of the impact of maintenance medication especially for a lithium combination therapy after acute electroconvulsive therapy

**Summary:**


The aim of the study was to evaluate the outcome of patients affected by major depression after the successful course of acute ECT.

**Method:** 84 patients recruited in a randomized double blind multicenter study designed to investigate the optimal stimulation placement in acute ECT (Eschweiler et al in press) had a follow up under naturalistic conditions between the 5th and 7th month. Outcome, maintenance therapy and patients’ attitude were evaluated with semi structured questionnaires by patients, their psychiatrists and the study raters.

**Results:** 69/84 (82.14%) questionnaires of the patients, 50/84 (59.5%) of the psychiatrists and 70/84 (83.3%) of the raters were returned. Most of the patients (78/84) had a combination of at least two antidepressants; only in 20/84 (23%) lithium was prescribed. According to psychiatrists 23/50 (46%) patients showed a relapse. 7/20 (35%) with lithium and 16/28 (57%) without lithium had a relapse within the first 6 months (OR 0.6) in a median of 2.5 months. Only one institution offered maintenance ECT in 7/84 (8.3%) patients.

**Discussion:** The results show a high relapse rate and highlight the meaning of maintenance medication especially for a lithium combination therapy, as stated before (Sackeim et al 2001, Kellner et al 2006).

**References:**


**NR72**  
**Monday, May 21, 9:00 AM - 10:30 AM**  
**Rapid-cycling and Suicide**

Margarita García-Amador University of Barcelona, Hospital Clinic, Bipolar Disorders Unit, Rosselló 140, Barcelona, 08036, 4700, Marc Valentí, M.D., Francesc Colom, M.D., Eduard Vieta, Ph.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to diagnose rapid-cycling bipolar patients and to understand how suicidal ideas or behaviours worsen functionality of these patient condition.

**Summary:**

**Background:** Rapid-cycling (RC) is a severe condition in bipolar disorder implicating a difficult functioning. However, suicide and suicidal ideation as a marker of worsening functioning has been understudied and data are scanty.

**Methods:** Three hundred and five patients (n=305) were included in a naturalistic, systematic retrospective study. Patient with rapid-cycling (RC) were defined as having four or more manic or depressive episodes of at least two weeks-duration in the year. The two groups were compared regarding clinical and sociodemographic variables. Moreover, functional markers have been studied with suicidal suicide and suicidal ideation.

**Results:** Fifty-five patients (18%) were classified as RC, whilst 250 (82%) were considered as non-rapid-cycling (NRC). No significant difference was found in the prevalence of RC amongst bipolar I and II patients. However RC was associated with depressive onset of bipolar disorder. The number of mixed episodes was significantly higher in RC (RC mean 0.86, NRC mean 0.39, t=2.12, p=0.001), and, RC patients presented a trend of history of psychotic symptoms. Functionality was represented by differ-
ences between both groups in occupational functioning ($\chi^2 = 7.691$, $p=0.006$) and a deficient autonomy ($\chi^2 = 5.555$, $p=0.018$). Around the topic of suicide, important data arouse: Patients that presented RC showed a marked increase of lifetime history of suicidal ideation ($\chi^2 =4.363$, $p=0.039$). On the other hand, the number of suicide attempts is significantly more frequent in RC than in NRC (RC mean 0.82 -SD 1.86- vs NRC 0.44-SD 0.94- t Student 2.09, $p=0.37$). Nonetheless, no significant differences were found between RC and NRC in committing suicide attempts. Finally, there were not any differences between RC patients and NRC in family history of suicide.

Discussion: Functionality is highly compromised in RC patients. Suicidal ideation as suicide attempts are important markers that impact not only in mortality but also in morbidity of RC patients.

References:

NR73
Monday, May 21, 9:00 AM - 10:30 AM
Suicide Attempt by Medication in Emergency: Month of Birth A Risk Factor for Violent Behavior?

Anne-Hélène Moncany, University Hospital, psychiatry, 2 bis rue Clémence Isiaure, Toulouse, 31000, 4279, Lionel Calhol, Coralie Lazignac, Andrei Cicotti, Susanne Maris, Remi Barbe, Cristian Damsa

Educational Objectives:
1. Be aware that numerous serious studies suggest a statistical significant link between the month of birth and somatic (cancers, Crohn disease, epilepsy) and psychiatric (schizophrenia, suicide) diseases. The viral hypothesis to explain those epidemiological findings is emphasized in almost all those studies.
2. Speculate about the results of this study, taking into account the epidemiologic literature. This study suggests a significantly higher incidence of violent behavior in subjects hospitalized in emergency for a suicidal attempt that where born at the end of winter and the beginning of spring, with a maximum for April and a minimum for December.

Summary:
Objective: Although there are numerous publications on the existing link between month of birth and suicide, only two studies focus on suicide attempts and auto-aggressive behavior. Research data suggest that month of birth is related to a variation of 5-HIAA in the cerebrospinal fluid, which correlates with violent behavior (VB). Therefore, the aim of this study is to search, for the first time, a possible link between month of birth and the occurrence of VB in emergency, for patients admitted for a suicide attempt with medication.

Method: This is a 10 months prospective study among all the patients of the canton of Geneva, Switzerland, admitted to the emergency for a suicide attempt with medication. The presence of VB was assessed by means of a questionnaire which describes the nature and the circumstances of the violent acts.

Results: During a 10 months study period we included 493 patients, of which 77 (15,62%) presented VB. A significantly higher incidence of VB was found in subjects that where born at the end of winter and the beginning of spring, with a maximum for April and a minimum for December.

Conclusion: Taking into account the significant differences found, in spite of a relatively small number of subjects, it seems promising to study the occurrence of VB as a function of month of birth in patients admitted in emergency for a suicide attempt with medication.

References:

NR74
Monday, May 21, 9:00 AM - 10:30 AM
Memory Functioning & Antidepressant Treatment: A Randomized Controlled Trial comparing Escitalopram and Bupropion-XL. Preliminary Report.

Beverley A. Bouffard, M.A. University Health Network, Psychiatry, 200 Elizabeth Street, EN-8-224, TORONTO, ON, MSG 2C4, 1220, Sidney H. Kennedy, M.D., Jill B. Rich, Ph.D., Rima Styra, M.D., Lakshmi Ravindran, M.D., Roger S. McIntyre, M.D.

Educational Objectives:
1) Evaluate outcome data involving multiple aspects of memory functioning (verbal, non-verbal, working, spatial and prospective memory) in a middle life MDD sample.
2) Recognize the differential performance of multiple aspects of memory performance at pre and post antidepressant treatment testing, both within subjects and across treatment groups (bupropion-XL or escitalopram).
3) Discuss implications for quality of life and workplace/school related functional outcomes.

Summary:
Cognitive impairment is frequently neglected in the assessment of Major Depressive Disorder. Despite clinical relevance, the neuropsychological profiles of both treated and untreated individuals with MDD have not been well characterized, and specific cognitive mechanisms responsible for cognitive dysfunction remain unclear. Older patients generally perform worse than healthy controls on tests of information processing, memory (Burt et al., 1995), attention and executive function; how these processes are affected in a younger population remains to be elucidated. Prior investigations have been compromised by incongruent test protocols and methodology such that the effect of disparate antidepressant treatment on memory functioning has not been clarified. Extant research has neglected to relate severity, course of illness, and comorbid diagnoses with quality of life and workplace disability measures to neurobehavioural memory outcomes.

Primary Outcome Variables: California Verbal Learning Test II (CVLT-II): Total Recall, Learning Slope, Recall Discriminability, Recognition Discriminability.

Secondary Outcome Variable: Hamilton Rating Scale for Depression - 17-Item.

Results: Memory performance was evaluated at baseline (n=29) and post-test (n=24). Raw scores were transformed into T-score or standard score equivalents according to norms provided in the CVLT-II manual. Preliminary analyses using blinded data indicate that at baseline, CVLT-II Immediate Recall scores were in the normal range, however both Recall and Recognition Discriminability were one-half to one standard deviation below norms. At post test, data support evidence for improvements in Immediate Free Recall, Learning Slope, and Recall and Recognition Discriminability. On tasks of Visuospatial Memory, improvements were
although all differences remain non significant. Full analyses of unblinded RCT data will be presented at the meeting.

References:

NR75  Monday, May 21, 9:00 AM - 10:30 AM
Is Fun Just Fun?: Teaching Psychopharmacology Through Games
Alfredo A. Massa, M.D. Maimonides Medical Center, Psychiatry, 914 48 street, Brooklyn, NY, 11219, 9000, Paulo R. Shiroma, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize implication of using an alternative method of teaching in the acquisition of knowledge in psychopharmacology.

Summary:
Introduction: All psychiatric programs provide lectures on basic principles of psychopharmacology. Yet, these traditional modes have been criticized for information overloads and passive transfer of expert knowledge.

An alternative teaching methods is “academic game”.

Objective: To investigate the effectiveness of an academic game in the acquisitions of knowledge in psychopharmacology in comparison with a traditional method of teaching.

Method: A randomized pretest-posttest control group design was carried out among medical students for three 6-week psychiatry rotation at Maimonides Medical Center. Demographic and feedback data were collected. These games happened over a 45-minute-period for 5 consecutive weeks and the module coincided with the topic taught during the previous psychopharmacology class. For the purpose of the study, the control group simultaneously received the same information played in the game but delivered in a lecture-type format. The game follows similar rules of the famous TV show, “Jeopardy” and a multiple-choice questions format was used. This project was IRB approved. Two-tail paired and pooled variance Student’s t test, chi-square and Pearson correlation were used as statistical methods.

Results: Forty three medical students participated. No difference was found between the groups in terms of age, gender, year of graduation, GPA and USMLE scores. Regarding the pretest-posttest scores, both groups improved [(game group t= 10.86,p<0.001); control t=4.82;p<0.001]) although no significant difference was found between groups (t=0.11;p=0.05). The scores showed a moderate correlation with the GPA in both groups [(game group r=0.54,p=0.01); control group r=0.61,p=0.05]) but not with USMLE scores, gender, age or year of graduation.

Conclusions: We did not find a significant difference between teaching methods as previous research in medical education described. The acquisition on knowledge is associated with previous academic performance rather than the method of teaching.

References:
Educational Objectives:

Personality is generally defined as the characteristic manner and style of an individual’s behavior and encompasses vigor, temper, and persistence of the resulting behavior. Human personality is shaped by both genetic factors as well as environmental influences, and the proportion between both varies for different traits, with some traits having a substantial genetic impact, whilst others are influenced more by environment. Our research suggested that coping style, social support, positive life events and NET G1287A gene polymorphism maybe the possible influential factors of the personality character in healthy Han Chinese.

Summary:

Purpose: To assess the influential factors of the personality character in healthy Han Chinese.

Methods: 120 unrelated healthy Han Chinese individuals were assessed with the Eysenck personality Questionnaire (EPQ), 5-HTT and NET gene polymorphisms were determined by PCR, life events, social support, coping style were evaluated by LES, SSS and SCGQ. Association between 5-HTT, NET gene polymorphisms, age, education, life events, social support, coping style and the EPQ personality were analyzed by multiple linear regressions.

Results: In male, passive coping style entered the psychotics personality regression equation \( R^2 = 12.0\% \), positive coping style, social support availability entered the exterior and interior personality regression equation \( R^2 = 23.5\% \), passive coping style, subjective social support, social support availability entered the neurotic personality regression equation \( R^2 = 58.8\% \). In female, positive life events entered the psychotics personality regression equation \( R^2 = 7.2\% \), NET G1287A gene polymorphism, social support availability entered the exterior and interior personality regression equation \( R^2 = 15.8\% \), passive coping style, age entered the neurotic personality regression equation \( R^2 = 39.6\% \).

Conclusion: Our study suggests that in male healthy Han Chinese, coping style is the possible influential factor of psychotics, exterior and interior, neurotic personality; social support is the possible influential factor of exterior and interior personality; in female healthy Han Chinese, positive life events is the possible influential factor of psychotics personality; NET G1287A gene polymorphism, social support is the possible influential factor of exterior and interior personality; coping style, age is the possible influential factor of neurotic personality.

References:


NR78  Monday, May 21, 9:00 AM - 10:30 AM
Oxidative Imbalance in Adult Attention Deficit / Hyperactivity Disorder
Salih Sele, M.D. Gaziantep University Sahinbey Research Hospital, Psychiatry Department, Gaziantep UNV Sahinbey Arastirma Hastanesi, Psikiyatri AD, Gaziantep, 27310, 4890, Haluk A. Savas, M.D., Hasan S. Gergerlioglu, M.D., Mahmut Bulut, M.D., Haci R. Yilmaz, Ph.D.

Educational Objectives:

Having been seldom diagnosed up till now, Adult Attention Deficit / Hyperactivity Disorder (A-ADHD) is a popular issue on which awareness is growing. There are few studies evaluating the biochemical basis of (A-ADHD). Oxidative status of other psychiatric disorders have already been studied and some clues pointing out the possible etiological role of those molecules have been reported. In this study, we evaluated whether nitric oxide (NO), an oxidant, and superoxide dismutase (SOD), an antioxidant, are associated with A-ADHD or not. At the conclusion of this presentation, the participant should be able to understand the possible underlying oxidative issues in A-ADHD.

Summary:

Objective: There are few studies evaluating the biochemical basis of Adult Attention Deficit / Hyperactivity Disorder (A-ADHD). In the present study, we evaluated whether nitric oxide (NO), an oxidant, level and superoxide dismutase (SOD), an antioxidant, activity are associated with A-ADHD or not. This study also aims to evaluate the NO levels and SOD activities, which were already measured and found to be associated in other psychiatric disorders, in A-ADHD and hopes to find some clues underlying the biological basis of the disease.

Method: Twenty A-ADHD patients from Gaziantep University Sahinbey Research Hospital, Psychiatry Clinic, diagnosed according to The Turkish version of Adult ADD/ADHD DSM IV-Based Diagnostic Screening and Rating Scale by two psychiatrists (H.A.S. and S.S.), and twenty one healthy volunteer controls were included. Blood samples were collected, NO levels and SOD activities were measured.

Results: The mean NO levels in patients (181.9 ± 35.85 μmol/L) were significantly higher than those of controls (40.1 ± 7.71 μmol/L) and SOD activity of patients (7.00 ± 1.34 U/L) was significantly lower than controls (11.18 ± 1.31 U/L) (t= 17.64, df= 39, p< 0.01 and t= -10.09, df= 39, p< 0.01 respectively).

Conclusions: Remarkable high levels of oxidant NO, and low SOD activities suggest an oxidative imbalance in A-ADHD. This is the first study evaluating the oxidative metabolism in A-ADHD. Our findings may pioneer the further clinical enzymology and biochemical studies on that disorder.

References:


NR79  Monday, May 21, 9:00 AM - 10:30 AM
Association Study Between 5-HTTLPR and Severity and Suicide Idea of Major Depression in Chinese Han Population
Xiaohong Cui The 1st Hospital of Shanxi Medical University, Psychiatry Department, No. 85 South Liberates Road, Taiyuan, Shanxi, Psychiatry Department, Taiyuan, 030001, 5700, Hong Yang, Yan Ren, Kerang Zhang

Educational Objectives:

Depression is an etiologically heterogeneous group of brain disorders characterized by a wide range of symptoms that reflect alterations in cognitive, psychomotor and emotional processes. Affected individuals differ remarkably regarding the profile of clinical features, severity and course of illness as well as their response to drug treatment and reintegration efforts. More and more studies were suggested the vulnerability to the disorder was the result of interaction effect of gene and environmental events.

Summary:

Objective to analysis the association between 5-HTTLPR and severity and suicide idea of Major Depression(MD) under controlling the effect of social-psychic factors.
Objective: To assess the association between the 5-HTTLPR, 5-HTTVNTR gene polymorphisms and the Eysenck personality Questionnaire (EPQ) personality dimensions in healthy Han Chinese.

Methods: 130 unrelated healthy Han Chinese individuals were assessed with EQP, and genotypes were determined by polymerase chain reaction (PCR). Association between two polymorphisms and personality were statistically analysed.

Results: 1. There were no association among the 5-HTTLPR allele, genotypes and any of the EPQ dimensions neither in male nor in female healthy Han Chinese (P>0.05). 2. In male, the 5-HTT STin2.10 allele frequency was significantly higher among extraversion compared with introversion subjects (P<0.05); subjects with STin2.10 allele showed more neurotic personality (P=0.004); in female, subjects with STin2.10 allele showed low N scores (P=0.013).

Conclusion: Our study suggests that no association was found among the 5-HTTLPR gene polymorphism and any of the EPQ dimensions; the 5-HTT STin2 gene polymorphism is associated with EPQ personality, STin2.10 allele is probably a risk factor of E and P personality in healthy male, and a protectant factor of N personality in healthy female.

References:
References:

NR82 Monday, May 21, 9:00 AM - 10:30 AM
Association Study Between EPQ Personality and Major Depression Symptom Severity
Liang Niu First Hospital of Shanxi Medical University, Psychiatry Department, No. 85 South Liberates Road, Taiyuan, Shanxi, Psychiatry Department, Taiyuan Shanxi, 030001, 5700, Hong Yang, Yan Ren, Xiaohong Cui, Kerang Zhang

Educational Objectives:
Depression is an etiologically heterogeneous group of brain disorders characterized by a wide range of symptoms that reflect alterations in cognitive, psychomotor and emotional processes. More and more studies were suggested the MD patients has different personality characters. Our research suggested that MD patients show more psychoticism, nervousness and endo-form tendency, and the neurotic personality is positive correlation with MD symptom severity.

Summary:
Objective: To assess the Eysenck Personality Questionnaire (EPQ) personality of Major Depression patients and association between EPQ personality and Major Depression symptom severity.
Methods: 120 MD patients were assessed with EPQ, HAMD; 120 normal controls were assessed with EPQ; association between personality and MD symptom severity were analysed.
Results: In MD patients, the P and N scores were obviously higher than normal controls; the E scores were obviously lower than normal controls (P<0.01). There were positive correlation between the neurotic personality and MD patients HAMD scores (P<0.05). There were no correlation between the P.E personality and MD patients HAMD scores (P>0.05).
Conclusion: Our study suggests that MD patients show more psychoticism, nervousness and endo-form tendency, and the neurotic personality is positive correlation with MD symptom severity.

References:

NR83 Monday, May 21, 9:00 AM - 10:30 AM
Comparison of Low Resolution Electromagnetic Tomography (LORETA) Imaging Between Patients with Mild and Severe Obstructive Sleep Apnea Syndrome
Hyun Kwon Lee Seoul National Mental Hospital, Psychiatry, treeself@hanmail.net, Seoul, Jungkook Dong, 5800

Educational Objectives:
The purpose of the study was to identify brain regions associated with nocturnal recurrent chronic hypoxia of untreated obstructive sleep apnea syndrome (OSAS) patients by means of low-resolution brain electromagnetic tomography (LORETA) and quantitative EEG.

Summary:
Objectives: The purpose of the study was to identify brain regions associated with nocturnal recurrent chronic hypoxia of untreated obstructive sleep apnea syndrome (OSAS) patients by means of low-resolution brain electromagnetic tomography (LORETA) and quantitative EEG.
Methods: Nocturnal polysomnogram (NPSG) and subsequent morning electroencephalograph (EEG) were measured in subjects. 10 severe and 10 mild right-handed male OSAS patients were selected by interview, scales (Beck depression inventory, Beck anxiety inventory, Epworth sleepiness scale and Pittsburgh sleep quality index) and NPSG. LORETA and quantitative EEG was compared between two groups by frequency bands (delta 1-3 Hz, theta 4-7 Hz, alpha 8-12 Hz, beta1 13-18 Hz, beta2 19-21 Hz, beta3 22-30 Hz and total 1-30 Hz) made by spectral analysis during rest.
Results: This study showed that severe OSAS was related to decreased alpha activity in the rt. posterior cingulate gyrus (Brodman area 23) compared with mild OSAS in LORETA (p<0.05). In quantitative EEG, the absolute powers of alpha activity (8-12 Hz) were decreased in P3 (-52.52 uV^2), PZ (-60.34 uV^2) and O2 (-41.51 uV^2) in severe OSAS group compared to mild OSAS group (p=0.047, p=0.039, p=0.04). Comparing LORETA with quantitative EEG result, similar results showed with regard to band, activation, location.
Conclusion: Severe OSAS patients shows the decreased LORETA activities of alpha frequency in rt. posterior cingulate gyrus compared with mild OSAS patients. This finding suggests that chronic repeated short-term hypoxias during sleep in OSAS can provoke cortical brain dysfunction.

References:

NR84 Monday, May 21, 9:00 AM - 10:30 AM
Awareness of Bipolar disorder in an Urban Community in South Korea
Soohyun Joe Seoul National University Bundang Hospital, Neuropsychiatry, Department of Neuropsychiatry 300 Gumidong Bundang, Seongnam, 463-707, 5800, Taehyon Ha, Bo Seok Cha, Jung Eun Choi, Kyooseob Ha

Educational Objectives:
The purpose of this study is to show low awareness on bipolar disorder compared to other prevalent disorders.

Summary:
The purpose of the study was to identify brain regions associated with nocturnal recurrent chronic hypoxia of untreated obstructive sleep apnea syndrome (OSAS) patients by means of low-resolution brain electromagnetic tomography (LORETA) and quantitative EEG.

Objectives: The purpose of the study was to identify brain regions associated with nocturnal recurrent chronic hypoxia of untreated obstructive sleep apnea syndrome (OSAS) patients by means of low-resolution brain electromagnetic tomography (LORETA) and quantitative EEG.
Methods: Nocturnal polysomnogram (NPSG) and subsequent morning electroencephalograph (EEG) were measured in subjects. 10 severe and 10 mild right-handed male OSAS patients were selected by interview, scales (Beck depression inventory, Beck anxiety inventory, Epworth sleepiness scale and Pittsburgh sleep quality index) and NPSG. LORETA and quantitative EEG was compared between two groups by frequency bands (delta 1-3 Hz, theta 4-7 Hz, alpha 8-12 Hz, beta1 13-18 Hz, beta2 19-21 Hz, beta3 22-30 Hz and total 1-30 Hz) made by spectral analysis during rest.
Results: This study showed that severe OSAS was related to decreased alpha activity in the rt. posterior cingulate gyrus (Brodman area 23) compared with mild OSAS in LORETA (p<0.05). In quantitative EEG, the absolute powers of alpha activity (8-12 Hz) were decreased in P3 (-52.52 uV^2), PZ (-60.34 uV^2) and O2 (-41.51 uV^2) in severe OSAS group compared to mild OSAS group (p=0.047, p=0.039, p=0.04). Comparing LORETA with quantitative EEG result, similar results showed with regard to band, activation, location.
Conclusion: Severe OSAS patients shows the decreased LORETA activities of alpha frequency in rt. posterior cingulate gyrus compared with mild OSAS patients. This finding suggests that chronic repeated short-term hypoxias during sleep in OSAS can provoke cortical brain dysfunction.

References:
Results: The rate of correct answer of questions about knowledge was 34.2% for bipolar disorder, 38.3% for depressive disorder, 44.2% for schizophrenia and 59.2% for diabetes mellitus. About 12% (88/776) respondents have never heard of bipolar disorder before participating the survey. While less than 5% of respondents have never heard of each of other diseases. About 13% (104/776) of respondents did not think bipolar disorder is an illness. While less than 10% of respondent did not think each of other diseases is an illness. About 16% (124/776) of respondents answered that they would avoid telling other people about illness relatives with bipolar disorder if they had them. Possible avoidance to tell others about ill relatives was reported 16.4% when the relatives have depressive disorder. It was 34.8% when they have schizophrenia and 6.8% when they have diabetes mellitus.

Conclusion: There is low awareness of bipolar disorder compared to that of depressive disorder, schizophrenia and diabetes mellitus. People with bipolar disorder are stigmatized more than people with medical illness. This study highlights the significance of public education for bipolar disorder.

References:

NR85 Monday, May 21, 9:00 AM - 10:30 AM
Effect of Lifetime Alcohol Consumption and Apolipoprotein E 4 allele on Cognitive Function of Elderly
Kyung Ryeol Cha, M.D. Yonsei University College of Medicine, Psychiatry, Psychiatry, YongDong Severance Hospital, 146-92, Dogok-dong, Kangnam-gu, Seoul, 135-720, 5800, Chang Hyung Hong, M.D., Chan-Hyung Kim, M.D., Byung Hoon Oh, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the effect of alcohol consumption on cognition in elderly.

Summary:
Objective: The purpose of this study is to find out the effect of ApoE genotype on correlation between lifetime alcohol consumption and cognition of the elderly in community.

Methods: A total of 2,004 subjects (653 men and 1351 women) aged 60-98 years were analyzed from preliminary data of GDEMCIS (Gwangju Dementia and MCI Study). The study questionnaire consisted of demographic characteristics, current and past illness history, drug history, family history of dementia and stroke, K-MMSE (Korean version-Mini Mental State Examination). We also examined ApoE genotype and analyzed associated factors with metabolic syndrome. The participants also underwent the CAGE questionnaire, the Geriatric Depression Scale, and a lifestyle questionnaire for alcohol consumption.

Results: There was an inverted J-shaped relation between lifetime alcohol consumption and K-MMSE scores (covariates: sex, age, years of education). Small to moderate amount of lifetime alcohol consumption showed a positive-trend effect on K-MMSE scores, but this effect is negative in case of large amount of consumption. These trend effects were more distinct in the presence of ApoE ε4 allele.

Conclusion: Moderate lifetime alcohol consumption might be helpful to elderly cognitive function, but large amount of alcohol consumption is harmful.

Keywords: Alcohol, Cognition, MMSE, Elderly, ApoE genotype

References:

The Psychiatric Manifestations of Mitochondrial Disorders: A Clinical and MR Spectroscopy Investigation
Rebecca E. Anglin, M.D. McMaster University, Departments of Psychiatry and Behavioural Neurosciences and Medicine (Neurology), 1 Mountain Ave, Hamilton, ON, L8P 4E8, 1220, Patricia I. Rosebush, Michael Mazurek, Mark Tamopolsky, Michael Noseworthy

Educational Objectives:
At the conclusion of the presentation, the participant should be able to (1) Appreciate the potential role of mitochondrial dysfunction in the pathobiology of psychiatric disorders. (2) Recognize aspects in a patient's history and clinical presentation that point to an underlying mitochondrial disorder. (3) Diagnose and understand the treatment implications of mitochondrial disorders in psychiatric patients (4) Understand how magnetic resonance spectroscopy can be used to investigate the metabolic abnormalities and potential pathophysiology associated with psychiatric illness in these patients.

Summary:
Background: The brain, as an intensely energy-dependent tissue, is one of the most vulnerable organs to the effects of mitochondrial dysfunction. One might therefore predict a high prevalence of psychiatric disturbances in patients with mitochondrial disease. Surprisingly, there has been very little attention to this issue in the existing literature. The purpose of this study was to identify mitochondrial disorders in patients with primary psychiatric symptomatology, and use proton Magnetic Resonance Spectroscopy (H-MRS) to look for associated metabolic abnormalities in candidate brain regions associated with psychiatric illness.

Methods: Patients referred for psychiatric evaluation were screened for personal and family histories of medical and neurological illnesses and received a neurological examination. Those with findings suggestive of a mitochondrial disorder were referred for muscle biopsy and mitochondrial DNA analysis. Patients diagnosed with a mitochondrial disorder, as well as age and sex matched controls, underwent psychiatric screening using standardized rating scales as well as H-MRS using a 3-Tesla magnet to measure lactate, creatine, choline and N-acetylaspartate (NAA) in regions of the brain implicated in psychiatric illness (prefrontal cortex, cingulate, caudate, and hippocampus).

Results: Nine patients (5 women, 4 men; mean age 43) presenting with primary psychiatric symptomatology were found to have mitochondrial DNA mutations, specifically: MELAS 3271 (N= 2); MELAS 3243 (N=2); MERRF (N=1); CPEO (N=1); Kearns Sayre syndrome (N=1); novel SCA mutation (N=1) and MNGIE (N=1). Psychiatric disorders included depression (N=8), anxiety (N=6), psychosis (N=3), frontolobesyndrome (N=1), catatonia (N=1), and borderline personality disorder (N=1). Preliminary MRS data shows elevated lactate and decreased NAA, creatine and choline in candidate brain regions compared to controls.
Conclusions: 1. Mitochondrial DNA mutations may present with primary psychiatric symptomatology and be a more common source of psychiatric illness than previously appreciated. 2. Psychiatric symptoms in mitochondrial disorders may arise from identifiable metabolic abnormalities in specific brain regions.

References:

NR87 Monday, May 21, 9:00 AM - 10:30 AM
1-year Follow Up After ECT Treatment of Depressed Patients: Comparison Between the Elderly Group and the Middle-Age Group

Yoshitoshi Shingai, M.D. Nippon University, Neuropsychiatry, 1-1-5 Sendagi, Bunkyo-ku, Tokyo, 113-8603, 5880, Kohei Ogawa, M.D., Masahiro Yamamoto, M.D., Amane Tateno, M.D., Takuya Saito, M.D., Yoshiro Okubo, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the outcome of ECT in elderly depressive patients compared to middle age patients.

Summary:
Objective: Although electroconvulsive therapy (ECT) for the depression in elderly is as beneficial as in middle age, it is not clear whether or not the outcome of ECT in follow-up period is different between elderly and middle age group. We compared the 1-year outcome of ECT for depression between the elderly and the middle age.

Method: We reviewed the charts of 34 depressed patients (male 13, female 21, mean age 56.8 years old) who met the criteria of major depressive episode by DSM-IV and were successfully treated by ECT. We divided patients into elderly group (age over 64 year old)(N=12, male 3, female 9, mean age 70.7 years old) and middle-age group (age under 65 years old)(N=22, male 10, female 12, mean age 49.3 years old). Follow-up period was 1-year after ECT. The definition of relapse were follows: 1) readmission, 2) increasing antidepressant in consecutive two outpatient visits, 3) switching of medication, 4) addition of another psychotropic. We studied the rate and mean duration until relapse. Statistical analyses were performed using Student t-tests (two-tailed) for the parametric data and Fisher’s exact probability test for the non-parametric data.

Result: There were no significant differences between elderly and middle-age in the rate of relapse (6 of 12 for the elderly and 15 of 22 for the middle-age, p=0.46) and the mean duration of relapse (96.0±93.5 days for the elderly and 48.1±34.4 days for the middle-age, t(19)=1.761, p=0.09).

Conclusion: There has been considerable debate concerning the outcome of ECT in the elderly depressed patients. Recent review demonstrated that the outcome of ECT for depression in elderly group was not different from the middle-age group. Our result also indicates that the outcome of ECT is not different between the elderly and the middle-age group.

References:

NR88 Monday, May 21, 9:00 AM - 10:30 AM
Effectiveness of Atypical Antipsychotic Augmentation After Successful Electro Convulsive Treatment

Kohei Ogawa, M.D. Nippon Medical School, Neuropsychiatry, 1-1-5 Sendagi, Bunkyo-ku, Tokyo, 113-8603, 5880, Yoshitoshi Shingai, M.D., Masahiro Yamamoto, M.D., Amane Tateno, M.D., Takuya Saito, M.D., Yoshiro Okubo, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand effectiveness of atypical antipsychotic augmentation after successful electro convulsive treatment.

Summary:
Objective: Continuation pharmacotherapy is important for the relapse prevention after electroconvulsive therapy (ECT) for depression, but it has not been established the standard strategy of treatment. Although atypical antipsychotic augmentation is used for the treatment of medication resistant depression, it is not clear that atypical antipsychotic is useful for the prevention of relapse after ECT. In this study, we investigate if atypical antipsychotic augmentation after successful ECT is effective.

Method: Medical charts of 28 consecutive patients with DSM-IV-TR major depressive patients who successfully responded to ECT were reviewed. Evaluation period was one year after successful ECT treatment. Of 28 patients, 10 patients (mean age 60.5) were treated with atypical antipsychotics and antidepressants and 18 patients (mean age 56.5) were treated with antidepressants but without atypical antipsychotics. Relapse was defined as 1) rehospitalization, 2) increasing antidepressant in consecutive two outpatient visits due to significant worsening depressive symptoms, 3) switching medication due to significant worsening depressive symptoms, or 4) adding another class of psychotropic medication. Fisher exact test was used for statistical analysis.

Results: 6 of ten patients (60%) with atypical antipsychotics augmentation were relapsed and 11 of eighteen patients without atypical antipsychotics augmentation were relapsed. There is no statistically significant difference in relapse rate between patients with and without atypical antipsychotics augmentation (p value = 1.0).

Conclusions: Recently atypical antipsychotics have been used to augment antidepressant effect for treatment resistant depression. In this study atypical antipsychotics augmentation does not appear to decrease relapse of major depressive episode after successful ECT treatment.

References:

NR89 Monday, May 21, 9:00 AM - 10:30 AM
Detrimental Effects on Mental Health in Primary Caregivers of Bipolar Patients

Allison M. Lee, M.D. Beth Israel Medical Center, Psychiatry, First Avenue at 16th Street, New York, NY, 10003, 9000, N.
Simay Gokbayrak, B.A., Samantha S. Yard, B.A., Nancy C. Maruyama, M.D., Susan Tross, Ph.D., Igor I. Galynker, M.D.

Educational Objectives:

Educational Objectives: At the conclusion of this presentation, the participant should be aware of the frequency, scope, and predictors of significant psychiatric symptoms in our sample of primary caregivers of bipolar outpatients.

Summary:

Objective: Caregivers of bipolar patients have been found to bear considerable burden. This burden contributes both to poorer clinical outcomes in bipolar disorder and to increased cost of the illness to society. Though many have explored the sources of caregiver burden, few have examined its specific effects on the mental health of caregivers. In a psychiatric clinic of an inner-city, community hospital, we initiated systematic assessment of psychiatric symptoms and quality of life in the primary caregivers of bipolar outpatients.

Methods: Using standardized measures in a consecutive sample of clinic patients and their caregivers, we assessed symptoms of depression, anxiety, and panic, as well as stress, perceived stigma, and quality of life. The following instruments were used: Beck Depression Inventory, Center for Epidemiologic Studies Depression Scale, State-Trait Anxiety Inventory, Sheehan Panic and Anxiety Scale, Perceived Stress Scale, Internalized Stigma of Mental Illness Scale (Adapted) and Quality of Life Enjoyment and Satisfaction Questionnaire.

Results: To date, in this ongoing study, 50% of caregivers for patients with bipolar illness met threshold for depression; of those none were treated with antidepressants. Thirty seven percent met threshold for anxiety and 50% reported 'feeling stressed' often or very often in the past month. All reported at least one experience of stigma related to their close other's disorder.

Conclusions: These interim results demonstrate the feasibility and utility of monitoring caregivers' psychiatric symptoms, and suggest high prevalence of significant psychiatric symptoms in the caregivers of bipolar patients. Our results detailing the frequency, scope, and predictors of psychiatric symptoms in our sample of bipolar caregivers will be discussed.

References:

NR91 Monday, May 21, 9:00 AM - 10:30 AM
The Clinical Significance of Anxiety Symptoms in Depressed Psychiatric Outpatients Without a DSM-IV Anxiety Diagnosis
Jennifer Resch Brown University, Human Behavior and Psychiatry, 235 Plain Street, Suite 501, Providence, RI, 02905, 9000, Mark Zimmerman, M.D., Iwona Chelminska, Ph.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to describe the ways in which the presence of anxiety symptoms affects the psychosocial functioning of depressed patients without a comorbid anxiety diagnosis.

Summary:

Many studies have shown that depression and anxiety are often comorbid disorders. In fact, anxiety disorders are the most frequent comorbid diagnoses with MDD. The presence of anxiety disorders in depressed patients is associated with poorer psychosocial functioning and predicts poorer outcomes. Little research has examined the clinical significance of anxiety symptoms in the absence of diagnosable anxiety disorders in depressed patients. In the present study from the Rhode island Methods to Improve Diagnostic Assessment and Services (MIDAS) project we examined whether the anxiety symptoms in depressed patients without a comorbid anxiety diagnosis results in poorer psychosocial functioning.

Method: Two thousand five hundred psychiatric outpatients were evaluated with a semi-structured diagnostic interview of 344 of whom had a current principal diagnosis of MDD and no comorbid anxiety disorder diagnosis. Symptom levels of somatic and psychiatric anxiety were rated on the Schedule for Affective Disorders and Schizophrenia (SADS). The patients completed the Medical Outcomes Study 36-item short form, and psychosocial functioning items of the SADS.

NR90 Monday, May 21, 9:00 AM - 10:30 AM
Adult ADHD and Bipolar Disorder—A Systematic Review of Comorbidity Rate and Diagnostic Validity
Aliza P. Wingo, M.D. Emory University, Psychiatry, 3009 Green Oaks Circle, Atlanta, GA, 30345, 9000, Megan M. Filkowski, B.A., S. Nassir Ghaemi, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the frequency of comorbidity of adult ADHD and bipolar disorder, become familiar with diagnostic validity studies such as phenomenology, course, and treatment studies.

Summary:

Introduction: Adult ADHD and bipolar disorder are reported to be frequently comorbid. We examined the validity and clinical implications of coexisting adult ADHD and bipolar disorder (BD), particularly, the rate of comorbidity, phenomenology, course of illness, family history, and treatment.

Methods: We conducted a literature search using Medline, Embase, PsycINFO, Cochrane, and the keywords manic, bipolar, attention deficit hyperactivity, adult. Exclusion criteria were pediatric only subjects, review articles, case reports, and articles that only assessed BD or ADHD but not both. Overall, 13 articles met our criteria. Computer search was supplemented with bibliographic cross-referencing.

Results: Four studies of BD samples reported adult ADHD rates of 5.9-21.2%. Five studies of adult ADHD samples reported BD rates of 4.5-47%. Two studies assessed phenomenology (overlap of symptoms, suicide attempt, violence, other comorbid psychiatric illnesses, etc); 4 studies assessed course (age of onset, number of mood episodes, severity); only one study each assessed family history and treatment response (a small, open, non-randomized, 6-week study).

Conclusions: The comorbidity of adult ADHD and BD has been insufficiently studied, with relatively more emphasis on comorbidity rate and course, but very few data on phenomenology, family history, or treatment. BD appears somewhat more likely to be diagnosable in adult ADHD than vice versa. It is not clear whether these are two separate illnesses or one illness with a broad manifestation of emotional and cognitive symptoms.

References:
Results: On the SF-36 subscales, depressed patients without anxiety symptoms had significantly better social functioning, better role-emotional functioning, and less bodily pain than depressed patients with anxiety symptoms. There was a trend for better overall mental health in depressed patients without anxiety symptoms compared to those without anxiety symptoms. A lack of anxiety symptoms in depressed patients was associated with longer duration of the current episode and greater number of prior episodes of depression.

Conclusions: The differences we found between depressed patients with and without anxiety symptoms were similar to those studies comparing depressed patients with and without comorbid anxiety disorders. Thus it may be just as important to evaluate patients for anxiety symptoms that do not meet criteria for an anxiety disorder diagnosis.

References:

NR92 Monday, May 21, 9:00 AM - 10:30 AM
Effect of Ziprasidone on Aversion-induced Dopamine Release: Correlation with a Classical Model of Anxiety
Luigi Pira, Ph.D. Pharaness, General Pharmacology, loc. Piscinamanna, Building 5, e/o Scientific and Technological Park of Sardina, Pula, 90100, 4759, Carla Pisu, Ph.D., Stefania Marcello, Ph.D., Luca Panì, M.D.

Educational Objectives:
After the conclusion of this presentation the participant should have learned the preclinical tests might give useful information on the mechanisms of action of drugs and might support or predict clinical effects. More specifically, this presentation should transfer preclinical suggestions on the potential anxiolytic-like effect of the atypical antipsychotic ziprasidone as assessed using two paradigms based on electric shock-induced aversion, the foot-shock-induced cortical dopamine release and the Vogel conflict-drinking test.

Summary:
Introduction: Psychological stress is thought to play a central role in the development of anxiety disorders. Exposure to stressful events can exacerbate anxious episodes, which are characterized by impairments in concentration, attention and memory, reduced socialization and an altered state of arousal. These impairments are accompanied by abnormalities in the responsiveness of the dopaminergic transmission, mainly in the mesocortical pathway.
Aims: The effect of the atypical antipsychotic ziprasidone @ on the changes in cortical dopamine output induced by stress was assessed on C57Bl/6 N mice, using the microdialysis technique. Furthermore, the effects of ziprasidone @, were assessed in a classical paradigm of anxiety: the Vogel conflict-drinking test.

Results: The acute administration of ziprasidone @ produced a marked increase of dopamine extracellular levels compared to basal values, whereas vehicle had no significant effect. The following exposure to the foot-shock stress, produced a marked increase of dopamine concentrations compared with basal levels in animals treated with vehicle (both in acute and sub-chronic route), but it failed to further increase dopamine in ziprasidone @ pre-treated animals.
Sub-chronic treatment with ziprasidone @ dramatically reduced the effect of foot-shock stress observed in control mice.

In the Vogel conflict-drinking test, animals pre-treated with the classical anxiolytic diazepam received a significantly higher number of shocks associated to water licks compared to control mice. Both acute and sub-chronic administration of ziprasidone @ determined a non-significant trend to increase the number of shocks accepted.

Comments: These results indicate that ziprasidone possess a marked anti-stress effect associated with a tendency to an anxiolytic effect, considering shock-induced cortical dopamine release and shock-induced conflicting behaviour as correlates of stress and anxiety, respectively.

A more prolonged treatment or the use of different behavioural paradigms might highlight a more clear anxiolytic effect of ziprasidone @.

This study was supported by a grant from Pfizer Inc.

References:

NR93 Monday, May 21, 9:00 AM - 10:30 AM
Comparative Analysis of the Short Portable Mental Status Questionnaire (SPMSQ) and the Telephone Interview for Cognitive Status (TICS) in the Evaluation of Cognitive Impairment Among African Americans.
Jared Kiddoe, B.S. Duke University Graduate School/School of Medicine, Psychological & Brain Sciences, 6366 Monterey Creek Dr., Durham, NC, 27713, 9000, Keith E. Whitfield, Ph.D.

Educational Objectives:
At the conclusion of the presentation the participant should be able to recognize the limitations of cognitive impairment screens when used in the African American population.
At the conclusion of the presentation the participant should be able to recognize the effect depression has on cognitive impairment screens.
At the conclusion of the presentation the participant should be able to recognize the effect age and mental health have on cognitive well being.

Summary:
Purpose: To determine if the Telephone Interview for Cognitive Status (TICS) is a reliable screener of cognitive impairment (CI) among African Americans (AAs).
Importance: Ensuring that there are accurate diagnostic tools for CI in African Americans will help prevent misdiagnosis of dementia. The TICS is a popular assessment tool for CI, but has not been validated as an accurate assessor of CI among AAs, therefore its use could be leading to increased misdiagnosis of CI in AAs.
Content: We examined if the TICS over-represented AA CI relative to the racially sensitive Short Portable Mental Status Questionnaire (SPMSQ), the impact of depressive disorders (depressive symptoms assessed via the CES-D) on accuracy to detect CI and if there were age differences in CI prevalence between younger subjects (ages 50 - 64) and older ones (> 64).
Methods: We did a secondary analysis on 419 AA subjects to estimate the TICS's sensitivity, specificity and assessment of CI prevalence among the entire sample and sub-samples differentiated by depressive symptoms and age using chi-square.
Results: TICS sensitivity and specificity was 91.6% and 79.6% respectively. The SPMSQ measured C.I. prevalence at 19.7%; the TICS, 34.4%. TICS sensitivity and specificity among the depressed was 85.7% and 68.8% respectively, among the non-depressed 92% and 80% respectively. The TICS measured depressed group C.I. prevalence at 47.6%; the SPMSQ, 30.4%. Among the non-depressed TICS C.I. prevalence was 33.7%; the SPMSQ, 19%. The TICS measured younger group C.I. prevalence at 51.9% and 80% among the older group. Within the younger group SPMSQ C.I. prevalence was 37% and 53.8% among the older.

Findings are consistent with our hypotheses that the TICS would be a less accurate assessor of CI, depressed subjects would have higher rates of CI and that there would be a higher rate of CI within the older group.

References:

NR95  Monday, May 21, 9:00 AM - 10:30 AM
The Impact of Substance Abuse on Treatment Planning in Depressed Outpatients with Comorbid Anxiety Disorders
Charissa F. Andreotti Brown University, Department of Psychology, Brown University, Box 5179, Providence, RI, 02912, 9000, Timothy J. Petersen, Ph.D., Mark Zimmerman, M.D.

Educational Objectives:
1. At the conclusion of the presentation, the participant should be able to identify the prevalence of substance use disorders as well as specific comorbidity when a comorbid anxiety disorder is present.
2. At the conclusion of the presentation, the participant should demonstrate an understanding of the substance use disorders that are more common in depressed patients with comorbid anxiety disorders compared to those without.

Summary:
Background: Substance use disorders including abuse and dependence commonly co-occur in patients with anxiety and depressive disorders. The objective of this study was to investigate how the rate of substance abuse differs in depressed patients with and without comorbid anxiety disorders, and examine how clinicians modify treatment recommendations in depressed patients with a history of substance abuse when a comorbid anxiety disorder is present.

Methods: 346 case records of depressed outpatients, derived from the Methods to Improve Diagnostic Assessment and Services (MIDAS) project at Rhode Island Hospital, were examined to identify the prevalence of substance use disorders as well as specific treatment recommendations made immediately after diagnosis. Regression models were utilized, controlling for demographic and clinical characteristics, to determine how substance use disorders differed between depressed outpatients with and without comorbid anxiety disorders, and how co-occurring substance abuse may impact treatment recommendations made in this patient sample.

Results: Prevalence of substance use disorders was compared for patients with (n=248) and without (n=98) comorbid anxiety disorders. Patients with comorbid anxiety were significantly more likely to abuse alcohol and marijuana than depressed patients without a comorbid anxiety diagnosis. When substance abuse was not present, depressed patients with anxiety disorders had...
a greater number of psychopharmacological therapies added compared to those without. When substance abuse was present, a significant difference was found to exist in the frequency in which psychotherapy was recommended; depressed patients with comorbid anxiety disorders received more recommendations for psychotherapy than those without.

**Conclusion:** Findings suggest the importance of modifying treatments for mood and anxiety disorders when co-occurring substance abuse is present. While our results point to emerging modifications in the clinical treatments for these complicated cases, further research is needed to identify the link between comorbid anxiety and tendency for substance abuse, and how these patients are best treated.

**References:**


**NR96**

**Monday, May 21, 9:00 AM - 10:30 AM**

**Prevalence and Clinical Characteristics of Body Dysmorphic Disorder on a General Adult Inpatient Psychiatric Unit**

Michelle Conroy, M.D. Brown University/Butler Hospital, Resident, 345 Blackstone Boulevard, Providence, RI, 02906, 9000, William Menard, B.A., Kathym Fleming-Ives, M.D., Poornam Modha, M.D., Hilary Cerullo, D.O., Katharine A. Phillips, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant will be familiar with results from a prevalence study of body dysmorphic disorder in patients on a general adult inpatient psychiatric unit, and will also be familiar with clinical correlates of the disorder in this population.

**Summary:**

**Background:** Body Dysmorphic Disorder (BDD), a distressing or impairing preoccupation with an imagined or slight defect in appearance, is a serious, understudied disorder. This study determined the prevalence and clinical correlates of BDD on a general inpatient adult psychiatric unit. To our knowledge, only one previous BDD prevalence study has been done in this setting.

**Methods:** 142 consecutively admitted adults on a psychiatric inpatient unit were screened for participation: 14.8% (n=21) were not eligible, 9.2% (n=13) refused, and 5.6% (n=8) did not participate due to their brief stay. The remaining 100 subjects (67% female; mean age = 39.5 ± 12.7) completed the following self-report measures: the Body Dysmorphic Disorder Questionnaire (BDDQ), a BDD screening measure with good sensitivity and specificity; the Beck Anxiety Scale; and the CES-D, a measure of depressive symptom severity. Those who screened positive for BDD on the BDDQ were interviewed to confirm the presence of DSM-IV BDD and obtain data on BDD's clinical features. Charts were reviewed for demographic and clinical information.

**Results:** BDD was diagnosed in 16.0% (95% CI = 8.7 - 23.3%) (n=16) of patients. Of those with BDD, 37.5% reported their BDD symptoms were a contributing reason for their current hospitalization. Patients revealed BDD symptoms to a mean of 15.1% ± 33.7 of all mental health clinicians who had treated them over their lifetime, and only one (6.3%) reported their BDD symptoms to their current inpatient psychiatrist. The most common reason for not disclosing BDD symptoms was embarrassment. Compared to subjects without BDD (n=84), those with BDD (n=16) were younger (p=.008) and had higher CES-D scores (p=.008). The two groups did not significantly differ on BAI score, demographic characteristics, or comorbidity.

**Conclusions:** BDD is relatively common in inpatients and is associated with more severe depressive symptoms, yet is underdiagnosed in this setting.

**References:**


**NR97**

**Monday, May 21, 9:00 AM - 10:30 AM**

**An Open-Label, Rater-Blinded, 6-week Trial of Escitalopram in Major Depression with Atypical Features**

Neena Ajwani, B.A. Duke University, Psychiatry and Behavioral Sciences, 2213 Elba st, Suite 159A, DUMC Box 3074, Durham, NC, 27705, 9000, Chi-Un Pae, M.D., Prakash Masand, M.D., Kathleen Peindl, Ph.D., Paolo Mannelli, M.D., Ashwin A. Patkar, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to understand the role of escitalopram, a selective serotonin uptake inhibitor, in the treatment of major depression with atypical features.

**Summary:**

**Objectives:** Although the selective serotonin uptake inhibitor (SSRI), escitalopram has been approved for the treatment of major depression (MDD), there are limited data whether escitalopram is effective in MDD with atypical features. As a preliminary study, we investigated the clinical utility of escitalopram in a 6-week, open-label, flexible-dose, rater blinded trial.

**Methods:** After screening, consenting, and a minimum of 4 week washout from preexisting antidepressants, 13 subjects received escitalopram (10-20 mg/day) for 6 weeks. The primary outcome was a change in score from baseline to end of treatment on the Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorder Version (SIGH-SAD), which includes a set of items for atypical symptoms. Secondary outcomes included the Clinical Global Impression (CGI-S and CGI-I) ratings.

**Results:** The study participants (n=13) were 69% female with a mean age of 46 years. The dropout rate was 15.3%. The mean SIGH-SAD score at baseline was 23.4 (SD=7.34) indicating moderate to severe depression. There was a significant reduction in mean SIGH-SAD scores from baseline to end of treatment (mean change -6.15, t=14.35, p<0.001). The common side effects were dry mouth (n=4); insomnia (n=2), headache (n=1) and diarrhea (n=1). There were no significant weight changes during the trial. The mean dose of escitalopram was 18.3 mg per day.

**Conclusions:** Preliminary evidence indicates that escitalopram may have a role in the treatment of MDD with atypical features. Randomized, double-blind, placebo-controlled trials are necessary to determine the efficacy of escitalopram in MDD with atypical features.

**References:**

Behavioral Avoidance as a Predictor of Symptom Improvement During Acute Fluoxetine Treatment for Depression

Greg C. Feldman, Ph.D. Massachusetts General Hospital, Department of Psychiatry, 15 Parkman St (WAC 812), Boston, MA, 02114, 9000, Juliana A. Smith, B.A., Molly Kerrigan, B.A., Judith Katz, B.A., Patrick J. McGrath, M.D., Maurizio Fava, M.D.

Educational Objectives:

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

Summary:

Objective: Various markers of avoidance have been shown to be elevated among individuals with depression and predictive of worse response to treatment for depression. In the present study, we investigated behavioral avoidance as a predictor of symptom reduction and premature treatment discontinuation during acute fluoxetine treatment in patients with Major Depressive Disorder (MDD).

Method: Five hundred seventy subjects with MDD were treated with fluoxetine for 12 weeks [target dosages: 10 mg daily (week 1), 20 mg (weeks 2-4), 40 mg (weeks 4-8), and 60 mg (weeks 5-12)]. Behavioral avoidance was assessed at baseline using a single item from the Hopkins Symptom Checklist (SCL-90; Dero- gatis et al., 1974; Item 50). Depression severity was assessed at baseline and week 12 with the 17-Item Hamilton Rating Scale for Depression (Hamilton, 1960).

Results: Intent to treat analyses. Behavioral avoidance was predictive of responder status when baseline Hamilton was controlled (Odds Ratio = .86, SE = .059, p = .300). Behavioral avoid ance was also predictive of remission status (Odds Ratio = .87, SE = .057, p = .029), but not above and beyond initial depression severity. Greater behavioral avoidance predicted earlier drop-out from treatment (r = .26, p < .001). Complete analyses. Behavioral avoidance significantly predicted responder status when initial severity was controlled (Odds Ratio = .82, SE = .077, p = .032) but did not significantly predict remitter status.

Conclusions: Behavioral avoidance was predicted less symptom improvement during acute fluoxetine treatment for MDD; however, results were less robust in the complete sample, possibly due to reduced variability in baseline behavioral avoidance among this sample. Treatment-seeking individuals with MDD with high behavioral avoidance may reap less benefit from pharmacological therapy and may be prone to disengage from treatment. Such patients may benefit from adjunctive psychosocial interventions such as behavioral activation.

References:


The Effect of Having a History of an Eating Disorder

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate understanding about the suicidal behavior profiles that are common in patients with Bipolar Disorder and comorbid GAD and/or Panic Disorder.

Summary:

Objective: Suicidality in bipolar disorder with comorbid anxiety has not been adequately investigated. Compared to bipolar patients without anxiety, bipolar patients with anxiety have been shown to have an earlier age of illness onset; higher rates of mixed states, depressive symptoms, and suicidality (1, 2). To further elucidate the higher rates of suicidality, we used a suicidality module to assess the gradations of suicidal behaviors in bipolar patients with comorbid generalized anxiety disorder (GAD) and/or panic disorder.

Methods: We analyzed screen visit data from 182 patients who recently completed a multi-site, 8-week, double blind, placebo controlled trial. The clinical trial's aim was to evaluate the efficacy, tolerability, and safety of a study medication in the treatment of ambulatory bipolar disorder with comorbid lifetime panic disorder or GAD and current at least moderately severe anxiety. The MINI International Neuropsychiatric Interview was performed to establish whether patients met DSM-IV criteria for bipolar disorder I, II or NOS and for panic disorder or GAD. All patients completed a suicidality module as part of the MINI. This module was expanded during the trial into a 16-question suicidality module. This new suicidality module separated one domain, suicidality, into several components: accidents, suicidal ideation, suicide plan, suicide intent, self-harm with the intent to die, self-harm without the intent to die, recent suicide attempts, past suicide attempts, and frequency and intensity of suicidal thought.

Discussion: 182 patients were screened and 151 met criteria for bipolar anxiety and completed the suicidality module. We plan to report the suicidal behavior profile as described by the 16-question suicidality module for each of the bipolar anxiety comorbidities in the study. This will give greater understanding of the gradations of suicidality in bipolar anxiety and give future direction to suicide tracking in this patient population.

References:


Summary:

Anorexia nervosa (AN) and bulimia nervosa (BN) are psychiatric disorders that primarily afflict adolescent girls and women in their child-bearing years. Previous investigations have produced mixed results on the impact of eating disorders on obstetrical outcome, and there is limited prospective data on the impact of having a history of an eating disorder on the course of mood/anxiety disorders in pregnancy, exposures during pregnancy, and obstetrical outcome.

238 pregnant women with a lifetime Axis I diagnosis of depression or anxiety (SCID) were followed prospectively throughout pregnancy. 9.6% (23/238) had a lifetime diagnosis of AN (2 active), and 4.6% (11/238) had a lifetime diagnosis of BN (2 active). Preliminary analyses confirmed our hypothesis that a history of an eating disorder has an impact on the 3 outcomes measured to date, specifically: 1) Increased fetal exposures to psychotropic medications (150.6 versus 116.1, t=2.421, p<.05), habit-forming substances like caffeine and alcohol (74.0 versus 49.2, t=2.168, p<.05), and tobacco (20.3 versus 7.5, t=2.587, p<.01) for a greater percentage of gestational weeks compared to women without a history; 2) Lower body mass indices at delivery (26.2 versus 31.5, t=4.779, p<.01), infants with smaller head circumferences (33.1 versus 34.0, t=2.179, p<.05), who were also more likely to have low birth weight (X²=13.067, p<.01), and be small for gestational age (X²=13.064, p<.01); and 3) Higher peak scores on the Beck Depression Inventory (BDI) in pregnancy (20.6 versus 16.5, t=2.051, p<.05), postpartum (18.6 versus 14.6, t=3.382, p<.01), and at their first visit postpartum (17.7 versus 10.5, t=3.382, p<.01).

These findings suggest that special obstetric monitoring of pregnant women with a history of AN or BN is warranted, and that all women presenting with a history of an eating disorder may be at increased risk for depression during pregnancy and the first year postpartum.

Supported by P50MH68036, R01MH63979, R01MH071531

References:


NR103 Monday, May 21, 9:00 AM - 10:30 AM
Neuropsychological Phenotypes in Late-Onset Alzheimer’s Disease Associated With Apolipoprotein E (ApoE) Genotype

Cecelia A. Lynch St James’s Hospital, Dublin, Mercer’s Institute for Research on Ageing, Mercer’s Institute for Research on Ageing, Hospital 4, St James’s Hospital, Dublin, 08, 4190, Robert Coen, Cathal Walsh, Ziarah Hawi, Aiden Corvin, Michael Gill, Brian A. Lawlor

Educational Objectives:

By reading this poster, the reader should: learn about patterns of cognitive deficits in Late-Onset Alzheimer’s Disease update their knowledge on the influence of ApoE genotype in Late Onset Alzheimer’s Disease understand the concept of neuropsychological phenotypes in Late-Onset Alzheimers Disease appreciate how genotype may influence clinical variables in Late-Onset Alzheimer’s Disease
Summary:

Background: ApoE is the only unequivocal genetic risk factor identified in Late-Onset Alzheimer’s Disease (LOAD) to date. However, it remains unclear as to how exactly ApoE confers risk and influences phenotype in the disease.

Aim: To examine the relationship between ApoE genotype and patterns of cognitive impairment in LOAD.

Methods: 81 subjects were diagnosed as having Alzheimer’s disease on the basis of DSM-IV and NINCDS-ADRDA criteria. Each subject had an age of onset > 65 years. The mean age of subjects at the time of testing was 75.6 years, mean MMSE (7’s) was 20.8 and mean MMSE (W) 22.2. Each subject was examined for: (1) cognitive function by means of a battery of neuropsychological tests (including MMSE, CAMCOG, Delayed Word Recall, Boston Naming Test, category and letter fluency) carried out at the Memory Clinic (2) ApoE genotype and (3) standardized clinical and demographic variables. Subjects were divided into three groups on the basis of their ApoE epsilon 4 (e4) genotype. The neurocognitive characteristics of each group were examined.

Results: The data indicate that subjects who carry one or more ApoE e4 allele score significantly lower in tests of short term memory, working memory / attention than those who do not possess the ApoE e4 genotype.

Conclusion: These results suggest that ApoE genotype differentiates scores obtained in certain neuropsychological tests in LOAD and in particular that ApoE e4 is associated with particular neuropsychological characteristics in LOAD. This supports a biological basis for certain neuropsychological differences between patients with LOAD and the concept of neuropsychological phenotypes in the disease.

References:
NR106  Monday, May 21, 9:00 AM - 10:30 AM
Lack of Symptom Stability Between Two Consecutive Depressive Episodes in Bipolar I Patients
Marcia B. de Macedo-Soares, M.D. Bipolar Disorder Research Program, Institute of Psychiatry, University of São Paulo Medical School, R. Dr. Oviedo Pires de Campos 785, São Paulo, 05403-010, 3510, R. S. Dias, M.D., K. M. Almeida, M.D., R. Tamada, M.D., J. A. Amaral, M.D., C. Issler, M.D., C. Lafer, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to discuss the lack of symptomatic stability of bipolar I depression

Summary:

Introduction: Few data exist about the stability of the symptom profile through successive depressive episodes in bipolar patients.

Objectives: To analyze the correlation of the symptom profile between two successive depressive episodes in DSM-IV bipolar type I patients.

Methods: The first and the second depressive episodes of 136 bipolar I patients during a 6 year follow up period were identified. Depressive episodes were defined according to DSM-IV criteria (confirmed by the SCID) and total scores on HAMD-31 ≥ 12. The respective 31 HAMD items of the first and second evaluations of each patient were then submitted to a cluster analysis (Ward Method). The correlation of the symptomatic profile between the episodes was verified by the Spearman’s test.

Results: Of a sample of 136 outpatients (86 women/50 men, ages ranging from 22 and 63 years, mean 41.17, s.d. 11.08), 76 presented at least one depressive episode (49 women/27 men, ages between 22 and 63 years, mean 41.17, s.d. 11.08), and 42 showed at least two depressive episodes (31 women/11 men, ages between 22 and 63 years, mean 41.17, s.d. 11.08). We then analyzed 42 pairs of episodes. Only HAMD-31 item “increased appetite” presented a moderate correlation of r=0.52. All other 30 items presented either a poor or no correlation between episodes.

Conclusion: In this sample, we found no correlation between the symptomatic profiles presented in consecutive depressive episodes at follow-up.

References:

NR107  Monday, May 21, 9:00 AM - 10:30 AM
Divalproex Sodium-ER in Outpatients with Disruptive Behavior Disorders: A Three Months Open Label Study
Kirti Saxena, M.D. The University of Texas Southwestern Medical Center, Department of Psychiatry, 5323 Harry Hines Blvd, Dallas, TX, 75390-9030, 9000, Linda Mora, B.A., Erika Torres, B.A., Sanja Medic, B.A., Hans Steiner, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to better diagnose Disruptive Behavior Disorders and treat them more effectively.

Summary:

Objective: To expand findings indicating efficacy of Divalproex Sodium-ER (DVPX) in Disruptive Behavior Disorders (DBD). Most previous studies found DVPX to be efficacious in patients in sociotherapeutically structured settings. We also are testing the hypothesis that DVPX will be efficacious against Reactive/Affective/Defensive/Impulsive Aggression (RADI), as opposed to Proactive/Instrumental/Planned (PIPP).

Method: Twenty participants (30% girls, mean age 13.4 (SD:1)) diagnosed with oppositional defiant disorder or conduct disorder by K-SADS were entered sequentially into 12 weeks of openly titrated medication (DVPX). Another 20 subjects were studied at baseline only as an anchoring contrast group. Primary outcome measures included the Clinical Global Improvement - Change (CGI-C), CGI-S (Severity) scales. Secondary Measures were the Overt Aggression Scale (OAS), among others. Analyses used LOCF format.

Results: There were no significant differences between the treatment group and the contrast group on demographic variables. As reported in previous trials, 44.4 % of the treatment group improved significantly (CGI-C Ratings 1 or 2). Baseline and last CGI-S score carried forward were significantly different, t (11)= 6.09, p<.001. The DVPX group showed reduced RADI aggression, indicated by the OAS, t (9)= 2.39, p<.05, but not PIPP aggression. Blood levels reached were between 59.8 and 93.9 ng/ml. Mean dose was 750 mg/d (range 500 to 1500mg/d).

Conclusion: This study supports that DVPX is efficacious in decreasing RADI aggression in DBD patients. These results are particularly noteworthy because the sociotherapeutic structures supporting patients in previous trials were not present.

References:
NR108  Monday, May 21, 9:00 AM - 10:30 AM

Cluster Analysis of Depressive Symptoms in Bipolar Type I Patients

Marcia B. de Macedo-Soares, M.D. Bipolar Disorder Research Program, Institute of Psychiatry, University of São Paulo Medical School, R. Dr. Odivio Pires de Campos 785, São Paulo, 05403-010, 3510, Rodrigo Dias, M.D., Renata Tamada, M.D., Cilly Issler, M.D., Jose Amaral, Lafer Beny, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the symptomatologic profile of bipolar I depressive patients

Summary:

Introduction: There is some controversy regarding the symptomatologic profile of bipolar depression. Psychomotor retardation, along with hypomnia and psychotic symptoms has been proposed as its’ “signature”. On the other hand, it has been suggested that atypical depression was more frequent in bipolar II individuals.

Methods: DSM-IV bipolar I patients meeting criteria for Major Depressive Episode (SCID) and presenting a total score on HAMD-31 ≥ 12 were identified. The first depressive episode of every patient during the follow-up treatment (1997-2003) according to these criteria was recorded, and the corresponding HAMD-31 scale sub-items were submitted to a cluster analysis (Ward Method).

Results: out of a total sample of 136 BP I patients (86 women, 50 men, aged 22 to 63, mean 41.17 years, s.d 11.08), 76 presented at least one depressive episode (49 women, 27 men, aged 22 to 63, mean 41.17 years s.d 11.08). Mean HAMD-31 total score of the first episode during the follow-up was 22 (12-48, s.d 7.23). The analysis revealed 3 symptom clusters: cluster 1 - depressive mood, guilt feelings, suicide thoughts, insomina (initial, intermediate and final), reduced work and activities, retardation, somatic and gastrointestinal symptoms, decreased libido, psychic anxiety, psychic retardation, motor retardation, helplessness, hopelessness, low self-esteem, agitation, weight loss; cluster 2 - somatic anxiety, obsessive symptoms, hypochondria, depersonalization, paranoia, symptoms, insight; cluster 3 - hypomnia, increased appetite, weight gain. Mean scores on cluster 1 symptoms was 0.88 (0.35 - 2.35, s.d. 0.38), on cluster 2 symptoms was 0.57 (0.00 - 1.80, s.d. 0.35), on cluster 3 symptoms was 0.44 (0.00 - 1.60, s.d. 0.53).

Conclusion: we observed a tendency to a predominance of cluster 1 symptoms, which is in accordance to a preponderance of melancholic symptoms in bipolar depression.

References:

NR109  Monday, May 21, 9:00 AM - 10:30 AM

Genetic Predictors of Postpartum Relapse of Major Depression

Elizabeth Z. King, B.A. Emory University, Psychiatry, 1365 Clifton Rd, NE, Building B, Suite 6100, Atlanta, GA, 30322, 9000, D Jeffrey Newport, M.D., Elizabeth Binder, M.D., Ph.D., Joseph Cubells, M.D., Ph.D., Lori L. Altshuler, M.D., Lee S. Cohen, M.D., Zachary N. Stowe, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the import and potential contribution of investigating genetic influences on major depression.

Summary:

Previous investigations have demonstrated that depression during pregnancy and a history of depression are significant risk factors for postpartum depression (PPD). The perinatal course of depression has been a major focus of our collaborative efforts. The potential contribution of genetic variables shown to enhance vulnerability remains unexplored.

A total of 225 pregnant women (≤32 weeks gestation) with a history of major depressive disorder as determined by SCID were enrolled in a prospective study and followed through 6 months postpartum. DNA was collected at the initial visit and analyzed blind to clinical course. Follow up visits included depression rating scales (BDI, HRSD and SCID mood modules. Preliminary analysis employed a HRSD 17-item score of ≥ 15 to document depressive symptoms. To date, 143 of the women were euthymic at 36 weeks gestation have completed the postpartum follow up with ≥3 visits postpartum. We analyzed genetic polymorphisms in several areas: 1) Associated with increased vulnerability to stressful life events - serotonin transporter (5HTTLPR, SLC6A4); 2) HPA axis activity (FKBP5, CRHR1); and 3) Sensitivity to glucocorticoids (RS6196) and BDNF (RS6265).

Preliminary analysis of the 5HTTLPR in 72 subjects demonstrated an increased proportion of our population possessed two versions of the less common (SS) allele (29.7%) compared to the general population. However, there was not a marked difference in relapse rates between the LL, LS, and SS genotypes. The relapse rate for those possessing the homozygous non-vulnerable alleles was 27.3%, 33.3% for heterozygous, and 29.7% for homozygous vulnerability. Further analysis of the remaining genotypes is in progress and will be discussed.

Assessment of the role(s) of genetic influences on postpartum relapse may provide more accurate identification of persons at risk, allowing for early intervention and/or more efficacious treatment selection.

Supported by P50 MH 68036 and RO1 MH 063979

References:

NR110  Monday, May 21, 9:00 AM - 10:30 AM

Associations of Post Partum Depression with Spousal Military Deployment and Isolation

Jeffrey H. Millegan, M.D. NMCSD, Mental Health, 34800 Bob Wilson Dr., San Diego, CA, 92124, 9000, Daniel Robrecht, M.D., Lynn Leventis, M.D., Crescitelli Jo, R.N., Robert McKay, M.D., Ph.D.

Educational Objectives:

At the end of this presentation, the audience should gain an appreciation for the effect that a spousal deployment will have on risk of post partum depression.

Summary:

Military deployments can be a stress not just on Service Members, but also on their families. In order to identify individuals at risk for post-partum depression, isolation, or the combination of the two, Naval Medical Center San Diego instituted a screening system. New mothers are administered an Edinburgh Postnatal
Depression Scale\(^1\), and asked about previous depression, their spouse’s deployment, and feeling of isolation.

We retrospectively examined depression screenings from six-week-postpartum visits to look for any association between military deployment and postpartum depression. A score of 12 or greater on the Edinburgh scale was considered a positive screen. Odd’s ratios were computed, and Mann-Whitney Test used to calculate statistical significance. Also, stepwise linear regression was used to examine which risk factors might predict scores on the depression scale. Of mothers whose record was complete, 73 of 435 had spouses deployed at time of screening, and 92 of 436 during the pregnancy. Spousal deployment during pregnancy showed an odds ratio for depression of 2.79, and was a statistically significant risk (p=0.002). Spousal deployment at the time of screening had an odds ratio of 1.50, not a statistically significant increase (p=0.377). A linear regression model was calculated that significantly (R = 0.275, p < 0.001) predicted depression score. Self-reported isolation, spousal deployment during pregnancy, and previous depression were all found to be significant (p < 0.05) predictors of depression score in the model, whereas a history of being on antidepressants, age, and spousal deployment at the time of screening were not (p > 0.1). These results support the hypothesis that military deployment of a spouse during pregnancy may be an independent risk factor for depression. Ongoing, aggressive screening of this at-risk population is therefore supported.

References:


**NR111** Monday, May 21, 9:00 AM - 10:30 AM Rorschach and Serotonergic Function in Depression

William Pitchot, Sr., Ph.D. University of Liege, Psychiatry, Psychiatric Unit CHU Sart Tilman Liege Belgium, LIEGE, 4000, 4231, Jacques Wauthy, Sr., B.S.C., Marc Anseau, Sr., Ph.D.

**Educational Objectives:**

To better understand the relationship between serotonin and the Rorschach ratings

**Summary:**

**Background:** several lines of evidence suggest a relationship between depression, serotonin and some personality traits. Impulsivity traits and serotonin are strongly related. However, only partial results exist concerning the relationship between Rorschach and indirect indices of serotonergic activity. In this context, we may hypothesized some links between serotonin function and some Rorschach measures of aggressiveness, impulsive behaviour and avoidance tendencies. In this study, the serotonergic function was assessed by flesinoxan test. Flesinoxan is a full 5-HT1A agonist.

**Methods:** the study was performed in 24 major depressed patients (DSM-IV). The patients underwent a flesinoxan test. administered intravenously according to a method described by Pitchot et al. (1994). Flesinoxan mg was injected within 10 min and blood samples were collected at 10, 25, 30, 60, 90 a, d, t120 in order to measure GH, PRL, cortisol and ACTH. Rorschach was administered according to EXNERâ€”s system. We retain variables in relation with aggressiveness, hostility, lack of control of emotional reaction avoidance and affective stimulus avoidance.

**Results:** hormonal responses to flesinoxan were negatively correlated with indices of aggressiveness (AG) or of hostility (S), of obsessionality (CDI), the quality of the treatment of information.

**Conclusion:** a complex relationship exists between serotonin and the psychic functioning as assessed by the Rorschach particularly in the field of the treatment of information

**References:**


2. Pitchot W, Hansenne M, Pinto E, Reggers J, Fuchs S, Anseau M. 5-HT1A receptors, major depression, and suicidal behavior.

**NR112** Monday, May 21, 9:00 AM - 10:30 AM Gamma-Knife Anterior Capsulotomy for Obsessive Compulsive Disorder: Preliminary Results of a Follow-up Study

Antonio C. Lopes, M.D. Faculty of Medicine, University of São Paulo, Department of Psychiatry, Av Ministro Oswaldo Aranha 150 ap 11, Rudge Ramos, São Bernardo do Campo, 09628000, 3510, Maria E. Mathis, Anita Taub, Miguel M. Canteras, M.D., Benjamin D. Greenberg, M.D., Georg Noren, M.D., Enuperedes C. Miguel, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to recognize that a subgroup of obsessive compulsive patients are treatment refractory; a specific technique of radiosurgery may be considered as a treatment option for these treatment refractory patients.

**Summary:**

**Background:** Sixty to eighty percent of Obsessive Compulsive Disorder (OCD) patients respond to medications or psychotherapy. On the other hand, some remain treatment refractory; for this subgroup, a stereotactic radiosurgery called Gamma-Knife anterior capsulotomy is a treatment option.

An improvement of this technique has been recently developed at Brown University. However, there is a lack of studies reporting results with this new technique.

**Methods:** Eleven refractory DSM-IV OCD patients were selected. Five were operated as part of a pilot study. Six patients were randomized to either receive active or “sham” radiosurgery, in double-blind, randomized controlled trial (RCT). Every patient was assessed in the pre and post-operative follow-up periods, with psychopathological, global status, neuropsychological and personality scales being applied, as well as magnetic resonance imaging (MRI) scanings with voxel-based morphometry (VBM).

More than 35 % improvement in Yale-Brown Obsessive Compulsive Scale and “improved” or “much improved” scores in Clinical Global Impression scale were taken as the primary treatment response criteria.

**Results:** Four out of eight (50 %) patients who had received active radiosurgery fulfilled our response criteria 12 months or more after surgery. None of the three sham radiosurgery patients were responders until the 12th month of follow-up. One of the sham procedure patients became responder only after an active procedure was conducted. Mainly episodic headaches, dizziness, nausea, and transient worsening of symptoms were observed. Regarding neuropsychological changes, improved performances on verbal IQ (p=0.04), global IQ (p=0.04), logical memory (p=0.04), and simple visual attention (p=0.04) were noted in the pilot patients.

**Conclusions:** Preliminary results suggest that Gamma-Knife radiosurgery for refractory OCD shows some efficacy, with few adverse effects. More results from our ongoing RCT will better investigate efficacy and safety issues.
Funding Source: CAPES, Brazil (Dr Lopes). FAPESP (process n. 99/12205-7) and CNPQ (process n. 521369/96-7), Brazil (Dr Miguel).

References:

NR113  Monday, May 21, 9:00 AM - 10:30 AM
Sleep Spindle Deficits in Medicated Schizophrenics and Medication Effects: A Whole Night High Density (HD)-EEG Study
fabio ferrarelli, M.D. UW-Madison, Psychiatry, 6001 research park blvd, 1102 e. johnson, madison, wi, 53719, 9000, michael J. peterson, M.D., reto huber, Ph.D., michael J. murphy, adam watson, simone sarasso, giulio tononi

Educational Objectives:
At the conclusion of this presentation the participants should be able to recognize that:

a) Sleep abnormalities are often reported in psychiatric patients, including schizophrenics
b) Sleep electroencephalography (EEG) recordings can minimize, in schizophrenia patients, possible confounding factors related to waking activities, including changes in the level of attention, decreased motivation or cognitive capacity, and presence of active symptoms.

c) The recent introduction of high density (hd)-EEG is especially well-suited to investigating localized changes in the sleep EEG activity.
d) The local abnormalities in sleep rhythms reported in this presentation may be linked to the biological basis of schizophrenia.

Summary:

Background: High-density electroencephalography (hd-EEG) during sleep is a powerful tool to reveal abnormalities in sleep rhythms in psychiatric populations. We recently showed reduced spindle activity in medicated schizophrenics compared to depressed and healthy subjects during the first sleep episode. Here we present a whole night, medication-controlled investigation of schizophrenics using a 256-channel hd-EEG.

Method: We recorded medicated schizophrenics (n=21), depressed subjects (n=17), age-matched controls (n=16), and non-schizophrenics taking antipsychotics (n=7). EEG signals were digitized at 500 Hz together with electromyogram and electrooculogram, filtered (0.5-50 Hz), artifact-rejected, average-referenced, and sleep-staged. Recordings were analyzed by power spectral analysis and topographic mapping at spindle frequencies. We also detected individual spindles and analyzed several spindle parameters (number, amplitude, duration, and time integrated spindle amplitude or ISA).

Results: Compared to the other three groups, schizophrenia patients had reduced power in the 12-15 Hz band for all sleep cycles and for the entire night. This reduction peaked in the 14-15 Hz range (p<0.006, Bonferroni test controlled for multiple comparison) and showed a centro-parietal distribution. Over the corresponding scalp area, spindle number, amplitude, duration and ISA were also significantly reduced in schizophrenics. By contrast, non-schizophrenia subjects taking antipsychotics had values comparable to healthy controls.

Conclusion: In a previous study we reported a reduction in spindle activity in medicated schizophrenics during the first sleep episode. The present study shows that such spindle activity changes are seen throughout the night and indicates that they are unlikely to be due to medication effects.

References:

NR114  Monday, May 21, 9:00 AM - 10:30 AM
Neuroendocrine Markers of Stress Reactivity in the Infants of Women with Bipolar Disorder
Sandra Juric, B.A. Emory University, Psychiatry, 1365 Clifton Rd., Emory Clinic Building B, Atlanta, GA, 30322, 9000, Patricia Brennan, Ph.D., D Jeffrey Newport, M.D., Alsion Shea, M.S.C., Susana V. Fernandez, B.A., Meir Steiner, M.D., Zachary N. Stowe, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will be familiar with the impact of maternal BPD on infant HPA axis reactivity (salivary cortisol) and the sympathetic nervous system (salivary α amylase) at 6 months of age.

Summary:
Several investigations have demonstrated that maternal depression and anxiety during pregnancy and the early postnatal period can alter later infant and child reactivity and behavior. Similarly, the children of women with BPD appear to be at considerable risk for behavioral alterations. Remarkably few studies have included the infants of women with BPD. The current study evaluated the HPA axis (salivary cortisol) and indirect measures of the sympathetic nervous system (salivary α amylase) in response to laboratory stressors at 6 months of age. A total of 26 mother/infant dyads with maternal BPD by SCID, were matched with an equal number of women with Unipolar Major Depression, and control subjects (no Axis I diagnosis). Both psychiatric groups were followed through out pregnancy and controlled derived from community advertisement/psychology research pool. Laboratory procedures included baseline, aclimation, stressor sound burst and arm restraint, recovery period, and study exit. Maternal and infant saliva was collected at six time points throughout the three hour period. Preliminary analysis using ANOVA demonstrated significant differences in the mean cortisol level, F (2,75)=4.140 p<0.02 and the baseline cortisol level, F (2,75)=5.697 p=.005, with the infants of women with BPD having significantly higher salivary cortisol (log mean cortisol 2.37±0.04, log baseline cortisol 2.36±.03) compared to both the UPD (log mean cortisol 2.34 ±0.02, log baseline cortisol 2.34 ± 0.02 ) and control group (log mean cortisol 2.35±0.03, log baseline cortisol 2.34±0.03 ). In contrast, salivary amylase results were unremarkable, though highly variable across the psychiatric groups. Additional analysis will include maternal versus infant measures, scoring of the mother/infant interactions. These novel data suggest that the infants of women with BPD may have alterations in HPA, indicative of altered stress reactivity. Similarly, that such alterations may be influenced by maternal symptoms during pregnancy. Supported by MH059322 and MH68036

References:
treatments for NASH include: 1. Increased exercise, 2. Caloric restriction resulting in weight loss in the treatment of NASH. Realize the potential for zonisamide and topiramate to cause weight loss and for bupropion to cause TNF-alpha reduction. Further research is needed to determine the precise effects of these drugs on NASH.

Educational Objectives:
- At the conclusion of this presentation the participant should be able to:
  1. Appreciate the importance of Nonalcoholic Steatohepatitis (NASH) in light of the current obesity epidemic.
  2. Understand the basic pathophysiological mechanisms of NASH.
  3. Recognize patients at risk for having NASH.
  4. Initiate the diagnostic testing for NASH.
  5. Implement cognitive behavioral therapy with the goal of weight loss in the treatment of NASH. Realize the potential for topiramate and zonisamide to cause weight loss and for bupropion to cause TNF-alpha reduction. Further research is needed to determine the precise effects of these drugs on NASH.

Summary:
- Up to 40% of the US may be obese by 2008. Commonly prescribed psychotropic medications—valproic acid, typical antipsychotics, lithium, quetiapine and others, but preeminent olanzapine and mirtazapine, typically contribute to appetite increase and consequent overeating and weight gain. Nonalcoholic steatohepatitis (NASH), now the commonest cause of chronic liver disease, is highly associated with truncal obesity, insulin resistance, and type II diabetes. It results from two distinct “hits”: First, chronic overnutrition causes intracellular hepatic lipid accumulation [steatosis]. Second, oxidant stress, mitochondrial injury, or obesity related increase in inflammatory cytokines— including tumor necrosis factor-alpha (TNF), central to the pathogenesis of NASH—superimpose a steatosis-based inflammatory state. Psychiatrists should keep NASH in mind, particularly in obese individuals with elevated liver function tests (LFTs). After ruling out other causes of hepatitis (most commonly alcohol or viral hepatitis), the next step is a non-invasive imaging study by ultrasound (US). A finding of diffuse hyperechoic texture (bright liver) is suggestive of NASH. Hepatology usually confirms diagnosis by liver biopsy. Current treatments for NASH include: 1. Increased exercise, 2. Caloric restriction resulting in weight loss [difficult] 3. Bariatric surgery, 4. Insulin sensitizing drugs (e.g. metformin, pioglitazone, and others). Commonly, the offending psychiatric drug cannot safely be withdrawn or substituted. However, evidence suggests some psychotropic medications may augment lifestyle modifications in reducing weight and consequent NASH: topiramate and zonisamide have been shown to reduce weight and increase lean body mass. And other studies show bupropion may have TNF-alpha reducing effects. These drugs are widely available, safe, and inexpensive. Further research may show these to help manage NASH. Molindone is an antipsychotic associated with weight loss but its safety is now in question. Psychiatrists can help treatment of NASH by focusing on prevention, encouraging appropriate diet and exercise, and perhaps with zonisamide, topiramate and bupropion.

References:
Multiaxial Evaluation of Panic Disorder and Quality of Life Assessment by WHOQOL-BREF (World Health Quality of Life - Brief Version).

Valfrido L. de-Melo-Neto Federal University of Rio de Janeiro, Laboratory of Panic and Respiration, Av. Venceslau Brás, 71 Fundos, IPUB, Residência Méd, Rio de Janeiro, 22290-140, 3510, Alexandre M. Valenga, Isabella Nascimento, Fabiana L. Lopes, Anna Lucia King, Antonio E. Nardi

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that the Panic Disorder diagnoses is per se a marker of quality of life impairment. The participant should be able to identify that high levels of anxiety and smoking are important factors related to quality of life impairment among Panic Disorder Patients.

Summary:
Objectives: To compare quality of life between Panic Disorder (PD) patients and healthy subjects, and to correlate social, demographic and clinical data with quality of life scores.

Methods: A cross-sectional study was conducted with 20 PD patients (DSM-IV-TR) - under treatment at the Panic and Respiration Laboratory, Brazil - and 20 healthy controls. Anxiety aspects were assessed by the Beck Anxiety Inventory (BAI), Hamilton Anxiety Rating Scale (HARS) and State-Trait Anxiety Inventory (Form Y - STAI) while PD overall severity was evaluated by the Panic and Agoraphobia Scale (PAS). Quality of life was investigated by the World Health Organization - Quality of Life - brief version questionnaire (WHOQOL-BREF), in four domains: physical, psychological, social and environmental. Patients were also evaluated by the DSM-IV-TR Axis IV and V.

Results: No significant differences of gender, age, schooling, religion, marital status nor individual income were observed between groups, but family income was significantly higher among controls. PD patients were 65% female. Mean age=37.5±9.1. Quality of life domain scores: Physical= 57.86±17.6, Psychological= 56.04±18.3, Social= 56.25±25.9 and Environmental= 47.03±16.9. Smokers=20%, BAI=3.4±15.0, STAI-S= 43.5±8.8, STAI-T=50.1±9.2, PAS= 13.6±9.4. All domains were significantly impaired among PD patients.

Conclusions: Panic disorder per se compromises well being. Psychosocial problems and high levels of anxiety can also negatively impact quality of life of PD patients. Smoking is correlated with lower quality of life scores.

References:

NR118
The Impact of Maternal Bipolar Disorder on Obstetrical Outcome
Yara Betancourt, B.A. Emory University, Psychiatry, 1365 Clifton Road, Building B, Suite 6100, Atlanta, GA, 30322, 9000, D Jeffrey Newport, M.D., Martha R. Calamaras, B.S., Adele C. Viguera, M.D., Marisa Johnson, B.A., Zachary N. Stowe, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should recognize that continued psychiatric treatment may improve obstetrical outcomes for women with BPD.

Summary:
The impact of maternal psychiatric illness and/or treatment on pregnancy outcome has generated considerable attention, particularly for depression and antidepressants. Interestingly, there is sparse data on the impact, if any, of maternal Bipolar Disorder (BPD) on obstetrical outcome. The disentanglement of the impact of illness from treatment as well as the use of an appropriate comparison group remain significant impediments to isolating the impact of maternal mental illness. In the current study, 63 women with a lifetime diagnosis of BPD and 278 women with Major Depressive Disorder (MDD) as determined by SCID, were prospectively followed through pregnancy. Most women with BPD continued psychiatric medications (lithium, lamotrigine, atypical antipsychotics) throughout pregnancy. Preliminary analyses compared obstetrical outcomes between diagnostic groups and to the 2004 National Vital Statistics Reports (NVSP).

NR119
The Effects of Childhood Trauma on Obstetrical Outcome
Denicia K. Holley, B.A. Emory University, Psychiatry, Emory Clinic Building B, 1365 Clifton Rd. NE, Atlanta, GA, 30306, 9000, D. Jeffrey Newport, M.D., Bettina T. Knight, R.N., Zachary N. Stowe, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to familiar with the prospective data of the effects of childhood abuse and neglect on the obstetrical outcome in women with a history of major depression and the implications for treatment planning for this at risk population.

Summary:
Pregnancy is a time of increased psychiatric vulnerability for women with a history of childhood trauma. Previous studies demonstrated that pregnant women with a history of sexual abuse reported more functional impairment, health complaints, and substance use. In the current study, 217 pregnant women with lifetime diagnosis of major depression (SCID) were followed prospectively...
throughout pregnancy. Subjects completed the Childhood Trauma Questionnaire (CTQ) at study entry and both self and clinician rated scales on follow up visits. Obstetrical outcome was compared between women with CTQ component scores of moderate to high versus minimal to low. Women with a history of emotional abuse and emotional neglect were more likely to deliver preterm (29.2% versus 15.7%) \( x^2 = 4.14, p < .05 \) and (33.3% versus 14.9%) \( x^2 = 7.43, p < .01 \) or have their infant admitted to the NICU (63.6% versus 23.1%) \( x^2 = 6.48, p < .05 \) and (77.8% versus 21.4%) \( x^2 = 10.93, p < .01 \), respectively. Women were more likely to deliver preterm with a history of physical abuse (41.0% versus 15.3%) \( x^2 = 8.42, p < .01 \) and physical neglect (34.8% versus 17.1%) \( x^2 = 4.07, p < .05 \). These relationships persisted when controlling for central nervous system medication use throughout pregnancy. Women with a history of emotional abuse had higher scores on the Beck Depression Inventory (BDI), the Perceived Stress Scale (PSS), and lower scores on the Dyadic Adjustment Scale (DAS) \( p < .01 \). Women with a history of a history of emotional abuse had higher scores on the PSS, and lower scores on the DAS \( p < .01 \), respectively. Women were more likely to deliver preterm with a history of physical abuse (41.0% versus 15.3%) \( x^2 = 8.42, p < .01 \) and physical neglect (34.8% versus 17.1%) \( x^2 = 4.07, p < .05 \). These relationships persisted when controlling for central nervous system medication use throughout pregnancy. Women with a history of emotional abuse had higher scores on the Beck Depression Inventory (BDI), the Perceived Stress Scale (PSS), and lower scores on the Dyadic Adjustment Scale (DAS) \( p < .01 \). Women with a history of emotional abuse had higher scores on the BDI scores during pregnancy \( t = 4.07, p < .05 \). These relationships persisted when controlling for central nervous system medication use throughout pregnancy. Women with a history of physical abuse had higher BDI scores, lower DAS scores \( p < .05 \), while women with a history of sexual abuse had higher BDI scores, lower DAS scores \( p < .01 \), and higher PSS scores \( p < .05 \). This data demonstrates the need to critically evaluate treatment strategies during pregnancy for women with a history of depression and childhood trauma in order to diminish potential risks to the infant.

Supported by P50-MH-68036, R01-MH-063979, and R01-MH-071531

References:

NR120

Sleep Quality During Pregnancy in Women With Depression: Relationship to Clinical Course in Pregnancy and the Postpartum Period

Melanie B. Galanti, B.A. Emory University, Psychiatry. 1365 Clifton Rd NE, Clinic Building B Ste 6100, Atlanta, GA, 30322, 9000, D Jeffrey Newport, M.D., Elizabeth Z. King, B.A., Bettina T. Knight, R.N., Zachary N. Stowe, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be familiar with the relationship of sleep quality and depressive symptoms in women with a history of major depressive disorder (MDD) during pregnancy and the postpartum period.

Summary:
Sleep disorders are common during pregnancy, peaking in the third trimester. Hormone variations associated with pregnancy cause a decrease in REM latency which, in the first month postpartum, becomes even more pronounced as a result of increased awakenings (Lee et al 2000). Moreover, many pregnant women may take over-the-counter or prescription medications to improve sleep. There are considerable data linking alterations in sleep patterns to mood disorders; however, the relationship and/or the predictive value of such alterations in recurrence of depression during pregnancy are limited. Recent Collaborative prospective data from our group has demonstrated a high recurrence rate for MDD during pregnancy (Cohen et al, 2006). Two hundred twenty-six women with a SCID diagnosis of MDD were followed prospectively during pregnancy. At each visit women completed the self-rated Beck Depression Inventory (BDI), Pittsburgh Sleep Quality Inventory (PSQI), clinician-rated Hamilton Rating Scale for Depression (HRSD) and the SCID mood module. Using the seven component scores on the PSQI as well as a global sleep score, significant correlations were found between the PSQI global score and the BDI \( n = .45, p < .05 \) and the HRSD \( n = .65, p < .05 \) - component subscore analysis pending. Non-depressed patients had significantly lower sleep scores \( 6.6 \pm 3.9 \) than depressed patients \( 9.0 \pm 4.1 \), \( t = 7.00, p < .01 \). BDI scores during pregnancy \( 11.0 \pm 8.8 \) were not significantly different to those in postpartum \( 10.8 \pm 8.2 \), \( t = 0.06, p = .98 \). This may suggest an association between depression during pregnancy and relapse in the postpartum period. To address whether or not alterations in the PSQI preceded recurrence of major depression, we are assessing the time course of alterations in sleep quality relative to the SCID mood module, and risk for recurrence in the postpartum period.

Supported by P50 MH-68036, R01 MH-63979, K23 MH-63507, and R01 MH-71531

References:

NR121

Monday, May 21, 9:00 AM - 10:30 AM

Effect of Antidepressant Treatment on Depressive Relapse In Bipolar Disorder: A Randomized Study

Megan M. Filkowsk; B.A. Emory University, Psychiatry, Emory Clinic, Building B, Suite 6100, 1365 Clifton Road, Atlanta, GA, 30322, 9000, Vanessa A. Stan, B.A., David J. Borrelli, Michael J. Ostacher, Rf S. El-Mallakh, Claudia F. Baldassano, S. Nassir Ghaemi, G.S. Sachs, R.J. Baldessarini

Educational Objectives:
To determine if long-term antidepressant use affects time to first mood episode in bipolar disorder.

Summary:
Objective: Some studies suggest that antidepressant continuation improves outcomes following recovery from bipolar depression. We report secondary outcomes from the evaluation of time to first episode in the first year of a randomized, controlled study of long-term versus short-term treatment with modern antidepressants (ADs) in patients with bipolar disorder (BPD). This will be a final presentation of the data from a 5 year study.

Methods: BPD patients, who recovered from a major depressive episode with an AD plus mood stabilizer, were openly randomized to either continue (long-term, LT; \( n = 31 \)) or discontinue (short-term, ST; \( n = 38 \)) antidepressants, with a least 1 year follow-up. Effect of patient bias regarding ADs was measured prior to randomization by using a questionnaire (rated -2 to +2 each) rating patient opinion about taking antidepressants.

Results: An unadjusted analysis of time to first mood episode showed that the short-term group was more likely to relapse (HR=.19 \pm .155 \text{95\%CI: 1.35, 1.96}) after adjusting for confounding variables, the short-term group was less likely to relapse (HR=.19 \pm .0315 \text{95\%CI: 0.72, 1.19}).

Conclusions: Time to first mood episode is initially favorable for long-term antidepressant use, but after adjustment for potential confounding variables, especially patient attitude, antidepressant discontinuation appears to lead to better outcomes. Results demonstrate the need for future double-blind trials to control for patient....
attitudes and obtain more definitive results. Final data will be updated prior to presentation. Funding Source: Supported by NIMH grant MH-64189-03.

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

References:


NR122

Monday, May 21, 9:00 AM - 10:30 AM

Association of T182C Polymorphism in Norepinephrine Transporter Gene and EPQ personality traits in Chinese Han Population

Kerang Zhang First Hospital of Shanxi Medical University, Psychiatry Department, No. 85 South Liberates Road, Taiyuan, Shanxi, Psychiatry Department, Taiyuan Shanxi, 030001, 5700, Xinrong Li

Educational Objectives:

Personality is generally defined as the characteristic manner and style of an individual's behavior and encompasses vigor, temper, and persistence of the resulting behavior. Our study suggests that the C allele may be a risk factor of P (Psychoticism) dimension of health men and N (Neuroticism) dimension of MD men.

Summary:

Object: To explore the relations of Norepinephrine transporter (NET) T182C gene polymorphism and EPQ personality traits in people of Chinese Han.

Method: 100 control and 100 case were all informed consent. Personality traits was evaluated by Eysenck Personality Questionnaire (EPQ) and T182C gene was amplificated with PCR technology and detected with Pyrosequencing PSCE96MA. Association between genetic polymorphism and personality were statistically analyzed SPSS11.5.

Result: 1. In health group, the compare of means of P dimension (t=2.094, P=0.039) and allele distribution of different level of P dimension ($\chi^2=4.190, P=0.041$) of males’ T182C allele have statistical significance. The frequency of C allele was higher in high score group of P dimension(45.5%) than in low score group(22.7%), 2. In MD group, the same allele distribution tendency is at N dimension ($\chi^2=3.344, P=0.067$).

Conclusion: Our study suggests that the C allele may be a risk factor of P (Psychoticism) dimension of health men and N (Neuroticism) dimension of MD men.

References:


NR123

Monday, May 21, 9:00 AM - 10:30 AM

Suicide in Older Adults with Schizophrenia

Shilpa Diwan, M.D., M.P.H. SUNY Downstate Medical Center, Psychiatry, 415 100 Street, Brooklyn, NY, 11209, 9000, Paul M. Ramirez, Ph.D., Pia Natalya Reyes, M.D., Ipsit Vahia, M.D., Mamta Sapra, M.D., Azziza O. Bankole, M.D., Carl I. Cohen, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate the importance of continued monitoring of suicidality in older adults with schizophrenia and examine the factors associated with it.

Summary:

Objective: To determine the prevalence of current suicidality and prior suicidal attempts in older adults with schizophrenia and examine associated factors.

Methods: The Schizophrenia Group (S) consisted of 198 persons aged 55+ living in the community who developed schizophrenia before age 45. We excluded persons with substantial cognitive impairment. A Community Comparison Group (C) (n=113) was selected which closely matched the schizophrenia sample. We examined current suicidality (presence of the following in past 2 weeks: wishing to be dead, thoughts of suicide, or attempted suicide) and lifetime history of a suicidal attempt. For S, we used George’s Social Antecedent Model to examine 16 predictors of attempted suicide. Results: We found a higher prevalence of current suicidality among S when compared to C (10% versus 2%; p=.006) as well as past suicidal attempts (30% versus 4%; p=.001). We separately examined S. 19% of those who previously attempted suicide currently exhibited suicidality. 55% of those who currently expressed suicidality had previously attempted suicide. 55% of S who had previously attempted suicide currently had syndromal depression (CESD>16) versus 27% who had never attempted suicide (p=.01); among those who currently expressed suicidality, 70% were depressed versus 28% of those without suicidality (p=.001). In logistic regression, we found 3 significant predictors of previous suicide attempts: current syndromal depression (OR=2.36), number of lifetime traumatic events (OR=1.16), and diminished use of spiritualists (OR=.44).

Conclusions: Prevalence of current suicidality and previous suicide attempts is dramatically higher among older schizophrenic adults than their peers in the community. Schizophrenic persons with prior attempts continue to express suicidality and exhibit more depression. Risk factors for previous attempts include current depression and more lifetime traumatic events. This highlights the importance of monitoring for suicidality, obtaining a detailed suicidal history, and the potential value of pharmacotherapy for depression and psychotherapy for prior traumatic events.

References:


Educational Objectives:

Participants should understand that despite surface similarities between bipolar and unipolar depression, the underlying symptom associations are distinct. These differences should be taken into consideration in the diagnosis and treatment of bipolar and unipolar patients.

Summary:

Objective: Studies indicate high rates of misdiagnosis for bipolar (BP) patients(1). Our previous study found differences in neural substrates between depressed unipolar (UP) and BP patients(2). These correlated with four symptom clusters found with a combined sample of UP and BP patients(2). This study seeks to examine the differences in symptomatology between the two groups by comparing separate Principal Component Analyses (PCA) on the Beck Depression Inventory (BDI).

Method: PCAs were conducted (one for UP, one for BP) on BDIIs completed during screening for research studies. Patients with DSM-IV diagnosis of BP or UP depression and Montgomery-Asberg Depression Rating Scale (MADRS) or Hamilton Depression Rating Scale (HAM-D) scores of 16 and 18, respectively, were included. PCAs using a varimax rotation with Kaiser Normalization were conducted for each group. PCAs with four components accounted for approximately 50% variance while maintaining distinct components. Items with a loading of >0.5 were included. Preliminary analysis of 98 patients was conducted; full data will be presented.

Results: 50 UP and 48 BP patients were included in the final analysis, accounting for 49% of variance in UP and 53% in BP patients. Component one in the UP group was similar to the Psychomotor-Anhedonia component extracted in the PCA conducted by Dunn et al(2). In the BP group, component one included a mixture of negative cognitions, anhedonia, and vegetative symptoms. Component two was similar for both groups. Component four contained suicidality and negative thoughts in both groups. For UPS, negative thoughts were self-directed and past-oriented. In BPs, negative thoughts indicated hopelessness about the future.

Conclusion: Overall, negative cognitions segregated more clearly from other symptoms in UP patients. BPs were more likely to have psychomotor-anhedonia and vegetative symptom clusters with negative cognitions, indicating more complex symptom associations for BP depression. Full data will be presented.

References:


NR125  Monday, May 21, 9:00 AM - 10:30 AM
Effect of Adult ADHD Treatment on Cognition in Adult ADHD Patients
Abid Malik, M.D. Albany Medical Center, Psychiatry, 434 Hudson Ave, Albany, NY, 12203, 9000, Kara L. Shirley, Pharm.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to recognized the effect of adult ADHD treatment on cognition

Summary:

Although the childhood ADHD is recognized since the early 1900s, recognition of the disorder in adults did not occur until the 1970s. Adult ADHD causes significant disabling symptoms and the total excess cost of ADHD in the US in 2000 was $31.6 billion which include cost in ADHD treatment of patients, other healthcare costs of persons with ADHD, other healthcare costs of family members of persons with ADHD, and the work loss cost of adults with ADHD and adult family members of persons with ADHD. Recently there has been increased interest in the treatment of this illness. Improvement in cognition is one important aspect of treatment. This literature review is done in November 2006 to determine the effect of treatment on cognition in Adult ADHD patients. PubMed was searched in Nov 2006 using key words “adult ADHD cognition”. Abstract of relevant articles were reviewed and evidence of treatment effect on cognition is discussed.

References:

1. Jentsch JD, Roth RH: The neuropsychopharmacology of phencyclidine: from NMDA receptor hypofunction to the dopamine hypothesis of schizophrenia. Neuropsychopharmacology 1999;20:201-225.
Adaptive Functioning in Older Schizophrenic Persons

Nikhil J. Palekar, M.D. SUNY Downstate Medical Center, Psychiatry, 107 Saint Marks Avenue, Apt # 3, Brooklyn, NY, 11217, 9000, Carl I. Cohen, Paul M. Ramirez, Shilpa P. Diwan, Ipsit Vahia, Pia Natalya Reyes, Azziza O. Bankole

Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify the various factors, which influence adaptive functioning in elderly schizophrenic persons, and able to modify the treatment plan to include various service strategies to enhance functioning that target clinical, psychosocial, and environmental risk factors.

Summary:

Rationale: Adaptive functioning entails the ability to handle instrumental activities of daily living (IADL) and to establish socially meaningful relationships. We examine factors associated with IADL and close relationships (confidants) in older schizophrenic persons.

Methods: The Schizophrenia group (S) consisted of 198 persons age 55+ living in the community who developed schizophrenia before age 45. We excluded persons with substantial cognitive impairment. We used an adaptation of Berkman-Guralnik’s model of social functioning for our analyses that consisted of two dependent variables: instrumental activities of daily living (IADL) and number of confidants, and 14 independent variables. Using a community comparison group (n=113), we dichotomized the dependent variables into persons scoring in the lower third /upper two-thirds of the IADL scale and the confidant variable. We then used these cut-off scores for the S group; 37% and 41% fell in the high cut-off groups for the IADL and the confidant variables, respectively.

Results: In logistic regression, 4 of 14 variables attained significance for being in the high IADL group: non-white, fewer negative symptoms, fewer physical disorders, and non-group living. Three of 14 variables attained significance for being in the high confidant group: younger age, higher income, greater use of “finding meaning” as a coping strategy. Our model attained significance in both analyses.

Conclusion: The IADL and confidant groups were not associated with each other in the logistic regression analysis. Thus, they seem to be separate measures of functioning. Like older persons in general, there is a wide range of adaptive functioning among older schizophrenic persons that will require more individualized service strategies. Our findings suggest service strategies to enhance functioning must concomitantly target clinical, psychosocial, and environmental risk factors.

References:

A Study for Alexithymia in the Patients with Panic Disorder

Min-Sook Kim, Sr., M.D. Sanggye-Paik Hospital, Inje University, Department of Neuropsychiatry, Sanggye-Paik Hospital

Educational Objectives:

To evaluate and recognize the negative prejudices to sleep pills and demonstrate taking sleep pills with psycho-education could change this negative viewpoint.

Summary:

Objective: To evaluate and recognize the negative prejudices to sleep pill and demonstrate taking sleep pills with psycho-education could change this negative viewpoint.

Design & Method: We examined fifty psychiatric outpatients who never have experiences of taking sleep pills in 1st visit and follow up after taking sleep pills with psycho-education by using questionnaire of prejudices to sleep pills.

Result: We demonstrate that most of them had various negative prejudice to sleep pills and their erroneous idea came from the media, their neighbors, pharmacists even from their physicians. We also recognized that taking sleep pills with psycho-education could change some of their negative prejudices.

Conclusion: In this survey, we demonstrated the common prejudice about sleep pills and where these erroneous idea from. We also measured whether the experiences of taking sleep pills could change the negative prejudice. In conclusion, Psycho-education of corrective idea to sleep pills on general population and even general physicians can improve treatment compliance and help more patients suffered from insomnia.

References:
Subjective Well-being Under Neuroleptic (SWN) Scale in Korean Bipolar Patients

Chul Na, M.D., Ph.D. Chung Ang University, Seoul Korea, psychiatry, ynpceu@hanafos.com, rachul@hanmail.net, Seoul, 140-757, 5800

Educational Objectives:
To enhance the quality of life for bipolar patients.

Summary:
Objectives: Since the treatment goal of psychiatric disorder has been changed from relieving psychiatric symptoms to restoring to original functions and improving quality of life, subjective evaluation of the treatment by the patients has growing importance. This study investigates subjective well-being in bipolar patients, especially those under neuroleptics.

Method: 45 patients with bipolar disorder, according to DSM-IV, were investigated. Subjective well-being was evaluated by the Korean version of Subjective well-being under Neuroleptics scale (KmSWN) with 20 items, at baseline and four month later. Young Mania Rating Scale (YMRS), Hamilton Depression scale (HAMD), Global Assessment of Functioning (GAF), Clinical Global Impression Scale (CGI-S), Clinical Global Impression Index (CGI-I) were also checked with KmSWN. 36 of them were under neuroleptics at 4th month, but 9 stopped neuroleptics. All of them were under mood stabilizers.

Results: Pre-treatment average scores for KmSWN was 55.4, which significantly declined to 50.0 four months later. Pre-treatment KmSWN score for the neuroleptics group and non-neuroleptics group were 59.6 and 54.7, respectively, and they became 50.2 and 50.0 four month later, which showed no significant change in subjective well-being ness. No correlations were found between pre- and post-treatment subjective well-being and YMRs, HAM-D, CGI-S, GAF.

Conclusion: It seems that symptom improvement does not influence patients' subjective well-being. Since most of the bipolar patients are under any mood stabilizers, addition of the neuroleptics may not have direct impact on subjective well-being. Subjective evaluation of the treatment by the bipolar patients might be influenced by his or her mood, which may cause reliability problems.

References:

Correlates of Nicotine Dependence in a Non-Psychiatric Sample

José María Martínez-Ortega, Sr., M.D. Hospital, Psychiatry, Avenida de las Fuerzas Armadas, 2, Granada, 18014, 4700, Luis Gutiérrez-Rojas, Sr., M.D., Manuel Gurpegui, Sr., M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to demonstrate that Psychiatric morbidity, previous suicide attempts, lack of physical exercise, high caffeine intake and consumption of illegal drugs are significantly associated with high nicotine dependence. Smokers with high nicotine dependence should be distinguished from other smokers in evaluating health status populations.

Summary:
Objectives: It is well documented that mental disorders and suicidal behavior are associated with tobacco smoking. However, investigations in which there is a distinction between high and low nicotine dependence are more recent. The purpose of this study was to evaluate correlates associated with high nicotine dependence such as psychiatric morbidity, suicidal behavior, practice physical exercise and use of caffeine, alcohol and illegal drug.

Method: The analysis was based on sample of 290 participants, ages varying from 18 to 65, in a primary health service of Granada (south of Spain). All of them were assessed with the Fagerstrom Test for Nicotine Dependence (FTND) and with the General Health Questionnaire (GHQ-28).

Results: The prevalence of current smoking was 34.5% and the prevalence of high nicotine dependence was 9.3%. Psychiatric morbidity (GHQ-28>6), previous suicide attempts, lack of physical exercise, high caffeine intake and consumption of illegal drugs were significantly associated with high nicotine dependence. These results remained after controlling for gender or substance abuse. Also there was significant relationship between high nicotine dependence and antecedents of suicide attempts (OR=3.53; IC 95%: 1.53 - 25.98). In the logistic regression model, after adjusting for sex and age, the differences remained statistically significant (OR=0.87; IC 95%: 1.96 - 34.03), as well as the protective effect of married status (OR=0.08; IC 95%: 0.01 - 0.72).

Conclusions: Our results are similar than those found in a previous study (Schmitz et al., 2003) in which the authors suggest that individuals with high nicotine dependence have stronger psychiatric morbidity than those with low or without dependence. Smokers with high nicotine dependence should be distinguished from other smokers in evaluating health status populations. Serial cross-sectional and longitudinal studies of nicotine dependence are needed to determine whether certain groups are especially vulnerable to nicotine dependence when they start smoking.

References:

Holding On and Letting Go: Acculturation Versus Biculturalism Among International Medical Graduates in Residency Training

Tatiana Falcone, M.D. Cleveland Clinic, Psychiatry and Psychology, 1310 Forest Hills blvd, Cleveland Heights, OH, 44118, 9000

Educational Objectives:
1. After reading this poster the participant should be able to recognize multiple stressors that International Medical Graduates face during residency training, and how they go through the adaptation process during residency training.
2. At the end of this presentation the participant should be able to recognize multiple stressors of American Medical Graduates during residency training.

Summary:
Objective: Acculturation is perhaps the most difficult problem many International Medical Graduates (IMG) face during their
training in the United States. Yet little is known about how residents and fellows progress through this adaptation process. Our objective was to assess perceived stressors, mood states, cultural adaptation, consumption of alcohol and chemicals, opinions regarding their peers' responses to stress.

Methods: All residents and fellows at our tertiary care medical center received a demographic survey and trainee stress index. A second questionnaire was mailed to our IMG to measure their cultural adaptation.

Results: Recent immigrants found English as a second language as a significant stressor, while American graduates (USG's) reported medical school debt and family alcohol abuse as more problematic. Adjustment to a new culture, racial and ethnic discrimination and feeling homesick for 2-4 weeks after visits to their home country were significant concerns for international doctors. Contrary to our expectations, IMG reported fewer struggles with general adaptation perhaps due to pre-residency experience living in the US. Cultural adaptation and incorporation of American values are pervasive with most doctors feeling proud of the impact the American culture has in their lives. They celebrate American holidays, engage in American music, and go to American restaurants. While adapting to a new culture, they retain other important characteristics of their native culture such as naming children in their native language, praying in their mother tongue, and developing a mixed group of friends from their homeland and from the US.

Conclusions: For new IMG cultural adaptation process may initially be difficult but the longer they reside in the US, the easier the cultural transition. However racial and ethnic discrimination was perceived as a major stressor during residency training for some IMG. Programs focusing on the celebration of diversity in communities may help decrease this stigma.

References:
severity, comorbidity, and social functioning did not differ between groups.

Conclusions: These preliminary results suggest that although onset on or before age 10 years is fairly common among people with neurotic excoriation, individuals developing this behavior earlier in life have similar clinical characteristics as those with later onset but may be less likely to seek treatment.

References:

NR135  Monday, May 21, 12:30 PM - 2:00 PM
Association of the Polymorphism Ser9Gly in the Dopamine D3 Receptor Gene With Tardive Dyskinesia in a Sample of Greek Inpatients With Chronic Schizophrenic Disorder
Emmanouil N. Rizos, M.D. University of Athens, Medical School, 2nd Dpt of Psychiatry, panpsych@attikonhospital.gr, medrizos@yahoo.com, Athens, 12462, 4840, Nikolaos Siafakas, M.D., Loukia Zerva, M.D., Christos Ghristodoulou, M.D., Rossetos Gournellis, M.D., Konstantinos Katsafouros, M.D., Lefteris Lykouras, Ph.D.

Educational Objectives:
- As a conclusion of this presentation our results demonstrate the association between the Gly variant of the DRD3 gene with the development of TD through the probable malpartition of dopamine D3 receptor in the locomotor area of brain.

Summary:
Tardive dyskinesia is one of the most serious drug-related side effects with high prevalence and potentially irreversible nature. Several genetic polymorphisms were investigated for an association with tardive dyskinesia. The Ser9Gly variant in the Mscl restriction site of the dopamine D3 receptor gene was reported to be associated with increase risk for tardive dyskinesia. In this study we have investigated the association of Ser9Gly polymorphism of the dopamine D3 receptor gene with tardive dyskinesia in 73 Greek inpatients with schizophrenic disorder and in 31 healthy volunteers. Specifically the frequencies of the genotypes of Ser/Ser, Ser/Gly and Gly/Gly in 42 schizophrenics with tardive dyskinesia were 11 (26%), 27(64%) and 4(10%), while the corresponding frequencies in 31 schizophrenics without tardive dyskinesia were 12(20.5%), 20(64.5%) and 1(13%). Additionally the frequencies of the genotypes of Ser/Ser, Ser/Gly and Gly/Gly in 31 healthy volunteers were 11(34%), 17(53%) and 4(12.5%). There was found a significant difference in the Abnormal Involuntary Movement Scale (AIMS) in patients homozygous for the glycine variant of the DRD3 gene, as compared to both heterozygous and serine homozygous patients (X² = 8.126, df =2 and P = 0.017, Kruskal-Wallis test). In particular the homozygous Gly/Gly group scored higher in AIMS than the patient subgroups of Ser/Gly and Ser/Ser genotypes. Although the sample was small these findings support a role for the Gly/Gly homozygotes in the Mscl polymorphism site of the dopamine D3 receptor in the pathogenesis and development of TD.

References:

NR136  Monday, May 21, 12:30 PM - 2:00 PM
Patient Knowledge About the Metabolic Syndrome: A Washington Heights Community Service (WHCS) Patient Survey
Christina Manguri, M.D. Columbia University / New York State Psychiatric Institute, Psychiatry, 1051 Riverside Drive, New York, NY, 10032, 9000, Erin Goss, B.A., Michael J. Devlin, M.D., David A. Lowenthal, M.D., Elizabeth Lequesne, M.D., Jean-Marie Bradford, M.D., John W. Newcomer, M.D.

Educational Objectives:
- At the end of the presentation, the participant should be able to:
  1. List the ATP III criteria for the metabolic syndrome.
  2. Recognize that Hispanic patients taking antipsychotic medications are at particularly high risk of developing the metabolic syndrome.
  3. Understand the variable knowledge that patients have about the metabolic side effects of the medications they take.
  4. Recognize the preferred interventions to treat metabolic side effects of medications by patients on a predominantly Hispanic community inpatient unit.

Summary:
Background: Research indicates that Hispanic patients with major mental illness have a higher prevalence of the metabolic syndrome (MS) than schizophrenia patients in CATIE or Hispanics in NHANES, suggesting additive risk. This study aims to address the limited knowledge available on screening for MS criteria within this high risk group, what Hispanic patients actually know about the MS, and what intervention strategies these patients prefer.

Study Population: The Washington Heights Community Service (WHCS) serves acute psychiatically ill inpatients, many Hispanic, in northern Manhattan.

Methods: We are recruiting 60 WHCS patients taking antipsychotic medications. Participants answer a brief survey covering their knowledge about their medications and preferred intervention strategies. After discharge, charts are reviewed for demographic information; ATP III criteria for the MS; weight; and evidence of provider education/treatment/documentation of the MS.

Results: Of the 29 patients recruited so far, 68% were overweight or obese (BMI ≥25). No patients had waist circumferences measured. Among those patients who had all remaining ATP-III MS criteria measured (63%), 21% fit criteria for the MS. All patients who met full criteria for the MS received treatment. However, many patients fitting only partial criteria were not adequately treated. Most patients (59%) knew that antipsychotic medications could cause symptoms of the MS, but only one knew the definition of the MS. Behavioral interventions were generally preferred over pharmacological treatment, especially among Spanish-speaking patients.

Discussion: Despite some screening for MS criteria, few patients were treated if they did not meet full criteria for the MS. The majority of patients are aware of metabolic risk associated with antipsychotic medications. Our pilot data indicate that these patients may prefer behavioral interventions over pharmacological interventions.

References:
Impact of Cannabis Use on Injection Patterns and Syringe Sharing among Injection Drug Users

Didier Jutras-Aswad Centre Hospitalier de l'Université de Montréal, Research center, 4821 St-Laurent blvd #302B, Montreal, PQ, H2T 1R6, 1220, Julie Bruneau, Geng Zang

Educational Objectives:

At the conclusion of this presentation, the participants should be able to recognize patterns of drug use, injection practices and sociodemographic characteristics of regular cannabis users among injection drug users (IDU). They should also be able to critically assess the relation between cannabis use and risky injection practices during an injection episode, taking into account previous individual pattern of cannabis use.

Summary:

Background: Injection drug users (IDU) are vulnerable to social, mental and health problems, one of the most important being the risk of HIV acquisition. Cannabis is the most frequently used illicit drug around the world and some studies have showed that almost 75% of IDU use this substance.

Objectives: The main objectives of this study are to assess the socio-demographic characteristics and drug use of regular cannabis users among IDU and to examine the relation between cannabis use and risky injection behaviors during injection episodes among regular and non-regular cannabis users.

Methods: Participants were recruited from a prospective cohort study of IDU followed between 2004 and 2006. They were asked to describe their socio-demographic status, pattern of drug use, injection behaviors and their last week (day by day) of drug use. Regular cannabis users (RCU), defined as IDU having used cannabis on average every second day for the past six months, were compared with non-regular cannabis users (NRCU). Chi-square, t-test and logistic regression were used for analyses and Generalized Estimating Equations (GEE) method to control for repeated measures.

Results: 527 participants were included, 189 (35.9%) were classified as RCU and 338 (64.1%) as NRCU. No difference was found between the two groups regarding most socio-demographic characteristics, drug use and injection practices. However, univariate analyses showed that, among RCU, cannabis abstinence on a given day was associated with an almost five fold increased risk of syringe sharing (OR= 4.713, p<0.05).

Conclusions: Our study suggests few differences in injection practices and high-risk behaviors between regular and non regular cannabis users. Yet, cannabis use during an injection drug episode seems to have a protective effect on syringe sharing among regular cannabis users. This finding has to be further explored, as it could have implications for treatment and prevention strategies.

References:


findings and show no difference for the ASD group in relation to with no history of SUD.

distinctly different personality profile than the never-, or current-
the high persistence profile in ADHD prior to treatment of SUD is
Tatiana Falcone, M.D.
Cleveland Clinic, Psychiatry and
showed a lower self-directedness (p<0.05) than ADHD subgroup 
SUD status. The ADHD subgroup with previous SUD shows a
treatment effectiveness. ASD personality profiles for all SUD sta-
2. Carey KB, Carey MP, Simons JS: Correlates of substance use 
tuses as well as the ADHD profile for SUD is in agreement with
earlier findings in literature.

**Summary:** Objective: The authors present preliminary data of personality characteristics in relation to the presence of Substance Use Disorder (SUD) in adults with attention deficit and hyperactivity disorder (ADHD) or autism spectrum disorder (ASD).

Substance Use Disorder (SUD) occurs more frequently in adults with ADHD and ASD. For effective SUD prevention and treatment programs for people with ADHD or ASD, more insight in this comorbidity is needed

**Method:** Consecutive newly admitted adults with ADHD (N=36) or ASD (N=35), were assessed for substance use disorders and completed the abbreviated Temperament and Character Inventory (VTCI-105). Raw data for each personality dimension were compared to the addiction-, age- and sex-matched norm groups using ANOVA analysis.

**Results:** Patients with ASD reported high harm avoidance, low reward dependence, and low self-directedness. Patients with ADHD reported high novelty seeking, high harm avoidance, low self-directedness, and low cooperativeness. Within the ADHD sample, the subgroup with a previous SUD showed significantly higher Persistence (p<0.005). The ADHD current SUD subgroup showed a lower self-directedness (p<0.05) than ADHD subgroup with no history of SUD.

**Conclusion:** The results for ADHD and ASD replicate previous findings and show no difference for the ASD group in relation to SUD status. The ADHD subgroup with previous SUD shows a distinctly different personality profile than the never-, or current-SUD subgroups. Prospective follow-up studies need to verify that the high persistence profile in ADHD prior to treatment of SUD is associated with a high response rate. This will greatly enhance treatment effectiveness. ASD personality profiles for all SUD statuses as well as the ADHD profile for SUD is in agreement with earlier findings in literature.

**References:**

**NR140 Monday, May 21, 12:30 PM - 2:00 PM**
**First Psychotic Episode In Children a Retrospective Review of 102 Cases**
Tatiana Falcone, M.D. Cleveland Clinic, Psychiatry and Psychology, 1310 Forest Hill Blvd, Cleveland Heights, OH, 44118, 9000, Kathleen Franco, M.D., Barry Simon, D.O.

**Educational Objectives:**
At the conclusion of this presentation the participant should be able to recognize prognostic factors for the development of psychosis in children and adolescents also recognize importance of laboratory testing in children with psychosis and start the treatment early enough.

**Summary:**
**Introduction:** Lengthy delays of 3 months to 6 years are not uncommon for children with first episode psychosis. We hoped to identify variables that could lead the clinician to earlier consideration of psychosis and factors that may lengthen the course.

**Methods:** We collected psychiatric admission data from 2003-2006 from our child and adolescent psychiatric unit. Of the 1500 cases reviewed, 102 patients younger than 18 years old had their first episode of psychosis. According to the developmental model 127 variables were identified as possible risk factors of conversion to schizophrenia. All the data recorded from the medical records was analyzed using a multivariate model and SAS 9.1 software. Psychotic symptoms were compared to demographic, diagnostic and treatment responses using a chi square model.

**Results:** Variables associated with only partial improvement of psychosis included male gender, disorganized behavior, motor symptoms specially catatonic behavior. CBC abnormalities were present in 75% of the patients, the most common abnormality was monocytosis. Fifty percent of all the patients were already treated with antipsychotics before arriving on the ward, and from that group, 47.05% had EKG abnormalities. A history of psychosis in a first degree relative or grand parent was highly associated with psychosis. Patients with negative symptoms were more likely to have family psychiatric history. Fifty percent of our population had a previous history of ADHD. Separation anxiety was associated with the development of childhood psychosis. Patients with a history of legal problems were more likely to consult first to the legal system and also have history of smoking and substance abuse. The majority (79%) reported a history of physical, emotional or sexual abuse. The suicide attempt rate was 32%, higher than rates in schizophrenia.

**Conclusions:** Family history, prior psychiatric disorders increase the risk for childhood psychosis. Gender, disorganized behavior and motor symptoms may predict poorer outcome.

**References:**

**NR141 Monday, May 21, 12:30 PM - 2:00 PM**
**Pathways to Substance Use: A Structural Model Approach Exploring the Influence of Temperament, Character and Childhood Adversity in 998 Randomized Prisoners**
Michael Lukasiewicz, M.D. Hopital Paul Brousse, Centre de recherche et de traitement des addictions, 12 avenue P v coutrier, Villejuif, 94800, 4278, Xavier Neveux, M.A., Bruno Falissard, Michel Reynaud, Isabelle Gasquet, Ph.D.

**Educational Objectives:**
To give the audience: a) information on structural modeling; b) information on TCI; and c) explain how the structural model may help to understand the contribution of personality and environment to substance use disorder.
Objective: Biological and environmental factors are believed to share the responsibility for vulnerability to substance abuse. A better knowledge of their interaction and respective influence remains an important and unsolved goal of addiction research. Cloninger's model of personality proposes two set of explanatory variables, three stable innate temperaments and four more environmentally-driven characters. Our objectives are 1/to study the relative influence of temperament, character and childhood adversity in the development of addiction. 2/to compare the patterns found among alcoholics and drug addicts. Our population was a group of prisoners, at high risk of substance abuse and past history of childhood adversity.

Method: A stratified random strategy was used to select 1) 23 prisons among the different types of prison in France, 2) 998 prisoners. Each prisoner was assessed by two psychiatrists, one junior, using a structured interview (MINI 5 plus), and one senior, completing the procedure with an open clinical interview. At the end of the interview the clinicians met and agreed on a list of diagnoses. Cloninger's TCI was used to measure personality. Structural models which have been advocated to disentangle the respective influence of complex risk factors were also used.

Results: The "novelty seeking" temperament was a crucial vulnerability factor, for both alcoholics and drug addicts, in the same proportion. Environmental factors (character and childhood adversity) played a part only in the development of drug abuse. Contrary to expectation and theory, novelty seeking proved to be partially influenced by environment.

References:

NR142 Monday, May 21, 12:30 PM - 2:00 PM
An Innovative Model for the Management of Obstructive Sleep Apnea in Patients With Severe and Persistent Mental Illness
Anthony M. Tobia, M.D. UMDNJ, Psychiatry, 21 Harper Road, Monmouth Jct, NJ, 08852, 9000, Anita Mallya, M.D.

Educational Objectives:
At the conclusion of this session, the participant should have an increased awareness of the prevalence of obstructive sleep apnea (OSA) in the mentally ill, appreciate its sequelae, and understand a systematic model to improve the coordination of care for schizophrenia patients with co-occurring OSA.

Summary:
Introduction: Obstructive sleep apnea (OSA) is a public health problem in the United States. Approximately 1 in 5 adults has at least mild OSA and 1 in 15 adults has OSA of moderate or worse severity. Surprisingly about 75-80% of OSA cases in the U.S. that could benefit from treatment remain undiagnosed. This is a significant cause of preventable morbidity and mortality. Due to their underutilization of primary care services, OSA in the severe and persistently mentally ill may in part explain the increased morbidity and mortality seen in this population.

Methods: 20 Schizophrenic patients attending a Partial Hospitalization program were asked to participate in this pilot study. All patients had a comorbid diagnosis of OSA. Baseline data were taken for three parameters including a) Health-Related Quality of Life Questionnaire, b) Client Satisfaction Survey and a c) "Pre-Test" assessing the individual's knowledge of his or her medical illness (OSA). Patients were asked to participate in a medication group focusing on their mental hygiene and comorbid OSA. During the group, patients completed the three surveys to evaluate the impact of this specialized medication group on their psychiatric and medical illness.

Results: Patients attending a specialized medication group were found to have improved knowledge of their medical illness and greater rates of follow-up with their pulmonologists. A preliminary review of the data revealed improved scores on the Health-Related Quality of Life Questionnaires and Client Satisfaction Surveys.

Conclusions: Treating psychiatrically ill patients in a medication group setting, specifically focused on medical comorbidity, is a unique and efficient model leading to improved quality of care and patient satisfaction.

References:

NR143 Monday, May 21, 12:30 PM - 2:00 PM
Antipsychotics Dosage and Antiparkinsonian Prescriptions
Eric Acquaviva INSEERM U669, PSIGIAM (Paris Sud Innovation Group in Adolescent Mental Health Methodology), Psychiatry, 97 Boulevard du Port Royal, 75679 Paris Cedex 14, Paris, 75679 Paris Cedex 14, 4279, Isabelle Gasquet, Ph.D., Bruno Fallassard

Educational Objectives:
Recent meta-analyses point out that the dosage of antipsychotics is decisive for the occurrence of adverse neurological events. Randomised trials have limitations in the analysis of the link between neurological adverse events and antipsychotic dosage. Observational studies make it possible to study antipsychotic dosage as it is prescribed in ordinary practice. Antiparkinsonians are prescribed for neurological side effects in schizophrenia. The frequency of their prescription reflects the frequency of neurological side effects.

The aim is to study the link between antipsychotic dosage and the prescription of antiparkinsonians in an observational study.

Summary:
Objective: To study the link between the dosage of several antipsychotics and the prescription of antiparkinsonians in an observational study.

Methods: In the context of a national naturalistic prospective observational study, a database containing all the prescriptions from 100 French psychiatrists during the year 2002 was analysed. The inclusion criteria were a diagnosis of schizophrenia or schizoaffective disorder and age over 18. The mean dosage of antipsychotics with and without antiparkinsonians was compared. Since there were multiple prescriptions for a given subject, generalised mixed linear models were also used to study the link between antiparkinsonian prescription and antipsychotic dosage.

Results: Antiparkinsonians were prescribed to 32.9% of the patients. Two groups of antipsychotics were observed relating to differences in dosage when an antiparkinsonian was co-prescribed or not: a first group, where the mean dosage was higher with antiparkinsonians (risperidone, amisulpride and haloperidol) and a second group (clozapine, olanzapine), in which antiparkinsonian co prescription was not related to the dosage of antipsychotics.

Conclusion: As a conclusion, it can be said that it is important to consider the dosage and the type of antipsychotic in the treat-
ment of patients suffering of schizophrenia, because neurological side effects are frequent and can impair quality of life. Moreover the prescription of antiparkinsonians can lead to different side effects such anticholinergic effects.

References:


**NR144**

**Monday, May 21, 12:00 PM - 2:00 PM**

**Adolescents Suicide Attempt With Their Parents Psychotropic Medication: Descriptive Study**

Daniel Matusevich Hospital Italiano, Psychiatry, Florida 336, Buenos Aires, 1005, 3570, Martin Ruiz, Carolina Vairo, Carlos Finkelsstein, Alfredo Job

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to recognize the risk of adolescents’ suicide attempt with their Parent's psychotropic medication

**Summary:**

**Objective:** To determine the frequency in adolescents under 21 years old hospitalized in the Psychiatric Unit of Hospital Italiano of Buenos Aires (HIBA) because of suicide attempt with pills taken by their parents.

**Population and sample**

This study was carried out in a population of patients under 21 years old hospitalized in the Psychiatric Unit of Hospital Italiano of Buenos Aires between September 2004 and February 2006.

**Method:** This is a quantitative, prospective, observational and transversal study

The variables considered were age, gender, cause of admission, suicide method. When the attempt was done with pills we considered what kind of pills and whom they belong to; we also asked about familiar psychiatric history and familiar history of suicide attempt and suicide.

**Results:** We analyzed data from 85 patients. 67% (n=57) were female and 33% (n=28) male. Age range was between 13 and 21 years with a media of 18.05 ± 2 years.

The principal cause of admission was suicide attempt (40.5 ± 3.68%) (n=45).

The suicide attempt method most frequently used was the ingestion of pills (77.8 ± 9.6%) (n=35).

**Discussion:** The majority of adolescents who took pills did it with medication belonging to their parents (82.8 ± 16.32%) (n=29). Within this medication 93% (n=27) were psychotropics.

The availability of suicide methods is related directly to suicide. Without these methods near many autoaggressive impulses may be restrained. The importance of this availability of these methods is often underestimated instead of being modified by prevention.

**References:**


cognitive impairment in ADHD, revealed by the change of Hb during different levels of cognitive load to the participants. At the conclusion of this presentation, the participant should be able to conceptualize ADHD as a functional impairment closely related with the nature and difficulty level of the cognitive demand.

Summary:

Functional Near Infrared Spectroscopy (fNIRS) is a portable, non-invasive brain imaging method measuring the changes in oxygenated hemoglobin (HbO2) and deoxyhemoglobin (HbH) levels particularly in prefrontal cortex. The purpose of this study was to compare the prefrontal HbO2 and HbH levels of adult cases with Attention Deficit Hyperactivity Disorder (ADHD) during a Stroop test with varying levels of difficulty and to evaluate the effects of methylphenidate (Ritalin®) with fNIRS. 10 adult, right handed cases with ADHD and 10 age, gender, handedness, education matched controls were included. There were three Stroop stimuli with increasing difficulty: neutral (NS), congruent (CS) and incongruent (IS). Results showed that 1) the behavioral performance of ADHD subjects on MPH and controls on Stroop test was better than ADHD subjects off MPH, while there were no significant differences between the former two; 2) despite lower behavioral performance during NS, HbO2 was higher in unmedicated ADHD cases, 3) when compared to NS, during the IS, bilateral prefrontal HbO2 and tHb levels were increased and HbH levels were decreased in controls and ADHD subjects on MPH; 4) ADHD subjects on MPH had significantly higher HbO2 in the mid and left lateral prefrontal regions during CS and in the right and left lateral prefrontal regions during IS when compared with ADHD subjects off MPH; 5) despite similar behavioral performance, ADHD subjects on MPH and controls did not show increases in HbO2 in the same prefrontal regions during CS and IS. These results indicated that, unmedicated ADHD cases did not utilize higher HbO2 during the NS effectively, and that they could not increase HbO2 further with increasing cognitive load as the controls did, suggesting a dynamic hypofrontality in unmedicated cases, which methylphenidate (Ritalin®) helped to overcome by increasing HbO2 in broad regions of prefrontal cortex with increasing cognitive load.

References:


NR147  Monday, May 21, 12:30 PM - 2:00 PM
EKG Changes in Psychotic Children After Atypical Antipsychotics
Tatiana Falcone, M.D. Cleveland Clinic, Psychiatry and Psychology, 1310 Forest Hills blvd, Cleveland Heights, OH, 44118, 9000, Kathleen Franco, M.D., Barry Simon, D.O.

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize the importance to do an EKG before starting an atypical antipsychotic in children and whenever possible repeat the EKG when levels have reached steady state.

Summary:

Introduction: Atypical antipsychotics are frequently used in child psychiatry for schizophrenia and off label for symptoms other than psychosis. Recent studies in adult populations caution using some atypical antipsychotics in patients with cardiac problems. In this study we analyzed all EKG's of patients admitted to our inpatient child and adolescent psychiatric unit with first psychotic episode. Methods: Psychiatric admission data was collected from 2003-2006. From 1500 cases reviewed retrospectively, 102 patients younger than 18 years old with first psychotic episode were identified. Analysis was done using SAS 9.1 software, one hundred twenty seven variables were collected including EKG's and the use of antipsychotics at the time of admission and at the time of discharge. Univariate associations between the presence or absence of EKG abnormalities were analyzed using chi-square or Fisher exact test.

Results: Fifty of 102 patients were already taking atypical antipsychotics. There was a significant association between EKG abnormalities and antipsychotic medications used prior to admission. Some of the medications were changed during the course of hospitalizations. There were no significant associations between EKG abnormalities and antipsychotic use at the time of discharge. Conclusions: Anti-psychotics are frequently used in children to control many other psychiatric symptoms different than psychosis. Even before the diagnosis of schizophrenia, 50% of our patients were already treated with antipsychotics. We believe early recognition and treatment of schizophrenia is important but we also advocate for initial EKG's prior to starting medication whenever possible and during follow up when levels have reached steady state.

References:


NR148  Monday, May 21, 12:30 PM - 2:00 PM
Antipsychotic Medication Effect on Glycemic Control in Mentally Ill Patients with Diabetes
Anthony M. Tobia, M.D. UMDNJ, Psychiatry, 21 Harper Road, Monmouth Jct, NJ, 08852, 9000, Hanny Mabrouk, M.D.

Educational Objectives:

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

Discuss the effect antipsychotic medications have on the disease progression of diabetes in patients with severe and persistent mental illness (SPMI).

Recognize the role HbA1c values play in monitoring diabetes, and the relationship between HbA1c and fructosamine values.

Summary:

Introduction: While it is well known that atypical antipsychotics may promote the development of type 2 diabetes mellitus, little is known of their effect on patients with pre-existing diabetes. The purpose of this study is to investigate the relationship between antipsychotic use and the course of pre-existing diabetes in schizophrenic patients. A clearer understanding of the effect that antipsychotics have on diabetes can help guide future treatment and practice guidelines for mentally ill diabetic patients who are prescribed antipsychotics. A secondary aim of this study is to ascertain the relationship between serum HbA1c and fructosamine values.

Conclusions: Anti-psychotics are frequently used in children to control many other psychiatric symptoms different than psychosis. Even before the diagnosis of schizophrenia, 50% of our patients were already treated with antipsychotics. We believe early recognition and treatment of schizophrenia is important but we also advocate for initial EKG's prior to starting medication whenever possible and during follow up when levels have reached steady state.

References:


NR147  Monday, May 21, 12:30 PM - 2:00 PM
EKG Changes in Psychotic Children After Atypical Antipsychotics
Tatiana Falcone, M.D. Cleveland Clinic, Psychiatry and Psychology, 1310 Forest Hills blvd, Cleveland Heights, OH, 44118, 9000, Kathleen Franco, M.D., Barry Simon, D.O.

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize the importance to do an EKG before starting an atypical antipsychotic in children and whenever possible repeat the EKG when levels have reached steady state.

Summary:

Introduction: Atypical antipsychotics are frequently used in child psychiatry for schizophrenia and off label for symptoms other than psychosis. Recent studies in adult populations caution using some atypical antipsychotics in patients with cardiac problems. In this study we analyzed all EKG's of patients admitted to our inpatient child and adolescent psychiatric unit with first psychotic episode. Methods: Psychiatric admission data was collected from 2003-2006. From 1500 cases reviewed retrospectively, 102 patients younger than 18 years old with first psychotic episode were identified. Analysis was done using SAS 9.1 software, one hundred twenty seven variables were collected including EKG's and the use of antipsychotics at the time of admission and at the time of discharge. Univariate associations between the presence or absence of EKG abnormalities were analyzed using chi-square or Fisher exact test.

Results: Fifty of 102 patients were already taking atypical antipsychotics. There was a significant association between EKG abnormalities and antipsychotic medications used prior to admission. Some of the medications were changed during the course of hospitalizations. There were no significant associations between EKG abnormalities and antipsychotic use at the time of discharge. Conclusions: Anti-psychotics are frequently used in children to control many other psychiatric symptoms different than psychosis. Even before the diagnosis of schizophrenia, 50% of our patients were already treated with antipsychotics. We believe early recognition and treatment of schizophrenia is important but we also advocate for initial EKG's prior to starting medication whenever possible and during follow up when levels have reached steady state.

References:


NR148  Monday, May 21, 12:30 PM - 2:00 PM
Antipsychotic Medication Effect on Glycemic Control in Mentally Ill Patients with Diabetes
Anthony M. Tobia, M.D. UMDNJ, Psychiatry, 21 Harper Road, Monmouth Jct, NJ, 08852, 9000, Hanny Mabrouk, M.D.

Educational Objectives:

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

Discuss the effect antipsychotic medications have on the disease progression of diabetes in patients with severe and persistent mental illness (SPMI).

Recognize the role HbA1c values play in monitoring diabetes, and the relationship between HbA1c and fructosamine values.

Summary:

Introduction: While it is well known that atypical antipsychotics may promote the development of type 2 diabetes mellitus, little is known of their effect on patients with pre-existing diabetes. The purpose of this study is to investigate the relationship between antipsychotic use and the course of pre-existing diabetes in schizophrenic patients. A clearer understanding of the effect that antipsychotics have on diabetes can help guide future treatment and practice guidelines for mentally ill diabetic patients who are prescribed antipsychotics. A secondary aim of this study is to ascertain the relationship between serum HbA1c and fructosamine values. As serum fructosamine values may be used as indicators for short term glycemic control, they may prove useful as a more sensitive marker of glycemic control in diabetic mentally ill patients.
clinically diagnosed SUDs in a public mental health clinic, and the treatment. This study determined the prevalence of probable and demographics; psychiatric and SUD diagnoses; results from a of 105 out of 525 new patients presenting over a nine month identifying and managing co-morbid SUDs.

are common among people with mental disorders, many patients may contribute to the low rates of documented identification and values. Larger trials will be needed to further clarify the risk antipsychotic medications may have in the disease progression of diabe-

tics. The participant will learn that provider attitudes and beliefs chotic medications may have in the disease progression of dia-

References:
1. Lambert BL et al.: Diabetes risk associated with use of olanzap-


NR149 Monday, May 21, 12:30 PM - 2:00 PM Identification and Treatment Need for Substance Use Disorders Among Psychiatric Outpatients

Manuj Nangia, M.D. University of Southern California Keck School of Medicine, Psychiatry, 1251 Hern Drive, Walnut, CA, 91789, 9000, Isabel T. Lagomasino, Katherine E. Watkins, Lisa Perez, B.S.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to better understand the degree to which psychiatrists in the outpatient setting are not documenting clinical diagnoses for patients with a full range of co-morbid substance use disorders (SUDs). They should also better understand that only a small proportion of patients are getting documented treatment or referrals. The participant will learn that provider attitudes and beliefs may contribute to the low rates of documented identification and management of SUDs.

Summary:
Objectives: While co-morbid substance use disorders (SUDs) are common among people with mental disorders, many patients remain undiagnosed and little is known about the need for SUD treatment. This study determined the prevalence of probable and clinically diagnosed SUDs in a public mental health clinic, and the need for treatment. We also examined barriers providers face in identifying and managing co-morbid SUDs.

Methods: A chart review was conducted for a random sample of 105 out of 525 new patients presenting over a nine month period to a Los Angeles County mental health clinic. Data included demographics; psychiatric and SUD diagnoses; results from a mandated Department of Mental Health (DMH) DSM IV-based SUD screening tool; and treatment or referrals provided for SUDs. Provider attitudes and beliefs were assessed using a questionnaire distributed to 17 providers.

Results: Of the 105 patients whose charts were reviewed, 31 (30%) were given a clinical diagnosis of substance abuse or dependence, but only 12 (39%) of those had documentation of any type of SUD treatment or referral. Using the DMH screening tool, 22 (21%) and 16 (15%) who screened positive for abuse or dependence, respectively, were not given any SUD diagnosis by the clinician. Problem drinking and high risk drug use were not addressed by providers in the chart. The questionnaire demonstrated that most providers believed their involvement with patients with SUDs will not make a difference, although they knew treatment does work.

Conclusions: Despite using mandated screeners, psychiatrists are not identifying and recording individuals with probable SUDs in the chart and only a small proportion of those are receiving any type of documented treatment or referral. There is a need to implement interventions for a full range of SUD disorders in mental health settings. Provider attitudes and beliefs about SUDs need to be addressed.

References:
1. Rosenthal RN; Alcohol-Related Illness in the Mental Health Patient: Conundrums in Diagnosis and Pharmacologic Management; Reporter Supplement to Psychiatric Times; May 2006: 1-11.

NR150 Monday, May 21, 12:30 PM - 2:00 PM The Safety of Electroconvulsive Therapy in Patients With Severe Aortic Stenosis

Paul S. Mueller, M.D. Mayo Clinic, Internal Medicine, 200 First St, SW, Rochester, MN, 55905, 3000, Roxann D. Barnes, M.D., Ranji Varghese, M.D., Rick A. Nishimura, M.D., Keith G. Rasmussen, Jr., M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to identify aortic stenosis as a risk factor for non-fatal myocardial infarction and mortality in patients undergoing general anesthesia.

Additionally, the participant will learn recommendations that were used in this study for the periprocedural management of patients with aortic stenosis undergoing ECT. Finally, the participant should recognize that ECT was performed successfully and without any major complication, including myocardial ischemia/infarction, or mortality in several patients undergoing ongoing ECT procedures requiring general anesthesia.

Summary:
Background: Patients with severe aortic stenosis may also have depression and other psychiatric disorders for which electroconvulsive therapy (ECT) may be recommended. It is unknown whether ECT, which requires the administration of general anesthesia, can be safely performed in patients with severe aortic stenosis. We sought to investigate the safety of ECT in patients with severe aortic stenosis.

Methods: A retrospective review was conducted of the medical records of all of the patients with severe aortic stenosis who underwent ECT at Mayo Clinic, Rochester, Minnesota, between January 1, 1995 and June 30, 2006.

Results: Ten patients with severe aortic stenosis who also underwent ECT were identified. Of these, 7 (70%) were women. The median age was 79.5 years (range, 65-93 years). All patients had an aortic valve area of 1.0 cm\(^2\) or less (median, 0.9 cm\(^2\)). The median aortic valve gradient was 43.5 mmHg (range, 32-57). The 10 patients underwent a total of 144 ECT treatments (range, 1-
37 treatments). Despite this large number of treatments, only 2 patients experienced single episodes of hypotension during the period of treatment; these episodes were successfully treated. None of the patients died during the period of treatment.

Conclusion: ECT was safe among patients with severe aortic stenosis treated at our institution. However, a prospective study would be needed to determine the precise risk of complications in such patients undergoing ECT.

References:


2. American College of Cardiology/American Heart Association Task Force on Practice Guidelines; Society of Cardiovascular Anesthesiologists; Society for Cardiovascular Angiography and Interventions; Society of Thoracic Surgeons; Bonow RO, Carlo B.

NR151 Monday, May 21, 12:30 PM - 2:00 PM
Reducing Recidivism in Mentally and Cognitively Impaired Patients who reside in Boarding Homes: Results of a Pilot Clinician Study
phil whang, M.D. UMDNJ, psychiatry, 183 SOUTH ORANGE AVE, e level, newark, NJ, 07103, 9000, Michael Y. Hwang

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the inherent problems associated with current resource allocation in New Jersey in providing housing for mentally impaired.

Summary:

Assessments: Multi-item questionnaire titled, "Brief instrument to assess boarding home care and the rate of recidivism" was created. This was a questionnaire to assess for the current limitations of boarding home structure. This maximum score per item was 8 indicating strongest severity of response. Clinicians certified by the screening service of the State of New Jersey were approached and after consent was obtained given the questionnaires. The screening service is a distinct state mandated entity which provides clinicians who are explicitly trained in the state legal and clinical requirements of civil commitment. Clinicians not linked with the screening service of the state of New Jersey were not approached. Results were tabulated and analyzed using descriptive statistics.

Results: 5 screeners certified by the state of New Jersey were surveyed. The mean score on the item assessing for the presence of adequate patient supervision in boarding homes was 7.2. The mean score for the item assessing for the fair and equitable use of federal funds was 6. The mean score for the item assessing for adequate governmental oversight/supervision was 6.8. The item assessing for the impact of improving boarding home supervision and its impact on reduction of rate of recidivism was 8.

Discussion: As a whole groups of experienced clinicians generally expressed moderate to strong reservations about current state of boarding home care pointing explicitly to problems including lack of adequate supervision and training of the staff. Given the highest severity response of 8 on the impact of improved oversight on the quality of boarding homes and its impact on recidivism, this survey suggests that more active oversight by the state government will likely result in measurable improvement of the level of care and also result in overall cost reduction by indirectly reducing the rate of recidivism.

References:


NR152 Monday, May 21, 12:30 PM - 2:00 PM
A Case-control Study of Patients with Resistant Schizophrenia After Clozapine Discontinuation
Grignon Sylvain, Sr., M.D. Sherbrooke University, Psychiatry, 580 Bowen Sud, Sherbrooke, PQ, J1G 2E8, 1220

Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate the likely outcome of patients after clozapine discontinuation concerning symptomatology, metabolic profile, quality of life and medication compliance. The participant will be able to appreciate the distinctive outcome of treatment resistant schizophrenic patients who discontinue clozapine with those who are still on clozapine treatment.

Summary:

Introduction: Clozapine is considered to be the reference treatment for resistant schizophrenia, but a significant number of patients will discontinue it. This poster presents a summary of a case-control study of patients who had (DC group) or had not (CLZ group) discontinued clozapine.

Method: Patients with a diagnosis of schizophrenia were eligible if they had received clozapine for a minimum of two months for treatment resistance pathology. 44 subjects have been recruited. 22 subjects had discontinued the clozapine (DC group) and were matched with 22 subjects under clozapine (CLZ group).

Subjects were separated in two groups according to their current status: CLZ group or DC group. Assessments consisted of chart review, biometric measurements, CGI-5 evolution for patients in the DC group, and one clinical interviewing using scales: Positive And Negative Syndrome Scale (PANSS), Calgary Depression Scale (CDS), Abnormal Involuntary Movement Scale, Drug Attitude Inventory (DAI-10), Global Assessment of Functioning (GAF) and Quality of Life Scale (QLS), occupational status, metabolic parameters.

Results: Service utilization tended to be higher before clozapine treatment in the CLZ group, and during and after clozapine treatment in the DC group. CGI-5 evolution scores for the DC group obtained were suggestive of significant clinical deterioration (CGI-E=2.7; CI 1.7-3.8). The main finding of the study, was the unexpected similarity between the two groups who did not differ significantly for functional, occupational, clinical and metabolic status. Treatment regimens were also quite similar and were characterized by the high prevalence (50 %) of antipsychotic polypharmacy (mean: 1.6 antipsychotic/patient).

Occupational rates did not differ from the two groups. Higher scores on the QLS were associated with work.

Discussion: This study, in spite of the methodological limitations and limited sample size, suggests that clozapine discontinuation is not necessarily associated with a long term worsening of the clinical course.

References:

"Diabetes Integration of Care by Mental Health Providers"

Brian K. Cooke, M.D. University of Maryland Medical Center, Psychiatry, 701 W. Pratt St., Baltimore, MD, 21201, 9000, Ann L. Hackman, M.D., Richard W. Goldberg, Ph.D., Lisa B. Dixon, M.D., M.P.H.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the involvement of mental health providers in monitoring diabetes care.

Summary:

Background: Diabetes affects 16-25% of people with schizophrenia. Both mental health and primary care play a role in managing diabetes among persons with severe mental illness (SMI).

Objective: We examined the involvement of mental health providers (MHP’s) at a community mental health center in patients’ diabetes care and tested whether clinical or demographic variables were correlated with MHP involvement.

Methods: We assessed 100 persons with schizophrenia and Type 2 Diabetes. Participants were asked if in the past six months their MHP asked about diabetes behaviors, diabetes medications, asked to speak with their diabetes doctor, or provided diabetes education.

Results: About 49% of participants reported that their MHP’s asked about diabetes health behaviors. Close to 40% reported being asked about diabetes medication. Only 16% reported that their MHP’s asked to speak with their diabetes doctor. Finally, a smaller proportion (14%) reported being provided diabetes education.

Conclusions: Recent research establishing the link between genetic variants in the RGS4 gene and schizophrenia in this sample; even though the genetic analysis suggested that the Chilean sample showed similarities with ethnically different samples, previously described as having association with this gene. Among other explanations, these results might be the consequence of inadequate statistical power.

References:

RGS4 Genetic Variants and Schizophrenia: A Structured Case-control and Family Study in an Admixed Sample in Chile.

Aida Ruiz, M.D. Universidad de Chile, Psiquiatria y Salud Mental, Avenida La Paz 1003, Santiago, 70100, 3370, Robin Murray, M.D., John Powell, Ph.D., Eduardo Miranda, M.D., Carlos Encina, M.D., Mario Quijada, M.D., Pak Sham, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the most common study designs for genetic association analysis

Summary:

Introduction: Recent analyses have reported that polymorphisms in the RGS4 gene, on 1q21-22, are associated with schizophrenia. This study analysed this possible association in an admixed sample, ethnically different from populations examined in previous reports.

Methods: The study was carried out in a case-control sample composed of 112 cases with DSM-IV schizophrenia, and 240 unaffected control subjects; and a sample of 44 DSM-IV schizophrenia families, recruited in Santiago, Chile. Four RGS4 markers, previously associated with schizophrenia, and 10 ancestry-informative markers were genotyped. The data were analysed by means of the UNPHASED program. Intermarker linkage disequilibrium (LD), single marker and haplotype associations were evaluated using the Pedigree Disequilibrium Test (PDT) and COCO-PHASE. Analysis of population stratification, in the case-control sample, was carried out using L-POP software. The structured association analysis was performed with WHAP program.

Results: The analysis of population structure detected stratification in the case-control sample; however the cases and controls were well matched. All markers were in Hardy-Weinberg equilibrium. Significant LD was observed for all pairwise calculations. In both samples, none of the SNPs included in this analysis were found to be associated with illness (P >0.05), and no significant haplotypic association was observed (P > 0.05). The structured association analysis did not show confounding effects of population stratification.

Conclusions: No evidence was found to support an association between genetic variants in the RGS4 gene and schizophrenia in this sample; even though the genetic analysis suggested that the Chilean sample showed similarities with ethnically different samples, previously described as having association with this gene. Among other explanations, these results might be the consequence of inadequate statistical power.

References:
Summary:

Introduction: Evidence for association between schizophrenia and the Dysbindin gene in a Chilean admixed sample.

Methods: Forty-four families affected by schizophrenia; and a case-control sample composed of 112 schizophrenic patients, and 240 unaffected control individuals, were collected in Santiago, Chile. Diagnosis was made according to DSM-IV criteria. Ten Dysbindin SNPs reported to be associated with schizophrenia, and ten ancestry-informative markers were selected for genotyping. Inter-marker linkage disequilibrium (LD) was measured using UNPHASED program. The Pedigree Disequilibrium Test (PDT) and the COCAHPHASE program were used to analyse single marker and haplotype associations. A population structure analysis was performed using the L-POP program, to detect hidden population stratification in the case-control sample. The WHAP program was used to carry out the structured association analysis.

Results: Even though the analysis of population structure found evidence for population stratification, the cases and controls were well matched. In both samples, no deviation from the Hardy-Weinberg equilibrium was found and significant LD was observed for most pairwise calculations. No single marker achieved a significant allelic association (p<0.05), and tests for haplotype analysis showed no association (p<0.05). Structured association analysis of Dysbindin gene did not detect possible spurious findings in the case-control sample.

Conclusion: In comparison with previous studies in ethnically diverse samples, the Chilean samples showed a similar pattern of allele frequencies, LD patterns, and haplotype frequencies. However, association between Dysbindin gene and schizophrenia was not confirmed. Potential methodological limitations of association studies could explain these results.

References:

NR156 Monday, May 21, 12:30 PM - 2:00 PM
Genetic Overlap Between Bipolar Disorders and Schizophrenia?: Potential Advantages of Latin-American Admixed Populations for Genetic Studies
Aida Ruiz, M.D. Universidad de Chile, Psiquiatría y Salud Mental, Avenida La Paz 1003, Santiago, 70100, 3370, Pak Sham, M.D., Robin Murray, M.D., John Powell, Ph.D., Sonia Medina, M.D., Paul Voehringer, M.D., Jorge Cabrera, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the designs for genetic association analysis the role of genetic factors in the aetiology of complex disorders, and the possible genetic overlap between schizophrenia and bipolar disorders. The paper reviews candidate gene studies on schizophrenia and bipolar disorders in Latin-American samples.

Methods: All citations in Medline up to October 2006, and recent conference reports were collected. Family and case-control studies of candidate genes in bipolar disorders and schizophrenia were included. Statistical package SPSS v.12.0 was used for descriptive data analysis.

Results: A total of 25 studies, including case-control or family designs, were found. Twenty-four candidate genes were examined in schizophrenia and/or bipolar samples, obtained from five populations: Brazilian, Chilean, Colombian, Costa Rican, and Hispanic USA. Diverse and discrepant association results were reported. Ancestry-informative markers for controlling population stratification, and structured association analysis, were used only in the Chilean case-control samples.

Conclusion: Methodological limitations, associated with inadequate statistical power and insufficient control for population stratification, among others, might be an important source of inconsistent results. Structured association methods should be considered in case-control studies of admixed populations.

References:

NR157 Monday, May 21, 12:30 PM - 2:00 PM
Auditory Hallucinations in Schizophrenia Spectrum Disorders: Comparison Between Schizophrenia and Schizoaffective Disorder
Milena Djuric, M.D. Maimonides Medical Center, Psychiatry, 5001 10th Avenue 4A Apt., 914 48th Street, Brooklyn, NY, 11219, 9000

Educational Objectives:
The educational objective of this report is to increase awareness that the affective component in Schizophrenia spectrum disorders may be expressed in auditory hallucinations of music. Auditory hallucinations of music might contribute to distinguishing Schizoaffective disorder from Schizophrenia.

Summary:
Introduction: Auditory hallucinations are considered a core feature of psychosis. The influence of affective component on the form and the content of auditory hallucinations in Schizophrenia spectrum disorders has yet to be explored.

Method: 22 schizophrenic and 23 schizoaffective patients at Maimonides Medical Center were studied. Patients were interviewed using comprehensive questionnaire of fourteen questions, which were related to the form, content and subjective experience of auditory hallucinations. Comparison between the two groups was done using χ² and Fisher's exact probability tests. The study was approved by the Institutional Review Board.

Results: Patients with Schizoaffective disorder experienced hearing music more often than patients with Schizophrenia. The basis for this finding might be in the correlation between mood and music. Music may reflect the psychotic patients' inner mood. This finding might reflect the effect of the affective component on the form and the content of auditory hallucinations in Schizophrenia spectrum disorders and suggests that music should be consi-
Comorbid Obsessive Compulsive Disorder in Patients with Schizophrenia

Jee Young Kim, M.D. INHA University Hospital, Psychiatry, 7-206 3Ga, Shinheung-dong, Jung-gu, Incheon, Korea, 400-711, 5800, Young Kyung Sunwoo, M.D., Myung Ji Lee, M.D., Ji Suk Jun, M.D., Min Hee Kang, M.D., Chul Eung Kim, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate that obsessive-compulsive disorder is relatively frequent in schizophrenia patients and significantly correlated with the severity of psychotic symptoms and general functioning.

Summary:

Objectives: Obsessive-compulsive disorder have been observed in a substantial proportion of schizophrenia. This study aimed to evaluate the prevalence of obsessive-compulsive disorder in schizophrenia, and the relationship between obsessive-compulsive disorder and severity of psychopathology, depressive symptoms and quality of life.

Methods: We interviewed 87 patients, diagnosed with schizophrenia and classified patients according to the existence of OCD evaluated by the Structured Clinical Interview for DSM-IV. And we evaluated the clinical and demographic data. To investigate the interrelationship, Yale-Brown Obsessive-Compulsive Scale(Y-BOCS), Positive and Negative Symptom Scale(PANSS), Clinical Global Impression-Severity(CGI-S), Hamilton rating scale for Depression(HAM-D), Global Assessment of Functioning(GAF) scale, WHO Quality of life(OoL WHO) were applied.

Results: The prevalence of obsessive compulsive disorder in schizophrenia patients was 16.1%. Patients with schizophrenia and obsessive-compulsive disorder had higher mean PANSS-general psychopathology and total score than schizophrenia patients without obsessive-compulsive disorder. The total score on Y-BOCS was significantly correlated with PANSS-positive score, GAF scale.

Conclusion: Obsessive-compulsive disorder is relatively frequent in schizophrenia patients and significantly correlated with the severity of psychotic symptoms and general functioning.

References:


NR158 Monday, May 21, 12:30 PM - 2:00 PM

Comorbid Obsessive Compulsive Disorder in Patients with Schizophrenia

Summary:

Objective: Hospital staffs are usually under tremendous stress in work. High work-related stress might increase the vulnerability of mental illness, emotional exhaustion, and health complaints and also influence job performance leading to the poor quality of care for the patients. However, many health surveys conducted in the hospital most focused on doctors and nurses and less paid attention to other ancillary employees. The aims of this study are to investigate the point prevalence and risk factors for minor psychiatric morbidity or depression in all staffs working in general hospitals.

Method: The study was conducted in a regional hospital that employed around 1,005 staffs. Doctors, nurses, administrative and ancillary staffs were screened by self-rating questionnaires including Chinese Health Questionnaire (CHQ-12), Center for Epidemiologic Studies Depression Scale (CES-D) and WHOQOL-BREF. Participants were all voluntary, anonymous, and no incentives are offered.

Results: Of the 1,005 questionnaires sent out 719 were returned and the response rate was 71.5%. Most of respondents were nurses (46.7%) and administrative staffs (15.2%). Of the 232 (32.3%) respondents probably morbid with minor psychiatric disorder (CHQ-12 scores above 3). On the other hand, 236 (33.5%) respondents might be a case of depression (CES-D scores above 20). Forty-seven percents of subjects were cases of either minor psychiatric disorder or depressive disorder, and nurses were with the highest prevalence and followed by pharmacists. For further analyses, nurses and doctors were put together as a group and the rest staffs as another group for investigating any associating factors. After logistic regression, female and doctors or nurses and less paid attention to other ancillary employees. The aims of this study are to investigate the point prevalence and risk factors for minor psychiatric morbidity or depression in all staffs working in general hospitals.

Method: The study was conducted in a regional hospital that employed around 1,005 staffs. Doctors, nurses, administrative and ancillary staffs were screened by self-rating questionnaires including Chinese Health Questionnaire (CHQ-12), Center for Epidemiologic Studies Depression Scale (CES-D) and WHOQOL-BREF. Participants were all voluntary, anonymous, and no incentives are offered.

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Results: Of the 1,005 questionnaires sent out 719 were returned and the response rate was 71.5%. Most of respondents were nurses (46.7%) and administrative staffs (15.2%). Of the 232 (32.3%) respondents probably morbid with minor psychiatric disorder (CHQ-12 scores above 3). On the other hand, 236 (33.5%) respondents might be a case of depression (CES-D scores above 20). Forty-seven percents of subjects were cases of either minor psychiatric disorder or depressive disorder, and nurses were with the highest prevalence and followed by pharmacists. For further analyses, nurses and doctors were put together as a group and the rest staffs as another group for investigating any associating factors. After logistic regression, female and doctors or nurses and less paid attention to other ancillary employees. The aims of this study are to investigate the point prevalence and risk factors for minor psychiatric morbidity or depression in all staffs working in general hospitals.

NR160 Monday, May 21, 12:30 PM - 2:00 PM
Patients As Parents: A Survey of Mental Health Services Ability to Cater for the Needs of Inpatients Who Are Parents
Pradeep Peddu Vi, M.B.B.S. Gloucestershire Partnership NHS Trust, Psychiatry, 9 Katmandu Rd, Bromsgrove, b60 2sp, 4120

Educational Objectives:
- My poster presentation should increase awareness of parenting issues faced by inpatients who are parents. Particularly the reciprocal impact of mental health difficulties in both parents and children.

Summary:
- To investigate whether junior doctors and ward staff are aware of patients needs as parents by exploring in-patient's experiences and looking at the facilities available.

Background: Psychiatric disorder in an adult who is a parent is associated with an increased risk of psychiatric disorder in his or her child. On the other hand concerns about children may well have had an influence on the course and severity of a parent's mental disorder. Psychiatrists can act positively to help patients who are parents to meet the needs of their children and ensure their safety. A broader concern was whether issues related to childcare, safety and mental health education to children are recognized by the staff. Little research is done in this area.

Method: Patients were interviewed prior to discharge on 8 inpatient units in West Midlands. Information regarding hospital policy on children visiting and available facilities for them was compiled for each unit.

Results: 75 patients were interviewed. 36% of patients were not asked whether they had children when admitted. 88% of them felt that no help was offered with childcare arrangements during their admission. 87% of them felt that no information was given to the children. 48% had concerns about children visiting the ward. 70 of 8 units didn't have designated areas to see children nor had written information suitable for children. Few staff had up to date training in child protection.

Conclusion: There is a need to provide training for doctors and nurses to increase awareness of the needs of patients in their role as parents, and in child protection.

References:

NR161 Monday, May 21, 12:30 PM - 2:00 PM
A Comparative Study of Schizophrenia Outpatients With and Without a Comorbid Depression
Shakila Tanjim, M.D. Kansas University Medical Center, Psychiatry, 3901 Rainbow BLVD., Mail stop 4015, Kansas City, KS, 66160, 9000, Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.A., Ekkehard Othmer, M.D., Cherilyn DeSouza, M.D., William F. Gabriele, Jr., M.D.

Educational Objectives:
- At the conclusion of this presentation, the participants should be able to recognize important clinical differences between schizophrenia patients with and without major depression.

Summary:
- Objective: To compare a large group of schizophrenia outpatients with and without comorbid major depression on multiple clinical dimensions.
- Method: During a five-year period, all new patients in a large psychiatric outpatient clinic were administered a structured diagnostic interview, a psychosocial history, and the Symptom Checklist-90-R. Of the 1458 patients, 192 (13%) were diagnosed with schizophrenia (DSM-III criteria). Of the 192 schizophrenic patients, 136 (71%) also satisfied inclusive diagnostic criteria for major depression.
- Results: No sociodemographic differences were found between the two groups. More psychiatric disorders among first degree relatives were found for schizophrenia outpatients with major depression: Alcoholism (50% vs. 18%) and Somatization Disorder (30% vs. 14%), but not familial depression or schizophrenia, were significantly more prevalent in relatives. Similarly, significantly greater psychiatric comorbidity was found for schizophrenia outpatients with major depression including Obsessive Compulsive Disorder, Phobia, Panic Attack, and Mania. In addition, the SCL-90 symptom profiles of both outpatient males and females with major depression showed significantly higher levels of current distress.

References:

NR162 Monday, May 21, 12:30 PM - 2:00 PM
Haloperidol and Survival in Non-Intubated Intensive Care Unit Patients
Vanessa W. Wong, M.D. Wilford Hall Medical Center, Psychiatry, 2200 Bergquist Drive, Life Skills Support Center, Lackland AFB, TX, 78209, 9000, Jason E. Schillerstedt, M.D., Kaustubh G. Joshi, M.D., Jonathan Chang, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to recognize that administration of haloperidol to patients in an intensive care unit (ICU) setting does not increase mortality rates. Incidentally, participants should also become aware that patients who receive haloperidol in the ICU have increased length of hospital stay.
NR163 Monday, May 21, 12:30 PM - 2:00 PM
Ten-Year Outcomes of Male Alcoholics: Does Race Matter?

Tanya Scurry, M.D., University of Kansas Medical Center, Psychiatry, 3901 Rainbow Blvd, Mail Stop 4015, Kansas City, KS, 66160, 9000, Barbara J. Powell, Ph.D., Elizabeth C. Penick, Ph.D., Peggy Kriehok, Ph.D., Jan Campbell, M.D., Elizabeth J. Nickel, M.A., H. Mikel Thomas, M.D.

Educational Objectives:
At the conclusion of this poster presentation, the participant should be able to recognize the relationship between ethnic background and long-term treatment outcomes of male veterans with alcoholism.

Summary:
Objective: To determine the influence of race on the one and ten-year outcomes of hospitalized male alcoholic veterans.
Method: Two hundred fifty-five male inpatient alcoholics were comprehensively evaluated at intake, one year and ten years later. Assessment measures included structured interviews, psychometric tests, and rating scales. Both drinking and non-drinking clinical outcomes were examined.

NR164 Monday, May 21, 12:30 PM - 2:00 PM
The Factors Related to Tobacco Craving in Smoking Workers.

Ho Jin Choi, M.D., Eulji university hospital, Neuropsychiatry, Eulji university hospital, Dunsandong, Seo Gu, Daegon, 302-799, 5800, Burn Seok Jeong, M.D., Se Jin Kim, M.A., Chang Hwa Lee, M.D., Kyeong-Sook Choi, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that the alcohol habit and mood, as well as the smoking habit, have an effect on tobacco craving.

Summary:
Objective: The aim of this study is to examine the factors related to tobacco craving in smoking workers using Tobacco Craving Questionnaires(TCQ) and other measures.
Method: Subjects of this study were 212 male working smokers, 18 to 65 years of age. Subjects were divided into two groups determined by the measurement of their tobacco craving level using the TCQ. Depending on their scores, the upper 25% were classified into the group with high TCQ scores, and the bottom 25% were classified into the group with low TCQ scores. Between the two groups, we compared the social demographical scale, alcohol drinking and smoking habits, Job Stress Scale (JSS), Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), Alcohol Use Disorder Identification Test (AUDIT)-CAGE.
Results: A total of 212 subjects, of whom 55 were included in the group with high TCQ scores and 55 were included in the group with low TCQ scores. There were no significant differences between both groups in demographic factors. The daily maximum smoking, and the scores of JSS, STAI, BDI, AUDIT and CAGE were significantly greater for the group with high TCQ scores compared to the group with low TCQ scores. When logistic regression analysis was performed, the daily maximum smoking, BDI and CAGE score were identified as a significant risk factors for tobacco craving.
Conclusion: This study presents that tobacco craving is significantly related to daily maximum smoking, depression and alcohol dependence. Therefore, it is necessary to examine the alcohol
use history, mood symptoms, in addition to smoking history, for successful cessation of smoking.

References:

A Dysfunctional Cortico- striatal Network in OCD: Links Between Executive Functions and Functional Neuroimaging by Pet-Scan.
Aurélie Bourguignon Guillaume Régnier Hospital, G 03, 108 avenue Général Leclerc, Rennes, 35000, 4279, Florence Prigent, David Travers, Dominique Drapier, Marc Verin, Bruno Millet

Educational Objectives:
At the conclusion of this presentation, the participant should be able to explain the cognitive abnormalities in OCD and to describe the brain areas implicated in OCD.

Summary:
Background: Many studies have found cerebral metabolism abnormalities in OCD in favor of a dysfunctional cortico-striato-thalamo loop. The aim of this study was to correlate abnormalities of executive functions with abnormalities of cerebral activity. The existence of correlations between cognitive tests and neuroimaging could support the hypothesis of a cortico-subcortical circuitry dysfunction in OCD.

Materials and methods: Eight patients suffering from OCD, treat- ment free for at least 2 weeks (4 weeks for fluoxetine), and six healthy volunteers matched according to sex, age and educational level variables, had a 18F-FDG PET brain scan. Following neuroimaging, patients and healthy volunteers were assessed by neuro- psychological tests.
The images were analyzed according to two set of methods:
- ROI method: comparison of cerebral activity in twelve regions of interest defined according to the atlas of SPAM (Statistical Probability Anatomy Maps), combined in a same volume (mask) than adjusted for each PET-scan.
- SPM2 method: statistical analysis of brain activity with SPM2 software.
The cognitive tools evaluate the visuo-spatial memory, verbal and non-verbal memory, the abilities to develop a strategy and the abilities to recognition of emotions.

Results: Some significant differences (p < 0, 05) were observed for two cognitive tests (verbal fluency and Hopkines test) in patients comparing to healthy volunteers. SPM2 analyze showed also a significant difference (p < 0, 05) between patients and controls with an orbito-frontal bilateral hyperactivity and a bi-temporal hyperactivity predominating on the left side in patient group. ROI method did not find significant differences between both.

Discussion and Conclusion: The results seem to replicate previous studies showing an orbito frontal hyperactivity in OCD patients. Those abnormalities are in line with cognitive dysfunction observed between patients and controls. Correlations will be presented during the poster session. Inclusions progress with 15 patients and 15 healthy volunteers in perspective.

References:

NR166
Mon, May 21, 12:30 PM - 2:00 PM
Assessing the Impact of Mandatory Tobacco Screening Via the Electronic Record on Clinicians’ Involvements with Tobacco Cessation Efforts
Lindsay J. Jordan, M.D. Maimonides Medical Center, Department of Psychiatry, 914 48th Street, Brooklyn, NY, 11219, 9000, Andrew J. Kolodny, M.D.

Educational Objectives:
To demonstrate the methods involved in implementing a mandatory tobacco screening program for all outpatients in a Community Mental Health Center.
To evaluate the impact of the screening program and its accompanying educational campaign on the attitudes and prescribing practices of clinicians.

Summary:
Objective: This study describes the impact of a mandatory tobacco screening initiative accompanied by an educational campaign on psychiatrists’ awareness concerning tobacco cessation.
Method: A mandatory tobacco screening template was added to the electronic record of an outpatient psychiatric department. The electronic record annually prompts clinicians to screen patients for tobacco use and nicotine dependence during psychopharmacology visits. The initiation of the template was accompanied by a staff educational campaign that addressed tobacco screening, motivational interviewing, and nicotine replacement therapy. After three months, clinicians were surveyed on their frequency of tobacco screening and counseling. The electronic record allowed tabulation of how many patients were screened, diagnosed, and treated for tobacco dependence during the 3 month period.

Results: Within 3 months of the template’s initiation, screenings were done on 65.7% of the 852 outpatients, 30% of whom have schizophrenia. 17.5% of the 560 screened patients received a diagnosis of nicotine dependence, of which 45% have schizophrenia. Amongst these 98 patients with dependence, 32 patients received some intervention such as counseling, medication, or referral. The number of patients on nicotine replacement therapy as per prescription data rose from 25 to 28 of the total 852 outpa tients after 3 months. As reported in a survey of 22 clinicians with a 91% return rate, 35% recall regularly screening for smoking before the program began. At 3 months, 90% of clinicians report regularly screening for smoking and discussing tobacco cessation. The majority of clinicians cited the educational components of the program and its mandatory nature as most influencing their changing practices concerning tobacco cessation counseling.

Conclusion: A tobacco screening initiative involving mandatory and educational components has utility in encouraging clinicians to address tobacco use among psychiatric outpatients.

References:
Association Study of DISC1 and Cognitive Deficit in Schizophrenia
Hae Jung Park, M.D. Samsung Medical Center, Psychiatry, Samsung medical center #50, Ilwon-Dong, Gangnam-Gu, Seoul, 135-710, 5800, Kyung Sue Hong, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the effects of DISC1 genotype on the risk for schizophrenia and the cognitive functions of the patients and normal controls in the Korean population.

Summary:
Objectives: Disrupted-in-Schizophrenia-1 (DISC1) has been identified as a positional and functional candidate gene of schizophrenia. Recently specific allele or haplotype of this gene showed genetic association with working memory deficits of schizophrenia in a few Caucasian populations. This study investigates the effects of DISC1 genotype on the risk for schizophrenia and the cognitive functions of the patients and normal controls in the Korean population.

Methods: The subjects were 61 DSM-IV schizophrenia patient and 85 normal controls. A comprehensive neurocognitive test battery including attention and working memory tasks was administered. Genotyping for rs373840 (Gln264Arg) of DISC1 was done with RFLP method. Association analyses between genotype and cognitive functions were performed using General Linear Modeling. We could identify three characteristic cognitive domains, i.e., CD1) possible endophenotype markers: impaired both in the patients and siblings groups, CD2) possible state-dependent markers: impaired only in the patients group, CD3) cognitive functions of which impairment was not observed in the patients or siblings groups.

Results: Significant association was not observed between this polymorphism and schizophrenia disease entity. Significant or trend of differences of cognitive functions between the genotype groups were found only in the patients. Subjects having GG genotype showed significantly poor performance in Span of Apprehension test (p=0.027) tasks, and trend of poor performance in Trail making A (p=0.056), and B (p=0.058) tasks compared to other genotype groups. Analyzing the interactive effect of the diagnosis (patient vs. control) and the genotype, significant interactions and a trend of interaction were observed in Span of Apprehension test (p=0.045), verbal memory (p=0.023), Trail making B tests (p=0.007) and Trail making A tests (p=0.054), respectively.

Conclusion: These results suggest that Gln264Arg polymorphism of DISC1 gene might have a modulating effect on the risk of schizophrenia through the regulation of the cognitive processes.

References:

Outpatient Consultation-Liaison Experience in Resident and Fellow Education
Gayla B. Tennen, M.D. Mayo Clinic, Psychiatry and Psychology, 121 Avalon Cove Circle NW, Rochester, MN, 55901, 9000, James R. Rundell, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize differences in outcomes amongst alcohol-dependent youth of various ethnic backgrounds.

NR167
Monday, May 21, 12:30 PM - 2:00 PM
Association Study of DISC1 and Cognitive Deficit in Schizophrenia
Hae Jung Park, M.D. Samsung Medical Center, Psychiatry, Samsung medical center #50, Ilwon-Dong, Gangnam-Gu, Seoul, 135-710, 5800, Kyung Sue Hong, M.D.

Educational Objectives:
At the conclusion of this presentation, participants should be able to articulate clinical distinctions between inpatient and outpatient Consultation-Liaison (CL) patient populations and to implement educational opportunities for psychosomatic medicine fellows, psychiatry residents and other residents in outpatient CL settings.

Summary:
Purpose: To characterize demographic and clinical differences between inpatient and outpatient Consultation-Liaison (CL) populations and investigate the educational value of outpatient CL experience.

Methods: We reviewed medical records of 200 patients seen by the Inpatient CL Service and 200 patients seen by the Outpatient CL Service at a tertiary care medical center during 2005. Demographic and clinical data (consultation reason, DSM-IV-TR diagnosis, clinical severity and management) were collected. Categorical data were analyzed with chi square analyses or Fisher's Exact Test.

Results: There were no important demographic differences between the two groups. There were 17 group differences in 26 clinical domains. The outpatient CL group had more consultation requests for depression (71.0% vs 41.0%, p<.001), anxiety (32.5% vs 15.0%, p<.001) and unexplained physical symptoms (9.5% vs 3.5%, p=0.019); more DSM-IV-TR diagnoses of anxiety disorder (29.0% vs 11.0%, p<.001), pain disorder (10.0% vs 4.0%, p=0.023), and adjustment disorder (15.5% vs 6.0%, p=0.003); more psychotherapy referrals and more antidepressants initiated.

CL inpatients had more consultation requests for confusion (13.0% vs 0.5%, p=.001), alcohol-related concerns (5.0% vs 0.0%, p=.002), drug-related concerns (7.5% vs 1.5%, p=.009) and psychosis (5.5% vs 1.0%, p=.024); more DSM-IV-TR diagnoses of delirium (23.5% vs 1.5%, p<.001), alcohol use disorder (17.0% vs 5.5%, p=.001), drug use disorder (19.5% vs 7.0%, p<.001) and secondary psychiatric diagnoses (22.5% vs 15.0%, p<.001); more referrals to addiction treatment, psychiatric follow-up, and had more antipsychotic, anxiolytic and mood stabilizer regimens initiated. CL inpatients were more severely medically ill, with more medical diagnoses (7.5% vs 1.5%, p=.009), medications (11.0 vs 6.5, p<.001), and lower GAP scores (37.5 vs 54.7, p<.001).

Conclusion: Results of this analysis suggest that implementing outpatient CL experiences may better prepare fellows and residents for practice. The rich case mix and broader range of diagnostic categories data were analyzed with chi square analyses or Fisher's Exact Test.

References:

NR169
Monday, May 21, 12:30 PM - 2:00 PM
Secular Trends in Alcohol Dependence: All Youth Are Not At Equal Risk
Soraya Asadi, M.D. Washington University in St. Louis, Psychiatry, 5555 Pershing Ave. #1W, St. Louis, MO, 63112, 9000, Richard Gruca, Ph.D., Laura Bierut, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize differences in outcomes amongst alcohol-dependent youth of various ethnic backgrounds.
alcohol dependence has been rapidly rising amongst young adults. It has been suggested that this may be attributable to

**Methods:** Information on lifetime prevalence of alcohol dependence was derived from the 2001-2002 National Epidemiologic Survey on Alcohol and Related Conditions, which was administered via face-to-face interview with 43,093 noninstitutionalized respondents aged 18 to 65 years.

**Results:** Reported lifetime prevalence of alcohol dependence in those aged 18-29 was significantly increased amongst European Americans and Hispanic Americans as compared to older groups in these same populations with odds ratios (OR) of 2.7 (95% confidence interval [CI], 2.3-3.1) and 2.4 (95% CI, 1.8-3.2), respectively. However, age did not have the same significance with regard to lifetime prevalence of alcohol dependence amongst African Americans, OR 1.2 (95% CI, 0.9-1.7).

**Conclusions:** There is an increased reported lifetime prevalence of alcohol dependence amongst young adults in the European American and Hispanic American populations. This finding is most consistent with a true “epidemic” of alcohol dependence in European American and Hispanic American youths.

**References:**

**NR170**
**Monday, May 21, 12:30 PM - 2:00 PM**
**Comparison of Sexual Offenders Against Children to Sexual Offenders Against Adults: Data From the New York Sex Offenders Registry**


**Educational Objectives:**
At the conclusion of this session, the participant should be able to: (1) Understand importance of differentiating pedophiles from sexual offenders against adults; (2) Identify which attributes may distinguish sex offenders against children from those against adults, based on data from New York State Sex Offenders Registry; (3) Understand the potential clinical implications of identification of these attributes; (4) Understand the strengths and limitations of using legal records for studying this population.

**Summary:**
There remains little agreement as to the characteristic psychopathology of pedophilia or the extent to which pedophiles comprise a homogeneous group. Development of maximally effective treatment and prevention techniques depends on the identification of characteristic pathological traits.

**Method:** Data on 837 sex offenders from the New York State Sex Offenders Registry for the five counties of New York City were analyzed with bivariate multinomial logistic regression to examine differences between sex offenders whose victims were children and those whose victims were adults.

**Results:** Offenders against children robustly differed from offenders against older age groups: they were older, more likely to commit multiple acts, and less likely to use force or a weapon. They were also more likely to have known victims, male victims, and victims of both genders. They were also more likely to commit “deviate intercourse” and less likely to commit sexual intercourse.

**Conclusions:** Relative to sexual offenders against adults, pedophiles may be characterized more by aberrant sexual arousal than by impulsivity and aggression. Strengths of study design include that data are drawn from legal records rather than self-report measures (and therefore less subject to under-reporting) and that the clear and robust findings support the identification of unique characteristics of this understudied population.

**References:**

**NR171**
**Monday, May 21, 12:30 PM - 2:00 PM**
**The C/L Psychiatrist as Toxicologist: An Illustrative Case**

Joseph J. Rasimas, M.D. Mayo Clinic, Psychiatry and Psychology, 200 1st Street SW, Rochester, MN, 55905, 9000

**Educational Objectives:**
At the conclusion of this presentation, the participant should be able to identify features of presentation, diagnosis, and management of valproic acid induced hyperammonemic encephalopathy. At the conclusion of this presentation, the participant should be able to appreciate the role of consultation psychiatrist as toxicologist in the acute medical setting. At the conclusion of this presentation, the participant should be able to appreciate the need for intense liaison involvement in toxicologic cases involving psychiatric patients in the medical setting.

**Summary:**
Hyperammonemic encephalopathy is a rare but serious adverse event associated with valproic acid treatment. Liver damage, as measured by serum transaminase levels, is minimal despite profound impairment in hepatic function likely due to valproate metabolites disrupting the urea cycle in susceptible individuals. A major risk factor for emergence of this condition is psychotropic polypharmacy, thus making proper diagnosis challenging in the setting of multiple potentially offending agents and often severe underlying neuropsychiatric disease. The case below highlights these and other salient features of patients who present with valproate induced hyperammonemic encephalopathy (VHE).

Less than three weeks after an early summertime hospitalization for lithium toxicity, a 36 year old patient with treatment resistant schizoaffective disorder and quiescent hepatitis C returned to the emergency department in a state of lethargy and confusion. Sodium valproate had been started in the interim to address emerging hypomania; a nightly dosage of 1000 mg produced a serum level of 114 µg/ml. Upon admission, AST and ALT were normal at levels of 17 U/L and 44 U/L, respectively, while ammonia was elevated at 66 µg N/dL. Serum lithium was 1.2 mmol/L. Following psychiatric consultation, sodium valproate was discontinued on the basis of suspicion of hepatotoxicity, and the patient’s other psychotropic medications (including lithium) were resumed. Ammonia peaked at 111 µg N/dL within 36 hours of presentation, while AST and ALT never exceeded 38 U/L and 81 U/L, respectively. Lactulose and supportive care were provided. Delirial symp-
toms resolved slowly beginning 96 hours after discontinuation of sodium valproex.

This case is presented to outline challenges in diagnosis and management of VHE, a syndrome that requires a high index of suspicion and often persistent liaison involvement on the part of the consultation psychiatrist in the acute medical setting.

References:

NR172 Monday, May 21, 12:30 PM - 2:00 PM
Factors Affecting Empathy in Medical Education
Abid Malik, M.D. Albany Medical Center, Psychiatry, 434 Hudson Ave, Albany, NY, 12203, 9000, Jeffrey S. Winseman, M.D., Julie N. Morsion, Ph.D., Victoria Balkoski, M.D., Leigh A. Zeller, M.S.W.

Educational Objectives:
At the conclusion of this presentation, the participants should be able to:
1) Appreciate the use of concept mapping in research
2) Articulate an understanding of factors affecting empathy in medical education from the student's perspective
3) Demonstrate greater attunement to medical student and resident perspectives on empathy
4) Promote the student's perspective in medical education initiatives that aim to enhance empathy

Summary:
Background: Enhancing empathy is a prominent goal of medical education, yet little is known about the student's perspective. This study focuses on students' experiences and opinions on what occurs during the process of becoming a doctor that affects the ability to be empathic.

Method: 290 medical students and interns responded to an electronic brainstorming survey asking each to list the factors associated with medical education that affect one's ability to be empathic. 34 subjects participated in a sorting task, placing the aforementioned factors into related categories and rating the relative importance of each factor on a 5-point Likert scale. Factors and ratings were examined using multidimensional scaling and cluster analyses, Pearson's r and Student's t-test. This process, known as "concept mapping," was conducted using the Concept Systems program.

Results: 160 unique factors were identified and sorted into four clusters of conceptually related items: "Personal Experiences, Connections and Beliefs;" "Negative Feelings and Attitudes toward Patients;" "Mentoring and Clinical Experiences that Promote Professional Growth;" and "School and Work Experiences that Undermine Development of Empathy." "Mentoring and Clinical Experiences that Promote Professional Growth" was rated most important (mean rating 3.59). The least important cluster was "Negative Feelings and Attitudes toward Patients" (2.75). All students, regardless of level of experience, rated factors in similar hierarchical fashion across all four clusters (r > 0.86). The factor given the highest importance rating was "listening" (mean rating 4.65). Importance ratings for "Negative Feelings and Attitudes toward Patients" were lower for third year students than they were for first year students (p<0.01).

Conclusions: Medical students and interns consider "Mentoring and Clinical Experiences that Promote Professional Growth," especially listening, to be the most important group of factors affecting empathy in medical education.

References:

NR173 Monday, May 21, 12:30 PM - 2:00 PM
Ten-Year Drinking Outcomes of Male Alcoholics: The Influence of Psychiatric Comorbidity in the Family
Elizabeth A. Garwood, M.D. University of Kansas Medical Center, Psychiatry, 3901 Rainbow Blvd, Mail stop 4015, Kansas City, KS, 66160, 9000, Barbara J. Powell, Ph.D., Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.A., Jan Campbell, M.D., Barry I. Liskow, M.D., Peggy Krieshok, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the importance of psychiatric comorbidity in first degree relatives of male alcoholics in predicting long term drinking outcomes.

Summary:
Objective: To determine the effect of psychiatric comorbidity among close relatives on the long term clinical outcomes of treated alcoholic men.

Method: Male inpatient alcoholics (N=360) were extensively examined at entry to the study and one and 10 years later. The family history of first degree relatives was used to divide the sample into three groups: No history of psychiatric disorder or substance abuse/dependence in the immediate biological family (FH-, n=77); family history of substance abuse/dependence only (FHSA, n=104); family history of substance abuse/dependence in addition to another psychiatric illness (FHSA+, n=152).

Results: Originally the alcoholic men in the FHSA+ group reported more psychiatric comorbidity, greater lifetime alcoholism severity, an earlier onset of alcoholic drinking and, though younger, more medical problems than the other two groups. At one year, all three groups showed significant reductions in alcoholism severity. At the 10-year followup, drinking outcomes were significantly poorer for the FHSA+ group. In addition, greater psychiatric distress, more psychiatric treatment and lower levels of psychosocial functioning characterized the 10-year outcomes of the FHSA+ group. Abstinence at the 10 year followup was highest in the FH- group.

Conclusion: A family history of substance abuse plus at least one additional psychiatric disorder was associated with an earlier onset of problem drinking, greater psychiatric comorbidity, and poorer long-term outcomes in a group of treated alcoholic men.

References:

NR174 Monday, May 21, 12:30 PM - 2:00 PM
Prevalence of Obsessive-Compulsive Disorder (OCD) on Colombian Adolescents and Its Association With Working While Going to School
Álvaro A. Navarro Mancilla, M.D. UNAB, Psychiatry, calle 157 No 19 - 55, Bucaramanga, 1642, 3010, German Rueda, M.D.,
NR175  Monday, May 21, 12:30 PM - 2:00 PM
Bullying In Middle Schools: Results from a 5-School Survey
Fabiana Pergolizzi  Project Bully, Research, 6538 Collins Ave #446, Miami Beach, FL, 33141, 9000, Darren Richmond, Paul Auster, Samantha Macario, Zoe Gan, Duolao Wang, Ph.D., Joseph Pergolizzi, Jr., M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to:
  - Describe actions that constitute bullying in middle schools;
  - Understand the extent, and different types of, bullying within a culture of meanness;
  - Describe actions to resist bullying; and
  - Identify education resources whose common goal is to: sensitize youth to the problems of bullying, help students take personal and collective responsibility in bullying incidents, reintroduce the concepts of empathy and courage, empower the "silent majority" of students who witness bullying incidents to take a stand and safely intervene, and help students learn bully prevention strategies.

References:

NR176  Monday, May 21, 12:30 PM - 2:00 PM
Conventional IM Sedatives Versus Ziprasidone for Severe Agitation in Adolescents
William C. Jangro, D.O. SUNY Stony Brook, Psychiatry, Health Science Center T-10, Stony Brook, NY, 11794, 9000, Horacio Preval, M.D., Robert Southard, N.P., Andrew J. Francis, M.D.

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

Summary:
Background: Atypical antipsychotics are considered to have fewer side effects than typical neuroleptics. Accordingly, injectable atypical agents such as ziprasidone may supplant haloperidol for treatment of severe agitation. Published trials comparing intramuscular [IM] haloperidol to ziprasidone for agitation excluded adolescents.
Objective: Compare IM ziprasidone to conventional IM medica-
tions (haloperidol combined with lorazepam) in adolescents aged 12-17.
Method: We retrospectively identified episodes of severe agita-
tion [defined as requiring physical restraint] in adolescents treated
with either IM ziprasidone or conventional IM agents in a tertiary hospital psychiatric ER over a 4 yr period. We found 52 episodes, representing 27 males and 25 females with varied psychiatric diagnoses. Urine toxicology revealed 14 patients with cannabis and 13 with other substances. For ziprasidone, the dosage was 20 mg for 23 episodes and 10 mg for 5 episodes. For 24 episodes with combined haloperidol with lorazepam, the dosages were 4.8±0.3 SEM mg and 1.9±0.4 mg respectively. Outcomes were the duration of restraints and need for adjunctive 'rescue' medications within 60 min.

Results: No difference was found in restraint duration (ziprasidone, N=28, 55±5 min; haloperidol with lorazepam N=24, 65±7 min, P=NS). Use of 'rescue' medications did not differ between ziprasidone [2/28] and haloperidol with lorazepam [1/24]. No side effects were noted. EKGs were obtained in 4 episodes post-IM ziprasidone and showed normal QTc [387-451 ms]. No overall post-pre changes in BP were found, but pulse decreased 8.3±2.4 for haloperidol with lorazepam and 8.9±4.24 for ziprasidone (P=NS).

Conclusion: IM ziprasidone appeared effective, well tolerated, and similar in clinical profile to combined conventional IM medications for treating severe agitation in adolescents. Given the favorable side effect profile of atypical agents, they may supplant conventional antipsychotics for treating agitation in both adult and adolescent populations.

References:

NR177 Monday, May 21, 12:30 PM - 2:00 PM
Meta-Analysis of Data on Caucasian and Asian Subjects Associating Tardive Dyskinesia With the Ser9Gly Polymorphism in the Dopamine D3 Receptor Gene: A Lesson on Pharmacogenomic Research in Psychiatry

M. Shamsi, M.D., MSc. University of Missouri - Columbia, Resident Physician - Psychiatry, 3302 Fox Trot Drive, Columbia, MO, 65202, 9000, Leonard Hearne, Ph.D., Stanely Zammit, MRCPsych, Ph.D., Mike Owen, FRCPsych FMedSci, Ph.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to demonstrate an understanding of how genetic factors play a role in a patient's response to medications. Risk of Tardive Dyskinesia in the presence of the Ser9Gly polymorphism in the Dopamine D3 receptor gene is a good example. This presentation describes how research in this area has evolved into its current phenotype and the effect of genetic stratification.
- With the Ser9Gly polymorphism has illustrated some important principles of Pharmacogenomics in Psychiatry.

Method: Out of 12 studies that met our inclusion and exclusion criteria, 7 were on Asian subjects and 5 were on Caucasians. Frequency of the Gly allele in the Caucasian population was different from the Asian population. We conducted meta-analyses of all 12 studies and separately of Caucasian and Asian studies.

Results: The Gly allele was associated with a higher risk of TD (OR = 1.14, 95% CI: 0.99 - 1.30) in the combined analysis. In the Caucasian group, the OR was 1.2, 95% CI: 0.99 - 1.46. In the Asian group the OR was 1.08, 95% CI: 0.89 - 1.30. The two population groups showed a difference in allele frequency. The Caucasian population showed a higher Gly allele frequency of 0.34 as compared to the Asian population that had a Gly allele frequency of 0.29. However, the Ser allele frequency was 0.66 in Caucasians and 0.71 in Asians. In the genotype model with the Gly allele as a dominant allele, the risk of TD was slightly higher with a combined OR = 1.20, 95% CI: 1.00 - 1.44.

Conclusions: Variations in allele frequencies in different populations influence the outcome in pharmacogenomic research. Defining and standardizing the phenotype is absolutely critical. It may not always be possible to conduct large studies in pharmacogenomic research and pooling data from smaller studies may be one solution.

References:

NR178 Monday, May 21, 12:30 PM - 2:00 PM

Akihiro Nishio, M.D. Gifu University School of Medicine, Dept of Psychopathology, 1-1 Yanagido, Gifu, 5008705, 5880, Hirofumi Ueki, M.D., Taro M. Goto, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to recognize the potential danger of the physical restraint and to understand the importance of the countermeasures to prevent deep vein thrombosis.

Summary:
- Physical restraint (PR) is frequently used in the psychiatric department. While PR is an accepted practice, it can pose side-effects on the patients. Although it has been well recognized that immobilization is one of the major risk factors for the deep vein thrombosis (DVT), it has not been proven whether the risk of DVT in PR patients with psychiatric disorders, is increased. D-dimer is a degradation product of the circulating cross-linked fibrin formed during activation of the coagulation system and it has been reported that D-dimer concentration is a predictor of the DVT. In the present research, we measured D-dimer in the PR patients with psychiatric disorders and in the healthy volunteers as a control, in order to evaluate the risk of the DVT. The experimental protocol was approved by the Ethical Committee of the Gifu University and written informed consent was obtained. Blood sample was obtained at a certain interval, and the concentration of D-dimer was measured using Latex agglutination method. The change of the D-dimer level in PR and healthy volunteers groups were compared, thus the risk of DVT was quantitatively estimated. Fi-
nally, the countermeasures to prevent DVT during PR were discussed.

References:

NR180  Monday, May 21, 12:30 PM - 2:00 PM
BOLD MRI Deactivation of Limbic and Temporal Brain Structures by Transcutaneous Vagus Nerve Stimulation
Thomas Kraus Frankenelb-Klinik Engelthal, Psychiatry, Reschenbergstrasse 20, Engelthal, 91054, 4280, Katharina Hösü, Olga Kiess, Anja Schanze, Johannes Kornhuber, Clemens Forster

Educational Objectives:
In this presentation the participant is given a survey of the latest research results within the field of transcutaneous vagus nerve stimulation (t-VNS). The participant will be informed about a new therapeutic method of stimulating the vagus nerve.

Concerning previous findings of invasive vagus nerve stimulation, the novel non-invasive method will be discussed in respect of feasibility as well as socio-economic implication.

Summary:
Introduction: Invasive vagus nerve stimulation is successfully used for treatment of therapy-refractory epilepsy or depression for more than 20 years. Given the anatomical distribution of the vagus nerve, electrical stimulation of afferences within the outer auditory canal might facilitate a transcutaneous way of vagus nerve stimulation.

In the present study we investigated BOLD fMRI effects in response to transcutaneous electrical stimulation of the left sensory auricular branch of the vagus nerve (t-VNS) regarding different anatomical areas within the outer auditory canal.

20 healthy subjects, age 18-35 years, were stimulated in four different anatomical areas (left tragus, left back side of the auditory canal, left ear lobe, right tragus) on four successive days. The stimulation electrode (silver plate, 5 mm in diameter) was adjusted to a pulse width of 20 μs and frequency of 8 Hz. Psychometric (adjective mood scale, visual analogue scale, test for general intelligence) and cardiovascular testing (RR, heart rate, laser doppler flowmetry) were applied before and after stimulation.

The general linear model showed enhancement of mood (F[1,76]=20.700, p<0.001) and cognition (F[1,76]=3.439, p<0.05), without interaction of different anatomical areas.

Periperal Microcirculation, measured by laser doppler flowmetry, significantly increased after stimulation of the left tragus (T=2.42, p<0.05), but not at any other area of the outer ear. Blood pressure and heart rate did not show significant changes.

In this very first study to examine the effects of vagus nerve stimulation in healthy subjects, psychometric assessment revealed significant improvement of well-being during auricular transcutaneous nerve stimulation. Being both easily feasible and safe for the patient, lacking the side effects of the implantable VNS-device, t-VNS might to be promising as a novel method in treatment of neuropsychiatric disorders. In contrast to vagus nerve stimulation by an implanted prosthesis system, t-VNS might also be applied for reasons of enhancing well-being in healthy individuals.

References:

NR181 Monday, May 21, 12:30 PM - 2:00 PM
Evaluation of Dialectical Behaviour Therapy in a General Adult Psychiatry Setting
ChiKe Onkonwo, M.D. St. Ita’s Hospital, Psychiatry, St. Ita’s Hospital, Portrane, Co Dublin, Co Dublin, 4190, Paul Lyons, Ph.D., Kieman Teresa, Martin Durkan, Healy Cathy, Declan Murray

Educational Objectives:
From this presentation, the reader will learn how a general adult psychiatric team integrated DBT into their service and the benefits and problem that were observed.

Summary:
Abstract: A dialectical behaviour programme (DBT) (Linehan, 1993) has been established as part of the general adult psychiatric service in North County Dublin.

The programme commenced in September 2006 with 8 patients and is due to grow to 12 patients in January 2007. Patients are referred from the general psychiatric service and have repeated deliberate self-harm.

Six staff working in the service were trained in standard DBT (2 intensive weeks separated by 10 months weekly learning and programme development meetings). Staff delivering the DBT are part of the general psychiatry team.

The programme commenced in September 2006 with 8 patients and is due to grow to 12 patients in January 2007. Patients are referred from the general psychiatric service and have repeated deliberate self-harm, making heavy demands on the service and may (but not necessarily) a diagnosis of borderline personality disorder.

The programme is standard DBT (Linehan, 1993) the only modification being some individual therapists do telephone consultation for less than 24 hours daily (but are available 7 days a week)

Evaluation includes (retrospective) data for the 6 months prior to therapy and corresponding data for the first 6 months of treatment.

Data collected includes demographic data, the Clinical Outcomes in Routine Evaluation (CORE) outcome measure (Evans et al, 2002), dose of tranquillisers (in diazepam equivalents) number of self harm incidents, number of visits to emergency room, number of psychiatric admissions per month, number of inpatient days per month, number of school or work days missed for psychological reasons and number of days homeless.

Baseline data and data for the first 6 months in therapy data will be presented and discussed in the context of the DBT literature.

References:

NR182 Monday, May 21, 12:30 PM - 2:00 PM
A Review of Elderly Depression among Asian Americans
yantao ma, M.D. MGH, psychiatry, 50 stanford st. ste 401, BOSTON, MA, 02114, 9000

Educational Objectives:
To review the current literature on elderly depression among Asian Americans.

Summary:
Method: A literature search was performed in using online English databases, including Pub Med, Ovid, Medline, and Treadwell Library using the following key words: elderly depression, geriatric depression, older adult depression, suicide, mortality, acculturation, trauma, Refugees, Asian Americans, Chinese Americans, and Chinese.

Results: More than seventy articles were included, which cover topics including prevalence, associated factors, comorbidity, recognition, and treatment of elderly depression among Asian Americans.

Conclusion: The high prevalence and the low rate of recognition of depression among Asian American elders constitute a significant public health problem. Increased awareness and understanding of the illness is important to improve mental health services to this underserved population.

References:

NR183 Monday, May 21, 12:30 PM - 2:00 PM
Improved Hemisphere-specific 100 MS Auditory Gating Associated with the Use of Atypical Antipsychotics Among Schizophrenia Patients
Brett Y. Lu, M.D., Ph.D. University of New Mexico Health Sciences Center, Psychiatry, MSC 09-5030, 1 University of New Mexico, Albuquerque, NM, 87131-0001, 9000, Ashley K. Smith, B.A., Reza Safavi, Faith M. Hanlon, Ph.D., D., Christopher Edgar, Ph.D., Gregory A. Miller, Ph.D., Jose M. Canive, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to appreciate current research on the neurophysiological basis of poor sensory gating in schizophrenia using evoked brain potentials. The participant should have some understanding of the putative neuronal substrates as targets of antipsychotic-related improvement in sensory gating.

Summary:
Schizophrenia patients often present with complaints of sensory overload. To understand the neurophysiological basis of this phenomenon, the auditory paired-click gating paradigm has been frequently used. Individuals are presented with pairs of clicks (S1 and S2, 500 ms apart), and evoked Cz responses at around 50 ms (P50) are measured using electroencephalography. Schizophrenia patients exhibit deficient S2 suppression, resulting in larger (worse) P50 S2/S1 gating ratios. Other reports also suggest a schizophrenia gating deficit at Cz 100 ms (N100), likely under greater attentional modulation than P50. How these deficits can be reversed by antipsychotic treatment remains little studied. Although receiving atypical antipsychotics, in contrast to conventionals, has been shown to correlate with improved Cz P50 gating, whether such an effect is specific to certain brain areas or detectable at 100 ms remains unexamined. For example, it is unclear if antipsychotics directly affect gating at the primary auditory cortices (PACs), which contribute most of the evoked Cz signals. In this project, we used magnetoencephalography to assess 50 ms (M50)
and 100 ms (M100) gating at bilateral PACs. Because (1) 100 ms gating is reportedly under greater non-PAC modulation, such as that from the prefrontal cortex (PFC) and (2) atypical antipsychotics may confer a neuroprotective role on the PFC, we hypothesize that atypical antipsychotics are associated with less gating deficit at 100 ms. Our preliminary results (>50 controls, >60 patients) indicate a P50, N100, left M50, and bilateral M100 gating deficit in the patient group. More interestingly, the effect of better gating related to atypical antipsychotics is much more dramatic at 100 ms, consistent with our hypothesis. These results help to characterize the neurophysiological targets and outcomes of antipsychotic treatment. With an increasing sample size, we plan to investigate how region-, temporally-specific gating affects one another, as a function of antipsychotic medications.

References:

NR184  Monday, May 21, 12:30 PM - 2:00 PM
Psychological Characteristics of Child Sexual Molesters
Dae-Young Oh, M.D. College of Medicine, Hanyang University, Seoul, Department of Neuropsychiatry, Hanyang Univ. Guri Hospital, Gyeongn-do, Guri, 5800, Jooho Choi, M.D., Yong Chon Park, M.D., Young-Hwa Oh, M.D., Sun-Hea Lee, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that child sexual molesters form heterogeneity within psychological characteristics and majority of them have the possibility of alcohol related problems.

Summary:
Objectives: Sexual molesters show different sociopsychological characteristics from sexual offenders in general. The characteristics of sexual offenses also reveal difference between sexual molestation of adults and children. We hypothesized that sexual molesters of child consist of heterogeneous in characteristic in psychological aspect.
Methods: The 149 subjects, who participated in the education program provided by Korea National Youth Commission in Korea regarding sexual molesters, were requested to fill out self-report questionnaires and had diagnostic interviews with the six psychiatrists from May 1st, 2004 through October 15th, 2005. The participants were assessed by Symptom Check List-90-revised, Beck Depression Inventory, Beck Anxiety Inventory, Self-Administered Alcoholism Screening Test, The Minnesota Multiphasic Personality Inventory-Posttraumatic stress disorder subscale, Padua Inventory-Loss of control over motor behavior, Buss & Durkee Hostility Inventory. After the diagnostic interview, the subjects were classified according to DSM-IV, and the classification was divided into four groups: alcohol dependence, personality disorder, pedophilia, adjustment disorder/deferred.
Results: The results from self-reports reveal a mild depressive state and almost no anxiety in the participants. Majority of them have the possibility of alcohol related problems as well as that of PTSD. They have antisocial impulsivity and hostility within a normal range. Association between self-reports and diagnoses have significant differences only in Self-Administered Alcoholism Screening Test.

Conclusions: The sexual molesters of child form heterogeneity within psychological characteristics. Alcohol-related problems are important factors for them.

References:

NR185  Monday, May 21, 12:30 PM - 2:00 PM
Bipolar Men and Bipolar II Disorder Self-Report Hazardous Alcohol Consumption in the Depressive Phase of Bipolar Disorder: A Pilot Internet Survey
Osama A. Abulseoud UCLA, PSYCHIATRY, 300 UCLA Medical Plaza, Suite 1544, Los Angeles, CA, 90095, 9000, Gerhard Hellmann, Ph.D., Joseph R. Calabrese, M.D., Marcia L. Verduin, M.D., Lori L. Althshuler, M.D., Mark A. Frye, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to appreciate the high prevalence of comorbid alcoholism with bipolar disorder particularly in men, bipolar II subtype and during the depressive phase of the illness. Given the predominance of depressive symptoms in bipolar disorder and the increased risk of suicidality and criminality in bipolar disorder when comorbid with alcohol abuse or dependence, identifying these patients who have hazardous drinking associated with depression is a clinical imperative.

Summary:
Introduction: Despite the high rate of co-morbid alcoholism in bipolar disorder, the relationship between mood state, gender, and alcohol consumption patterns has not been well studied.
Methods: An anonymous Internet survey through the UCLA web site was conducted from August 2002 to September 2005. Hard copies of this survey were also displayed in clinics associated with UCLA, Case Western University and the Medical University of South Carolina. The survey asked bipolar subjects to self-report alcohol quantity consumed when euthymic, manic, or depressed.
Results: 366 individuals who identified themselves as having bipolar disorder returned the survey. There was no gender difference in reported overall alcohol consumption; both men and women reported increasing their alcohol use in both manic and depressive episodes in comparison to euthymic periods. Significantly more men (38%) than women (23%) and more bipolar II (31%) than bipolar I (16%) respondents reported consuming a hazardous amount (>5 drinks/day) of alcohol during depression.

Conclusion: These preliminary primary findings suggest that hazardous drinking in bipolar depression is more common in men and bipolar II disorder. Further study is encouraged to assess if this alcohol increase is a possible attempt at self-medication of mood symptoms or an independent comorbid factor related to alcoholism.

References:
Abnormalities in White Matter Structure in Autism Spectrum Disorders Detected by Diffusion Tensor Imaging

Roger J. Jou, M.D., M.P.H. Yale University, Psychiatry and Investigative Medicine, Yale University Dept of Psychiatry, 300 George St, Ste 901, New Haven, CT, 06511, 9000, Sarah J Paterson, Ph.D., Andrea P. Jackowski, Ph.D., Xenophon Papademetris, Ph.D., Nallakkandi Rajeevan, Ph.D., Lawrence H. Staib, Ph.D., Robert T. Schultz, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
1. Identify those areas of the brain thought to be implicated in autism
2. Identify major white matter tracts in the brain and discuss their function
3. Understand the basic principles diffusion tensor imaging, and how it was used in the current study to detect abnormalities in white matter connectivity
4. Understand the findings of the current study, and their relevance to the core symptoms of autism
5. Discuss the use of diffusion tensor imaging in future studies in autism and other neuropsychiatric disorders

Summary:
Background: The neurobiology of autism spectrum disorders (ASD) is currently unknown. One hypothesis states that ASD are attributable to impaired connectivity between those cortical areas responsible for social and language function. The objective of the current study was to test the hypothesis that abnormal white matter connectivity exists between those cortical regions implicated in social and language function.

Methods: Diffusion tensor magnetic resonance imaging was performed 20 males, ages 9 to 22 years: 10 with ASD and 10 typically developing controls (TDC). Subjects were group-matched according to age, handedness, and full-scale IQ. Fractional anisotropy (FA), a useful measure of the structural integrity of axonal tracts, was compared between groups using an integrated image analysis software package. Volumes of interest (VOIs) were identified using predetermined probability and cluster thresholds. Diffusion tensor tractography was performed to confirm anatomic localization of all VOIs.

Results: Significantly reduced FA values were observed along portions of the following white matter structures: corpus callosum, cingulum, superior and inferior longitudinal fasciculi, and inferior fronto-occipital fasciculus. Significantly reduced FA values were also observed bilaterally in the white matter adjacent to the fusiform gyrus. All findings survived after covarying for age, FSIQ, and TBV. Tractography yielded fiber bundles bearing strong resemblance to those major fiber tracts known to course through the identified VOIs.

Conclusions: These data provide evidence for impaired cortico-cortical connectivity in ASD. Aberrant axonal connections between those cortical areas implicated in social cognition and language function may contribute to the impairments characteristic of ASD.

References:

The Bible and Tao: Preliminary Psychiatric Investigation of Relationship between Korean Traditional Culture and Christianity

Seon-Cheol Park, M.D. Hanyang University, Seoul, Korea, Department of Neuropsychiatry, 17 Haengdang-dong Seongdong-gu, Seoul, 133-792, 5800, Yong Chun Park, M.D., Young Hwa Oh, M.D.

Educational Objectives:
Tao in the Bible of Korean Revised Version is similar to Tao which is the essence derived from the Korean traditional culture, such as Buddhism, Confucianism, and Taoism from the viewpoint of enlightenment.

Summary:
Objectives: It is known that Tao is one of the traditional therapeutic resource of psychiatric practice in Korea. For the preliminary investigation to understand the relationship between Korean traditional culture and Christianity, this study purposes the comprehension of Tao translated in the Bible of Korean Revised Version.

Methods: The authors searched the term "Tao" in the Bible of Korean Revised Version and compared it with the Biblia Hebraica Stuttgartensia, and Novum Testamentum Graece to detect the original expressions of Tao. The meaning of Hebrew or Greek original expressions were compared with English expressions of The Holy Bible, the King James Version.

Results: Tao was recorded 85 times in the Bible of Korean Revised Version. The majority of original expressions were "derek" (43 times) in Hebrew Old Testaments, and "hodos" (14 times) in Greek New Testament. The majority of English expressions corresponding to Tao were "way" or "ways" (59 times). "Derek" means the commandments of God. "Hodos" means the way of Jesus Christ.

Conclusion: Tao in the Bible of Korean Revised Version is similar to Tao which is the essence derived from the Korean traditional culture, such as Buddhism, Confucianism, and Taoism from the viewpoint of enlightenment. Korean psychotherapy can be elaborated further with the acceptance of Western psychotherapy on the basis of deep understanding of Korean traditional culture, such as Tao.

References:

Differential Manifestation of Alcohol Withdrawal Symptoms Related to Serotonergic Polymorphism

SamWook Choi, M.D. Kangbuk Samsung Hospital, Department of Psychiatry, Department of psychiatry, Kangbuk Samsung Hospital, 108 Pyeong-dong, Jongno-gu, Seoul, Korea, Seoul, 110-102, 5800, Doug Hyun Han, M.D., Young Sik Lee, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that the role for the 5-HT receptor subunit gene in the development of alcohol dependence and the differential manifestation of alcohol withdrawal symptoms related to serotonergic polymorphism in patients with alcohol dependence.

Summary:
Objectives: The purpose of this study was to address a role for the 5-HT receptor subunit gene in the development of alcohol...
dependence. The differential manifestation of alcohol withdrawal symptoms related to serotonergic polymorphism in patients with alcohol dependence was also examined.

**Method:** It was evaluated that the role of the 5-HT1A, 5-HT2A, 5-HT transporter (5-HTTLPR) polymorphism to manifest the individual differences in alcohol withdrawal symptoms by an association study of 97 male inpatients with alcohol dependence and 76 healthy controls. The patient’s alcohol withdrawal symptoms were assessed with the Clinical Institute Withdrawal Assessment for Alcohol (CIWA-Ar).

**Results:** In 5-HT1A receptor, the frequency of G- allele (CC) was significantly higher in the patients with alcohol dependence than the normal control group (X^2=5.03, p=0.025). The subscale score of nausea, anxiety, headache among CIWA-Ar scale and the total score of CIWA-Ar scale in G+ allele (CG+GG) was significantly higher than G- allele (p=0.01, p=0.00, p=0.01, p=0.01). In 5-HT2A receptor, the genotype frequency was significantly different between alcoholics and control subjects (X^2=23.41, p=0.00), but there was a significant deviation from Hardy-Weinberg equilibrium in the patients. CT genotype, allele, and CT genotype group frequencies of 5-HT2A among alcoholics and normal controls were not different in terms of all the subscale of CIWA-Ar scale. In 5-HTTLPR, the frequency of L- allele (SS) was higher in the patients with alcohol dependence compare to the normal control group, but this was statistically insignificant (X^2=3.162, p=0.075). Visual hallucination was more severe in L+ (SL+LL) allele than L- allele (p=0.01).

**Conclusions:** The results suggested that 5-HT polymorphism and allelic types revealed the difference in severity of each withdrawal symptom in alcohol dependent patients.

**References:**

**NR189 Monday, May 21, 12:30 PM - 2:00 PM**

**Innovative Approaches to Assessing Access to Care and Barriers to Help-Seeking: A Demographic Ethnic-specific Analysis of Patient Needs for Asian-American and Pacific Islander Victims of Domestic Violence**

Doris Chang, Ph.D. New School for Social Research, Psychology, 65 Fifth Avenue, New York, NY, 10003, 9000, Sophia Haeri, B.A.

**Educational Objectives:**
At the conclusion of this presentation, participants should be able to: (1) recognize patterns of referral to a psychiatric emergency room in a rural county; (2) identify factors that may lead to admission for further evaluations; and (3) discuss how timeliness may be an indicator of optimal care received in the psychiatric emergency room.

**Summary:**
At the conclusion of this session, the participant should be able to: (1) Identify reasons why API women may be less likely to seek help from mainstream agencies; (2) evaluate the possible implementation of an innovative model for collaboration between investigative research teams and domestic violence advocacy centers; and (3) Identify unique patient needs and potential barriers to help-seeking among API victims of domestic violence.

**Method:** In order to assess service needs and utilization patterns, an intake and follow-up protocol was developed in collaboration with a community-based domestic violence center serving API communities in Boston, MA. Instruments were selected for their cross-cultural psychometric viability and translated into Chinese, Vietnamese, and Cambodian. A relational database was constructed to make results available to researchers and clinic staff.

**Results:** Initial pilot data indicate that women most likely to use the center are older, less acculturated recent immigrants who have already made a decision to leave their abusers. Over two-thirds of respondents were foreign born; they were also more likely (59%) to be US citizens or permanent residents. Roughly three-quarters of the women had completed high school and 40% had at least some college; however, the majority of them were unemployed. Respondents also tended to rate their English speaking ability as being less strong than their English reading ability.

**Conclusions:** Alternate methods of outreach may be necessary to serve women who have not made a decision to leave their abusers and/or who do not have legal status. Efforts at securing employment for women in this community that focus on spoken English-language rather than vocational training may be more efficacious. Study method also presents an innovative model for collaboration between investigative research teams and domestic violence advocacy centers to enhance parity and access to care for traditionally underserved ethnic populations.

**References:**
negency physician) was 3.08 (2.88) hours. 80.0% (n=257) were
detained on a legal hold. The group referred by police (n=134)
and the group referred by mobile evaluation team (MET) (n=123)
were compared. Our findings indicated that the group referred by
MET were more likely to be admitted (X^2=18.1, d.o.f.=1, p<0.01).

**Conclusions:** Substantial amount of patients received a primary
diagnosis of substance disorders in the PES setting. Patients
brought in by MET are more likely to be admitted. While all PES
patients should receive appropriate psychiatric assessment,
nearly one quarter of patients were not seen by a psychiatrist
prior to discharge. Timeliness in PES should also be monitored
to enhance access and humane care.

**References:**
1. Hughes DH: Trends and Treatment Models in Emergency Psy-
chiatry. Hospital and Community Psychiatry 44(9): 927-28,
1993.
2. Woo BK, Sevilla CC, Obrocea GV: Factors influencing the
stability of psychiatric diagnoses in the emergency setting: review of 934 consecutively inpatient admissions. Gen Hosp

**NR191**  
**Monday, May 21, 12:30 PM - 2:00 PM**

The Impact of Positive and Negative Symptoms on
Caregiver Burden, Experience and Psychological
Well-being in the Relatives of Patients with
Schizophrenia

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22042, 5830, Sheng-Chang Wang, Hai-Gwo Hwu, Tzung J.
Hwang

**Educational Objectives:**
At the conclusion of this presentation, the participant should be
able to recognize that positive symptoms of schizophrenia led to
greater burden and impaired psychological well-being of the
caregivers. Negative and disorganization symptoms led to less
positive caregiving experiences.

**Summary:**
**Background:** Schizophrenia is a chronic debilitating illness,
which has diverse symptomatology. This disease results in great
burden and psychological impact on the caregivers. However, the
psychological well-being of the caregivers is frequently neglected.
The study is to investigate the relationship between the different
dimensions of psychopathology, caregivers' burden and caregiv-
ers' psychological well-being.

**Methods:** The patients of schizophrenia were recruited from
acute ward (n=23) and day hospital (n=40) of National Taiwan
University Hospital. The primary caregivers of every patient were
recruited. A primary caregiver was defined as the member of the
nuclear or extended family who was the most involved with the
care of the ill relative. The Positive and Negative Symptom Scale
(PANSS) was applied to evaluate the patients' mental status.
The primary caregivers were assessed by several instruments
including: 1) Overall Caregiver Burden Scale (OCBS), 2) Experi-
ence of Caregiving Inventory (ECI), 3) Brief Symptom Rating Scale
(BSRS). We used Pearson product-moment correlation and non-
parametric correlation (Kendall's tau) as statistical method to eval-
uate the correlation between PANSS and OCBS, ECI, and BSRS
respectively.

**Results:** More severe positive symptoms, but not negative
symptoms, of schizophrenia were significantly related to greater
burden of caregivers. The severity of positive symptoms was also
significantly related to the severity of obsession, depression, anx-
xiety and hostility in caregivers as measured by the BSRS. There
was positive correlation between BSRS and OCBS scores, but
the BSRS scores were not correlated to the scores of negative or
disorganization symptoms. In addition, the more severe negative
symptoms and thought disorganization, the less positive care-
giving experiences.

**Conclusions:** Positive symptoms of schizophrenia led to greater
burden and impaired psychological well-being, whereas negative
symptoms did not. In contrast, negative and disorganization symp-
toms led to less positive caregiving experiences.

**References:**
1. Kate Harvey et al: Relatives of patients with severe psychotic
illness: factors that influence appraisal and psychological dis-
2. Albina Veitman et al: The experience of proving care to relatives

**NR192**  
**Monday, May 21, 12:30 PM - 2:00 PM**

Psychological Factors and Physical Status after
Percutaneous Transluminal Coronary Angioplasty

Eric Bui, M.D.  Laboratoire du Stress Traumatique - CHU de
Toulouse, Service de Psychiatrie et Psychologie Médicale, 170,
av. de Casserard, Toulouse, 31059, 4279, Philippe J.R.
Birmes, M.D., Lionel Calhio, M.D., Remy Klein, M.D., Laurent
J. Schmitt, M.D.

**Educational Objectives:**
At the conclusion of this presentation, the participant should be
able to understand the relationship between psychological factors
and physical status in patients undergoing percutaneous translu-
minal coronary angioplasty.

**Summary:**
**Background:** Little data is available on psychological factors
involved in physical recovery after Percutaneous Transluminal
Coronary Angioplasty (PTCA).

**Objective:** To examine the impact of depressive symptoms,
anxious symptoms and alexithymia on physical status 6 months
after PTCA.

**Methods:** We continuously enrolled French speaking patients
admitted to a cardiology ward of Toulouse University Hospital for
PTCA. Within 24 hours of the PTCA, each subject was assessed
with the 20-item Toronto Alexithymia Scale (TAS), the short ver-

tion of the Geriatric Depression Scale (GDS), the state subscale
of the State-Trait Anxiety Inventory (STAI) and the 36-item Short
Form Health Survey (SF-36) which provides a Physical Compo-

tent Score (PCS). At 6 months, the SF-36 was re-administered
by telephone. Correlations analyses were performed controlling
for sex, age, cardio-vascular risk factors, number of dilated arteries
and baseline PCS score.

**Results and discussion:** Sixty-one subjects (85.2% male) com-
pleted the follow-up interview. Mean(SD) age was 66.6(10.6),
mean(SD) GDS was 3.2(6), mean(SD) STAI was 29.9(9.6),
mean(SD) TAS was 48.7(12) and mean(SD) PCS was 43.7(9.4).
Baseline GDS was not associated with 6 months PCS whereas
baseline TAS and STAI were correlated with 6 months PCS score
(p<0.05) suggesting that alexithymia and state anxiety at time of
PTCA may be predictors of poorer physical status.

**Conclusion:** According to our findings, baseline alexithymia and
state anxiety may be associated with poorer physical status 6
months after PTCA. Further studies are needed to replicate these
results. Addressing these psychological dimensions may improve
physical quality of life after PTCA.

**References:**
1. Mallik S, Krumholz HM, Lin ZQ, Kasl SV, Mattera JA, Roumains
SA, Vaccarino V: Patients with depressive symptoms have


NR193 Monday, May 21, 12:30 PM - 2:00 PM
Is Anakin Skywalker Suffering from Borderline Personality Disorder?

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the clinical features of the ADHD/ED comorbidity as well as be informed with the review of literature about this subject.

Summary:
Introduction: We present a review of literature on the comorbidity of Attention-Deficit/Hyperactivity Disorder (ADHD) and Eating Disorders (ED), and through three case reports discuss clinical and therapeutic issues concerning this comorbidity.

Methods and Results: After search over PubMed and active search of relevant papers, we found only three ‘case report’ papers, one analysis of four case-control studies paper, and one prevalence study of ED in an adult clinical sample of ADHD patients. The case reports describes a total of 10 patients with Bulimia Nervosa (BN) and ADHD. The analysis of case control studies found 17 patients with BN and ADHD, and the prevalence study found 9 ED patients (7 Binge-Eating Disorder(BED); 1 BN; 1 Eating Disorder not-otherwise specified(ED-NOS)) in the ADHD sample. We describe the case of one female patient with BN purging type with ADHD inattentive type, which started symptoms of ADHD at school age and never received treatment for it. Also, we describe the case of one male and one female patient with Binge-Eating Disorder comorbid with ADHD.

Conclusion: Most comorbidity studies of ADHD didn’t search for ED, although some studies suggests a higher prevalence of BN in ADHD women. Interestingly, there are fewer descriptions of BED and ED-NOS comorbid with ADHD in the literature, which are the most common ED, rather than BN/ADHD. In most case reports, patients were treated with psychotropic medication and had improvement of BN symptoms. However, we must question the safety of this modality of treatment on BN patients which have high levels of impulsivity and could abuse of stimulant medication. Further data over the treatment follow-up of these patients is needed to answer this important therapeutic issue.

References:

NR195 Monday, May 21, 12:30 PM - 2:00 PM
Speaking Out For Mental Health: Collaboration Between Future Psychiatrists and Journalists
Nioka N. Campbell, M.D. University of South Carolina School of Medicine, Department of Neuropsychiatry, 15 Medical Park, Columbia, SC, 29203, 9000, Jennifer E. Heath, M.D., Jamae C. Campbell, M.D., Brian S. Dundas, M.D., Laura G. Hancock, M.D., Ralph C. Pollock, M.D., Jesse A. Raley, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
1) Identify the understanding and comfort level of resident physicians in interacting with media outlets.
2) Assess the knowledge concerning the stigma of mental illness among upcoming journalists in training.
3) Recognize how collaboration between disciplines can affect attitudes, stigma, education, and mental health advocacy.

NR194 Monday, May 21, 12:30 PM - 2:00 PM
Attention-Deficit/Hyperactivity Disorder (ADHD) Comorbid With Eating Disorders (ED): Clinical and Therapeutical Implications
Bruno P. Nazar, Sr., M.D. IPUB-UFRI, Psychiatry, Rua Visconde de Albuquerque 1400/101, Leblon, Rio de Janeiro, 22450000, 3510, Paulo E. Mattos, M.D., Monica Duchesne, Eloisa Saboya

References:
4) Develop similar programs within residency training to enhance systems based learning for members in training.

Summary:

The U.S. Surgeon General warned in 1999 that stigma was the most formidable obstacle to the future progress in the area of mental illness. We developed a systems based learning project to strike at the core of this issue. Media outlets are the leading genre by which public opinion and understanding is formed. Reservations and discomfort with media interactions are the most common explanations for psychiatrists’ lack of participation in public advocacy. The primary goals of this project were to change the attitudes and understanding of mental illness within journalists in training, and to improve understanding and confidence in media interactions among psychiatry residents. Attitudes assessment surveys among rising journalists regarding psychiatry and mental illness, and psychiatry residents concerning comfort with the media were obtained. Designated speakers and workshop leaders from each discipline modeled appropriate, unbiased, and professional interactions among these two fields. Interdisciplinary teams were assigned group projects for collaboration and media/professional interactions over a six month period. Results included a demonstrated increase from 14% to 64% in resident comfort with media interactions, an increase from 80% to 100% in journalists’ self reported understanding of mental illness, and an increase from 60% to 100% in journalists’ recognition of stigma as a major problem for mental illness. The conclusion of this project demonstrates how a collaborative curriculum in systems based learning can improve attitudes and knowledge among representatives of the media, psychiatry, and mental health. Increasing public exposure to reliable, essential, health information concerning mental illness will be the necessary step in overcoming stigma. This project focused on our future media journalists and psychiatrists, making an impact on those same individuals who will be covering the crucial issues of mental health in the future.

References:


NR197 Monday, May 21, 12:30 PM - 2:00 PM

Intramuscular Olanzapine in Patients With Borderline Personality Disorder: An Observational Study in An Emergency Room

Cristian Damsa University Hospital, Emergency Psychiatry, Rue Micheli-du-Crest 24, Geneva, 1211, 4419, Eric Adam, Francois De Gregorio, Lionel Cailhol, Joseph Lejeune, Coralie Lazignac, Michael H. Allen

Educational Objectives:

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

• Recognize the key points of clinical guidelines about the differential diagnosis of agitation in emergency departments.
• Treat acute agitation of patients with Borderline Personality Disorder who refused oral medication.
• Be aware about the interest of intramuscular olanzapine in treating acute agitation of patients with Borderline Personality Disorder.

Summary:

Objective: Despite the frequency (25%) of Borderline Personality Disorder (BPD) in patients with acute agitation in emergency departments (ED), there are few data about the use of intramuscular (IM) psychotropics in those patients. This is the first open label study with olanzapine in this setting. This study did not receive any funding.
Method: Measures were collected prospectively for patients with acute agitation in ED. Consent were obtained subsequently and diagnosis ascertained using the Structured Clinical Interview for DSM IV. A group of 25 patients with severe agitation and BPD received olanzapine 10 mg IM. Agitation was assessed at entry, two hours after the first 10 mg OLZ IM administration and 12-24 hours after the first injection. Measures included PANSS-EC (Positive and Negative Syndrome Scale Excited Component: tension, uncooperativeness, hostility, poor impulse control, and excitement), ABS (Agitated Behavior Scale) and CGI-S (Clinical Global Impression-Severity). Vital signs and adverse effects were assessed at the same intervals. Movement disorders were assessed using the BAS (Barnes Akathisia Global Score) and SAS (Simpson-Angus Extrapyramidal Effects Scale).

Results: Significant reductions of agitation associated with good tolerance were observed two hours after first IM olanzapine. The study population was comprised of 19 females and 6 males. The mean age was 33.48 ± 8.65. Due to the severity of the agitation, physical restraint was required in 20 (80%) patients. Four patients (16%) required a second 5mg OLZ IM, 2 hours following the first IM, and one patient requiring a third 5 mg OLZ IM after the first 12 hours. There were statistically significant reductions in PANSS-EC, ABS and CGI scores 2 hours after the first IM.

Conclusions: Randomized, placebo controlled studies are needed to confirm the efficacy of intramuscular olanzapine in patients with acute agitation and BPD.

References:

NR198  Monday, May 21, 12:30 PM - 2:00 PM
Psychosis, Violence and Substance abuse in Minors: How strong Are the Ties?
Aditi Mehta, M.D. Cleveland Clinic foundation, Child and Adolescent Psychiatry, 6799 Sylmar Drive, Broadview Heights, OH, 44147, 9000, Tatiana A. Falcone, M.D., Kathleen May Quinn, M.D., Barry Simon, M.D., Kathleen N. Franco, M.D.

Educational Objectives:
The relationship between psychosis and violence is well understood in adults. However, little research has been done in adolescents. At the conclusion of this presentation, the participant will be able to identify the common substances of abuse in this population

Summary:
Introduction: The recent homicide of a psychiatrist by a psychotic patient created an uproar in the psychiatric community. This reopened the question of the possible correlation between psychosis and violence. We hypothesized an association between legal troubles related to violence in psychotic minors and substance abuse. Prior research supports correlation of increased risk of violence in psychotic adults who abuse substances.

Methodology: We reviewed psychotic admission data for minors with psychosis admitted to our inpatient child and adolescent psychiatric unit between 2003 and 2006. From 1500 charts reviewed, we identified 102 patients with first episode psychosis. We used non-psychotic patients on the same unit as control. Data were then analyzed using multivariate model and SAS 9.1 software to assess associations among psychosis, legal problems and abuse of substances.

Results: Of 102 psychotic patients, 40 had a history of violence against people and 29 had a history of documented legal problems predating the psychosis. The psychotic patients had significantly elevated rates of legal problems as compared to control. There was a significant correlation between legal problems and history of violence against people. Those with legal difficulties and psychosis had elevated rates of alcohol, nicotine (69%) and cannabis (53.3%) abuse.

Discussion: A wide range of studies have reported higher rates of violence in individuals suffering from schizophrenia, particularly with co-morbid substance abuse. Unfortunately, not many studies have been done in adolescents. In fact, a prior study of minors found no association between psychosis and violence.

Our multivariate analysis supports an association among psychosis, violence and legal concerns in minors. 29% psychotic minors encountered the legal system first, and this may have contributed to delay in mental health.

Treatment: Data from this retrospective review supports the association of substance abuse as an additional risk factor for violence in minors with psychosis.

References:

NR199  Monday, May 21, 12:30 PM - 2:00 PM
Parent Versus Teacher Reports of Attention Deficit Hyperactivity Disorder and Needs of Counseling: School-Based Mental Health in South Korea
Su-Jin Yang, M.D. Chonnam National University Hospital, Psychiatry, 5 Hakdong, Dong-ku, Kwangju, 501-746, 5800, Woongjang Kim, M.D., Samyoen Lee, M.D., Haewon Jung, M.D., Wooyoung Park, M.D., Seongshim Cheong, M.D., Jae-Min Kim

Educational Objectives:
At the conclusion of this presentation, the participant should be able to find that prevalence of Attention Deficit Hyperactivity Disorder (ADHD) was 6.5 percentage in South Korea Primary schoolchildren and recognized that teacher reports of ADHD may be a useful method for detecting clinical significant case of ADHD that would otherwise be missed when relying only on parent report. Parental need of counseling was related with children’s poor language ability. Intended audience is psychiatrists, child and adolescent psychiatrists, and school mental health professionals.

Summary:
Objective: To compare parent and teacher reports of Attention Deficit Hyperactivity Disorder (ADHD) and needs of counseling in a school-based sample. The associations between specific patterns of agreement/disagreement and other parent and teacher characteristics are examined.

Method: A cross-sectional survey of 2,429 children included in four primary schools at Seoul, South Korea. Parents and teachers completed the Korean ADHD Rating Scales (K-ARS) and the Korean version of the Strengths and Difficulties Questionnaire (SDQ-Kr). Two child psychiatrists interviewed the children, who demonstrated clinically significant scores on K-ARS or SDQ-Kr,
with Mini-International Neuropsychiatric Interview-Kid (M.I.N.I.-Kid).

**Results:** Of 2,429 children, 158 (6.5%) children had ADHD. Of 121 ADHD children without comorbidity diagnosed by M.I.N.I.-Kid, 21 (17.4%) had ADHD that was also identified by both parent and teacher report while 18 children (14.9%) teacher-reported ADHD that the parent did not identify. There were 35 children (28.9%) who were not identified as ADHD according to both parent and teacher report and 47 children (38.8%) were identified as ADHD by parent report alone. Children identified as ADHD by teacher report alone were significantly older age, boys, and fewer parental need of counseling than children who parent-reported ADHD. Of ADHD children, 37.5% of parents and 57.0% of teachers reported need of counseling. Parental need of counseling was related with children’s poorer language ability (Odds Ratio 2.3).

**Conclusions:** We found that obtaining teacher reports of ADHD may be a useful method for detecting clinically significant case of ADHD that would otherwise be missed when relying only on parent report.

**References:**

**NR200**
**Monday, May 21, 12:30 PM - 2:00 PM**

**Ability of Facial Affect Perception in Schizophrenia Patients and Their First Degree Relatives**

Seung-Hwan Lee *Inje University Ilsan Paik Hospital, Neuropsychiatry, 2240 Daehwa-Dong Ilsan-gu, Goyang, 411-706, 5800, Hyung-Seok Seo, Seung-Yeon Kim, Jong-Nam Kim, Hyun Kim, Young-Choo Chung

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to recognize the ability of facial affect perception in patients with schizophrenia, their first degree relatives, and normal control subjects.

**Summary:**

**Objective:** Recently, many studies have been investigated about social functioning of schizophrenia patients. There have been increasing reports that ability of facial affect perception has been decreased in schizophrenia patients. The purpose of this study is to compare the ability of facial affect perception among patients with schizophrenia, their first degree relatives, and normal control subjects.

**Method:** 23 Schizophrenia patients, 11 first degree relatives, and 26 normal control subjects were recruited in this study. The age range of all subjects were from 18 to 60 years old. The facial affect identification test (FAIT), which was developed and standardized in Korea, was applied. It displays pictures of human faces which were composed of six kind affects (sadness, happiness, fear, anger, surprised, disgust).

**Result:** We found that correctness scores (correct response rate to identify appropriate affect in displayed face) of sadness, anger, disgust were increased in order of patient, first relatives, and normal control group. But the significant statistical differences were observed only in sadness. The patients group showed significantly decreased ability to detect the sad affect compared with normal subjects. Also, the intensity scores (0-8 points, point of emotional intensity which subjects feel when they see the faces) were increased in order of patient, first relatives, and normal control group in all category. But the significant statistical differences was not observed. The reaction point scores (sensitive point which subjects can feel the affect, the lower point the more sensitive) were highest in first relative group. But, the significant statistical differences was not observed.

**Conclusion:** This study showed the ability to detect sad affect could be a core deficit of emotional processing of schizophrenia patients. Furthermore, this finding suggest that the deficit in the recognition of negative facial expressions such as sadness, anger, disgust may constitute a social cognitive marker of schizophrenia.

**References:**

**NR201**
**Monday, May 21, 12:30 PM - 2:00 PM**

**Left Amygdalar Hyperactivation During Emotional Task in Schizophrenic Patients: An 18FDG-PET Study**

Emilio Fernández-Egea, M.D. *Hospital Clinic de Barcelona, Psychiatry, C/Villarreal 170, Barcelona, 08036, 4700, Eduard Parellada, Francisco Lomeña, M.D., Javier Pavia, Carles Falcon, Anna Mane, Miguel Bernardo

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to understand the role of neurobiological aberrations (namely lack of habituation phenomena) behind emotional deficit misattributions of schizophrenic patients.

**Summary:**

The role of amygdala during facial emotion recognition (FER) tasks among schizophrenic patients remains unclear as its clinical implications. While most of authors have reported hypoactivation (related to their failure in emotion experience), recently few reports of medial temporal lobe (namely amygdala and hippocampus) hyperactivation have been published. It has been interestingly suggested that patients exhibit a lack or slower adaptive habituation phenomena (a neural mechanism for avoiding repetitive irrelevant stimuli) maybe due to their misattribution of affective meaning to neutral or ambiguous information. We propose to study FER task with [F] fluordeoxyglucose (FDG) PET techniques. Pharmacokinetics of FDG differs from the other brain techniques; because it includes 30 minutes of uptake period and assess accumulative activation. We have hypothesized that the most irrelevant stimuli should habituate faster and then be showed as hypoactive, in contrast to relevant stimuli with slower habituation. We studied amygdalar response during FER tasks with 18FDG-PET technique in ten right-handed healthy volunteers and twelve right-handed non acute schizophrenic patients, who underwent a 20 minutes of continuous emotional (ET), consisted in an emotional valence discrimination task of men and women with happy or sad expression. SPM2 was used for a ROI (amygdala - hippocampus) contrast of Schizophrenic patients - Healthy subjects, showing high left amygdalar response in schizophrenic patients (t=22, -2, -14; z = 2.98; p < 0.001) while no other ROI area exhibited statistically significant differential activation. In conclusion, schizophrenic patients exhibit amygdalar hyperactivation during a continuous emotional task, which could be related to their symptoms of misattribution.
References:

NR202  Monday, May 21, 12:30 PM - 2:00 PM
Burnout in Cancer Care Professionals and Other Staff in Ankara Oncology Hospital
Derya Iren Akbiyik, M.D. Ankara Oncology Training and Research Hospital, Psychiatry, Bulbulderesi Cad. 50 / 5, Ankara, 06660, 4880, Halduñ Seyyur, M.D., Erdem Karabulut, Ph.D., Eytem Sahin Cankurtaran, M.D., Elvan Ozalp, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that burnout of cancer care professionals and hospital staff could be seen in different levels mainly depending on the type of work, distance to cancer patients and the length of working period in the same area. The risk for psychiatric illnesses is high in the cancer care professionals experiencing burnout but most of them are not seeking psychiatric help until the decision to leave work.

Summary:
Introduction: Working with cancer patients is a source of stress in daily routine at work. Thus, it carries a special risk for burnout and psychiatric problems of which the prevalence and levels may differ according to the roles and responsibilities in the oncology team.

Aim: The aim of this study is to evaluate the mental health status and burnout levels in an oncology hospital and to show the differences between staff working with the same patients with different responsibilities.

Methods: In a six months period, confidentially enveloped instruments were given to all personnel to answer by themselves spending about 30-40 minutes and return personally to the research bureau. The groups were including; medical doctors (DRs), nurses (Ns), technical personnel and unqualified personnel. The measuring instruments were General Health Questionnaire12, (GHQ12), Symptom Check List-90, Maslach Burnout Inventory(MBI), and a questionnaire for sociocultural characteristics.

Results: Among 1010, 780 had returned the material fulfilled appropriately. The physical conditions of work place and interpersonal relations were the most important subjects affecting the presence and level of burnout. The mean GHQ12 scores of DRs and Ns were similar to each other and significantly higher than other groups. The mean scores of all personnel were as high as the type of work, distance to cancer patients and the length of working period in the same area. The risk for psychiatric illnesses is high in the cancer care professionals experiencing burnout but most of them are not seeking psychiatric help until the decision to leave work.

Conclusions: According to GHQ12 scores, all staff needed personal psychiatric evaluation at least once. This finding supports the studies reporting the potential higher levels of psychiatric conditions among cancer care workers. All of the groups are not suffering from the same dimensions of burnout, so they needed interventions with respect to their professions, positions at work and distance to the cancer patients.

References:

**NR204  Monday, May 21, 12:30 PM - 2:00 PM**

The Influence of Lithium on Hippocampal Volume in Elderly Bipolar Patients: A Study Using Voxel Based Morphometry

Stevin Zung, M.D. University of São Paulo Medical School, Institute and Department of Psychiatry, Rua Apinagés 866 Apto 21, São Paulo, 05017-000, 3510, Fabio Duran, Quirino Cordeiro, Ricardo Uchida, Cassio Bottino, Geraldo Busatto, Homero Vallada

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to understand the possible neuroprotective effects of lithium and its influence on hippocampal volume in elderly bipolar patients.

**Summary:**

**Introduction:** Recent studies have demonstrated that lithium exerts relevant neuronal protective and regenerative effects both *in vitro* and *in vivo*. The effects of the long-term lithium treatment in brain areas associated with memory impairment of elderly bipolar patients are still unknown.

**Objective:** To compare the volumes of the hippocampus and parahippocampal gyrus between elderly bipolar patients using lithium, elderly bipolar patients not using lithium and healthy controls.

**Methods:** Sociodemographic, clinical and MRI data were obtained from 30 elderly euthymic bipolar patients using lithium for at least one year, 27 elderly euthymic bipolar patients not taking lithium for at least eight months and 22 elderly healthy controls. Volumetric differences in the hippocampus and parahippocampal gyrus between groups were investigated with voxel-based morphometry (VBM) based upon the Statistical Parametric Mapping (SPM) technique.

**Results:** There were no statistical differences in sociodemographic and clinical characteristics and the course of bipolar disorder between the two bipolar groups. In the VBM analysis, one voxel cluster of statistical significance was identified at the left parahippocampal gyrus between groups compared to the non-lithium treated group. Post hoc unpaired t-tests showed that the volume of left parahippocampal gyrus was larger in the lithium treated group compared to the non-lithium treated group.

**Conclusion:** The use of lithium is associated with a larger volume of the left parahippocampal gyrus, possibly due to its neuroprotective effects.

**References:**


**NR205  Monday, May 21, 12:30 PM - 2:00 PM**

What Are We Measuring Using Quality of Life Instruments in Depressed Patients? The Lido Experience

Neusa S. Rocha, M.D. UFRGS-HCPA, Psychiatry, Avenida Iguacu, 119/201, Petropolis, Porto Alegre-RS, 90470-430, 3510, Marcelo PA Flack, Ph.D., Mick J. Power, Ph.D., Donald Bushnell

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to recognize the similarities among quality of life and depression.

**Summary:**

**Aims:** The WHOQOL-Bref (Bref) is a generic quality of life measure, which has been developed simultaneously in many cultures and languages. It has 26 items covering four domains: Physical, Psychological, Social and Environment. Our main objective was to look at items exhibiting differential item functioning (DIF) by a depression factor.

**Methods:** We investigated data from six countries (Australia, Brazil, Israel, Russia, Spain, and the USA) recently involved in a large international study, Longitudinal Investigation of Depression Outcomes (LIDO), assessing quality of life and economic aspects of undiagnosed depression among primary care patients. The sample consisted of 2359 subjects. The depression factor was defined by the diagnosis of depression using the Composite International Diagnostic Interview (CIDI) (n=1193). We have utilized the Rasch modeling as our method.

**Results:** We found that 11 items of 26 items showed uniform DIF for depression factor and only one showing non-uniform DIF. To elucidate what is being measured by WHOQOL-Bref, quality of life (qol) or depressive symptoms, we divided arbitrarily the items into “QOL items” (15 items, related to overall quality of life, general health, pain, medication, safety, environment, body, finances, information, mobility, relationships, support, home, services and transport) and “depression items” (11 items, defined as those similar to DSM-IV criterion for depression and/or Hamilton Depression Scale items related to positive feelings, spirituality, think, energy, leisure, sleep, daily life activities, work, esteem, sex and negative feelings). Interestingly, only 3 of 11 “depression items” did not show DIF for depression, whereas only 5 of 15 “QOL items” showed DIF for depression.

**Conclusions:** Our findings indicate a possible depression domain within the WHOQOL-Bref. In addition, as work continues including satisfaction within the quality of life construct, it may be affected by depressive symptoms

**References:**


**NR206  Monday, May 21, 12:30 PM - 2:00 PM**

Rhabdomyolysis, Acute Renal Failure and Delirium: Complex Manifestations of Tribulus Terrestris Extract’s Adverse Effects

Xiangyang Zhao Metro Health Medical Center, Psychiatry Department, 2500 Metrohealth Drive, 8th floor (PGY-1), Cleveland, OH, 44109, 8000, Mamta Singh, M.D., Alicia Norby, Robert Weiss, Robert T. Segraves, M.D.

**Educational Objectives:**

Tribulus terrestris extract (TTE)- an alternative of androgenic-anabolic steroids (AAS) is used as an enhancement supplement for libido and bodybuilding. We report one case of TTE caused rhabdomyolysis, acute renal failure (ARF) and delirium.

**Summary:**

**Case report:** A 35-year-old African American male, Mr. S was brought to emergency for confused behaviors. In ED, patient...
stated that he had been not feeling well and had general muscle soreness for about week. With careful questioning, patient said he had been taking Tribulus- an enhancement supplement for body-building in the past two weeks. Review of past medical history was significant only for acne and family history significant for deceased mother who was schizophrenia.

Physical examination elicited unremarkable results. Initial workup significant for serum creatinine 3mg/dL, Bun: 37mg/g ALT 115 IU/L, AST 307 IU/L and creatine kinase 15,391 IU/L. Head CT, chest x-ray and EKG did not reveal any abnormality.

The patient was admitted to the medicine service with the initial impression of altered mental status, renal failure and rhabdomyolysis. Further workup showed serum myoglobin 921 ng/ml, Ado- lase 41.6U/L and positive urine myoglobin. Rhabdomyolysis was confirmed. Mental status exam revealed change of cognition such as slow speech and delayed answers, a perceptual disturbance such as difficulty to understanding his medical condition. Delirium was diagnosed. TTE was discontinued. Risperdal 1mg twice a day was started and later up to 2mg twice a day. Patient was aggressively hydrated and responded well to IV fluids. On the 4th day of the hospital course, the patient’s serum creatine kinase and myoglobin began to trend down and mental status improved. Upon discharge, serum Creatine kinase was 3405 IU/L, creatinine 1.3 mg/dl, BUN 7mg/g. Patient was alert and orientated. He spoke spontaneously without sign of delay with good judgment and insight. He scored 29/30 in MMSE. Patient was advised not to take TTE in the future and was discharged with risperdal 2mg twice a day and was followed up by psychiatry as outpatient.

Conclusion: We report one case of TTE caused rhabdomyolysis, ARF and delirium.

References:

NR207 Monday, May 21, 12:30 PM - 2:00 PM Providing Quality Care for Long-Term Residents of State Institutions: A Continuum of Care for High End Users from the Years 2003-2006.

Anasuya Salem, M.D. Delaware Psychiatric Center, Psychiatry, 20 Capano Drive #C1, Newark, DE, 19702, 9000

Educational Objectives:
- The objectives of the High End User Project include:
  - Justify the need for a performance improvement project
  - Observe the effectiveness of integrated treatment planning involving the community treatment team and the public psychiatric hospital.
  - Examine if the HEUP results in a reduction of hospital re-admission for this population.

Summary:

Background: The High End User is an intensive system of case management that integrates multiple resources. Individuals in HEUP are pre-identified by the unit that monitors all involuntarily committed patient admissions in Delaware hospitals. Acute psychiatric hospitalization is pre-authorized for consumers in the HEUP for admission to the public funded hospital instead of frequent “short” stays in other acute inpatient settings.

Methods: Descriptive epidemiological study was done to justify the need for the project. Total number of subjects included in the study is 103. Study included admission data from 2003-2006.

Inclusion Criteria:
- 4 or more hospitalizations within any 12 month period.
- Patients with 30 days of inpatient care within any12 month,
- 3 admissions within any 90-day period,
- Aged 18 - 69+ years.
- Assigned to an intensive case management program or community based acute outpatient day treatment program.

Results: initial findings of the project are: After these patients were placed under high end user system, there is 10% reduction in inpatient treatment rate, 12% reduction in subsequent treatment episodes, 4% reduction in the average length of stay, and 44% increase in receiving treatment from provider 2 (provider 2 = High End User Unit).

Conclusion: This study justifies that there is a need for this kind of one system, which will provide improvement in performance by observing effectiveness of integrated treatment planning involving the community treatment team and the public psychiatric hospital.

References:
1. DHSS data.
2. DHSS data.

NR208 Monday, May 21, 12:30 PM - 2:00 PM Folk Treatment of Mental Illness in Korea

Sun Hea Lee, M.D. College of medicine, Hanyang university, Neuropsychiatry, Hanyang Univ. Hospital, Sung-dong, Hanyang Univ. Hospital, Sung-dong, Seoul, 133-792, 5800, Yong Chon Park, M.D., Jung Hyun Nam, M.D., Dae Young Oh, M.D., Young Haw Oh, M.D.

Educational Objectives:

At the conclusion of this presentation should be able to understand the recent illness behavior, the identification of concept and treatment about mental illness of the folk people.

Summary:

Object: To understand the recent illness behavior, the identification of concept and treatment about mental illness of the folk people is necessary. Many of the folk healings may influence the unconscious illness behavior. Comparison of the knowledge and attitude toward the folk healings between 1970s and 2000s also promote our understanding of the illness behavior.

Methods: Two scholars B.Y. Rhi and K.I. Kim were most prominent and their articles were enough to cover the folk healings of Korean psychiatry. The article list of them were searched and 34 articles were selected. Web site were searched with the key words of ‘folk healing’, ‘folk therapy’ and ‘folk treatment’ and then 20 articles were added. We investigated 54 articles in total from 1970s to 2000s.

Result:
1. The concepts of the mental illness in Korean folk treatment can be classified into four areas. “Shamanistic or supernatural”, “natural or primitive medicine”, “folk psychological”, and “others”.
2. The treatment of the mental illness can be classified according the concept of mental illness.

Discussion: Although the Western psychiatry was introduced in Korea about 100 years ago, the concept and treatment of the mental illness among the rural people were rarely influenced until 1970s. But the tendency changes slowly from “shamanistic” to “psychological” during recent three decades. Public education and mass media could influence the changes.

The classification of concept and treatment of mental illness is important because culture relevant treatment has developed according to the preference of the patients. For example, the “shamanistic” patient needs the intuitive technique, the patient prefers “primitive medicine” needs somatic concern attitude and the “psychological” minded patient needs Tao psychotherapy.
Sleep-Deprived Mice

1. Identify the signs and symptoms of neuroleptic malignant syndrome
2. Recognized the presentation of neuroleptic malignant syndrome with newer antipsychotics

Summary:

Neuroleptic Malignant Syndrome (NMS) is a rare but life threatening syndrome associated with antipsychotic treatment. The incidence of NMS with atypical antipsychotics is unknown, but it is thought to occur less frequently with newer antipsychotics than with conventional agents. Prompt recognition and treatment is essential to decrease the morbidity and mortality from this potentially fatal condition, making elucidation and comparison of signs and symptoms of NMS with atypical agents an important undertaking, especially as these newer agents continue to increase in market share. PubMed was searched in Nov 2006, using the keywords “neuroleptic malignant syndrome” with each atypical agent: “olanzapine,” “ziprasidone,” “quetiapine,” “risperidone” and “aripiprazole.” Abstracts and all relevant articles in English language were reviewed. References of the reviewed articles were examined to find additional articles on case reports of NMS associated with these atypical antipsychotics. Information from the articles was used to characterize and compare the presentation of NMS and description of affected patients with each antipsychotic. This synthesis of data advances the understanding of NMS in atypical antipsychotics, enhancing awareness and facilitating early detection and treatment. Avenues for further research are explored.

References:

Topiramate Increases The Expression of C-Fos and C-Jun in Mouse Hippocampus After Kainic Acid-Induced Seizure

Yong-Chul Park College of Medicine, Kyung Hee University, Seoul 130-701, Republic of Korea, Department of Neuropsychiatry, KHMC, Hoegi, Dongdaemun, Seoul, South Korea, Seoul 130-012, 5800, Ah-Rang Cho, Ji-young Song, Hwan-II Chang, Hae-Jeong Park, Joo-Ho Chung, Jong-Woo Kim

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize TPM might be reduced CA3 pyramidal cell death induced by KA through mediating c-Fos and c-Jun.

Summary:
Topiramate (TPM) is a broad spectrum antiepileptic drug used for the treatment of epilepsy. Its anticonvulsant mechanisms are known for activation of GABA receptors, sodium channel blocking, and activation of the kainate/AMPA subtype of excitatory amino acid receptor. However, the extent to which TPM’s different mechanisms of action contributed to its overall anticonvulsant effect remains unclear. In mice, kainic acid (KA) administered intracerebroventricularly (i.c.v) lead to morphological damage of hippocampus especially concentrated on the CA3 pyramidal neurons. Additionally, KA leads to the induction of several types of protooncogene products, such as Jun and Fos. In the present study, the effect of topiramate on the expressions of c-Fos and c-Jun in hippocampal cell death induced by KA (0.1 mg/kg, i.p, 3 h) administered i.c.v. was examined using immunohistochemistry. KA-induced CA3 pyramidal cell death was found by cresyl violet staining. TPM treatment (30 mg/kg) attenuated KA-induced CA3 pyramidal cell death. KA increased immunoreactive cells of c-Fos and c-Jun in hippocampal CA1 and CA3 region. TPM treatment significantly decreased the KA-induced c-Fos and c-Jun immunonecrosis. Body weight was lowered and memory function by Y-maze test was reduced in SD mice. Nine up-regulated proteins were identified by matrix-assisted laser desorption ionization time-of-flight (MALDI-TOF) analysis. Of 9 identified proteins (thioredoxin-like 1 (Txn1), 60S acidic ribosomal protein P0 (Rplp0), S-adenosylhomocysteine hydrolase (Achy), toll interacting protein (Tollip), serine-threonine kinase receptor-associated protein (Strap), tryptophane aspartate-containing coat protein (Coro1a), ARPA1 actin-related protein 1 homolog B (Actrb1), dihydroangiominidase-like 3 (Dpyt3), and enolase 1 (Eno1)), Txn1, Rplp0, and Acely are known as cell/organism defense proteins and Tollip, Strap, and Coro1a as immunity-related proteins. Little is known concerning the functions of Actrb1, Dpyt3, and Eno1. In summary, this work is the first report to identify changes in defense or immunity-related proteins caused by exposure to SD.

This study was supported by the SRG program of KOSEF(R11-2005-014).

References:

References:

NR209 Monday, May 21, 12:30 PM - 2:00 PM
Review of Neuroleptic Malignant Syndrome With Atypical Antipsychotics
Abid Malik, M.D. Albany Medical Center, Psychiatry, 434 Hudson Ave, Albany, NY, 12203, 9000, Victoria Balkoski, M.D.

Educational Objectives:
At the conclusion of this presentation, the participants should be able to:
1. Identify the signs and symptoms of neuroleptic malignant syndrome
2. Recognized the presentation of neuroleptic malignant syndrome with newer antipsychotics

References:
reactivities. These findings suggest that TPM might be reduced CA3 pyramidal cell death induced by KA through mediating c-Fos and c-Jun.

This study was supported by the SRC program of KOSEF(R11-2005-014).

References:

NR212 Monday, May 21, 12:30 PM - 2:00 PM
Single Nucleotide Polymorphism of Interferon: Influenced Genes From Korean Schizophrenics
Young Jong Kim Kyung Hee University, Department of Neuropsychiatry, KHMC, Hoe-gi, Dongdaemun, Seoul, South Korea, Seoul, 103-012, 5800, A-rang Cho, Jin-kyung Park, Geon-Ho Bahn, Jong-woo Kim, Hak-jae Kim, Sr., Joo-ho Chung

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to recognize SNP in schizophrenia in Korea people.

Summary:
Interferon-γ (IFN-γ) is a cytokine produced by T-helper cells which is known to lowered production in acute schizophrenia. Several lines of evidence point out the possible roles of IFN-γ on neuropsychiatric disorders. To examine the proteins regulated by IFN-γ we attempted to identify the proteins expressed differentially from the brain of IFN-γ knockout mice using the 2D gel-based proteomics. We identified 7 up- and 7 down-regulated proteins using silver-stained or fluorescent 2D-gel/MALDI-TOF-MS. Among the candidate proteins targeted by IFN-γ, we selected brain-specific creatine kinase (CKB) and triose phosphate isomerase I (TPI), based on the previous report of the candidate genes related to the brain function, for further study of SNP analysis in Korean population control (n=271) and schizophrenia (n=189). The genotype distribution at 5'-untranslated SNP sites, -40 C/T (rs2765042) of CKB, showed significantly higher frequency of CC (24.06% in schizophrenia and 14.44% in control, p<0.05). In contrast to this, the genotype at 5'-untranslated SNP sites, -850 C/T (rs2071064) of TPI, higher allelic frequency of T (37.5% in schizophrenia and 32.27% in control) may affect the binding of transcriptional factor AP2α to the predictive promoter. The number of microsatellite CA13 repeats in the first intron of INF-γ slightly decreased in schizophrenia, whereas CA12 repeats increased in schizophrenia. In addition, +874 T/A SNP (rs2430561) is weakly associated with schizophrenia in Koreans and SNP correlated with the number of CA12 repeats. In this report we demonstrate the proteomic approaches from transgenic mice system to find the candidate human ortholog genes involved in the SNP analysis in schizophrenia.

This study was supported by the SRC program of KOSEF(R11-2005-014).

References:
1. Avrut V: Production of interferon-gamma in families with multiple occurrence of schizophrenia.
2. Rothermundt M: Immunochemical dysfunction in schizophrenia: a systematic approach.

NR213 Monday, May 21, 12:30 PM - 2:00 PM
Relationship Between Neurocognitive Function, Psychological Defensiveness and Cognitive Insight in Psychosis: An Investigation Using the Beck Cognitive Insight Scale
Hyoun Jeong Kim, M.D. Seoul National Hospital, psychiatry, Seoul National Hospital, Jungok-3-dong, Gwangan-gu, SEOUL, 413-711, 5800, Jin Hun Kim, M.D., Hae Kyung Jhin, M.D., Ph.D., Eun Kee Chung, M.D., Ph.D., Dong-Won Chang, M.D., Ph.D.

Educational Objectives:
- Knowing the mechanisms of impaired insight may tell us about more general cognitive mechanisms in schizophrenia. We used two measures assessing insight: BCIS, SUMD. These instruments measure insight but place relatively differing emphasis on different aspects of the insight. At the conclusion of this presentation, the participant should be able to recognize the potential importance of combining insight with neurocognitive or psychological mechanism and the multidimensional concept of insight.

Summary:
Background: An increasing number of studies have observed poor insight to be a reflection of cognitive dysfunction in schizophrenia. The most consistent finding was an association between perseverative errors on the Wisconsin Card Sorting Test (WCST) and poor insight. We examined whether cognitive insight as well as clinical insight were associated with a neurocognitive or psychological defensiveness problem.

Method: 41 participants with a psychotic disorder (40 with schizophrenia, 1 with schizoaffective disorder) underwent an assessment of insight, psychotic symptoms, neurocognitive function and psychological defensiveness: the Beck Cognitive Insight Scale (BCIS), the Scale to Assess Unawareness of Mental Disorder (SUMD), Positive and Negative Syndrome Scale (PANSS), two scales from the Minnesota Multiphasic Personality Inventory (MMPI, Scales L(Lie) and K(Correction)), and neuropsychological battery. MMPI scales L and K were presumed to be indicative of psychological defensiveness and denial of problems. The neuropsychological battery included a wide range of tests that assessed global cognitive function, attention, memory, and executive functions: the trail marking test A and B, vigilance test, auditory verbal learning test, visual memory test, go-no-go test, Benton judgment line orientation test and Ekman 60 facial recognition test.

Results: Results showed that BCIS composite index and self-reflectiveness subscale were significantly correlated with MMPI scales L and K (BCIS composite index and MMPI scales L and K: r=-.528, p<.01; r=-.346, p<.05; BCIS self-reflectiveness subscale and MMPI scales L and K: r=-.456, p<.01; r=-.533, p<.01). No correlation between BCIS and neuropsychological battery was found. Some items of SUMD correlated with MMPI scales L and K. There was no correlation SUMD and neuropsychological battery.

Conclusion: These results suggest that in contrast with previous investigations using SUMD, cognitive insight correlates with psychological defensiveness and the concept of insight is multidimensional and these instruments measure insight but place relatively differing emphasis on different aspects of the insight.

References:
NR214  Monday, May 21, 12:30 PM - 2:00 PM

Stigma of Residents Living Around Large Mental Hospital Towards Psychiatric Patients: A Pilot Study in South Korea

Hyun Kwon Lee, Seoul National Mental Hospital, Psychiatry, tresself@hanmail.net, Seoul, Jung kok dong, 5800

Educational Objectives:

This pilot study investigated stigma toward psychiatric patients from residents living around large mental hospital in South Korea that expected to contact with psychiatric patients.

Summary:

Background: As the extent of stigma varies according to the some social demographic variables and sociological backgrounds of each society, this pilot study investigated stigma toward psychiatric patients from residents living around large mental hospital in South Korea that expected to contact with psychiatric patients.

Methods: A total of 96 Korean-speaking persons living around Seoul National Mental hospital were interviewed in private household using questionnaires. Factors of stigma scale that constructed validity in Korean language were un-recoverbility, peril, visibility and discriminative behaviors toward people with mental illness.

Results: Female showed significantly high stigma in peril (p=0.016) and resident period correlated with significantly high stigma in peril (p=0.031), discriminative behavior (p=0.028). Residents that had lived within 1km showed high tendency stigma in visibility factor (p=0.085) and people that had not actually seen psychiatric patients showed high tendency stigma in discriminative behaviors factor (p=0.07). People that answered any experience whether actually had been injured by psychiatric patients showed high tendency of stigma in peril (p=0.072), visibility factor (p=0.073) and answered any experience that had heard any harm due to psychiatric patients showed significantly high stigma in discriminative behaviors (p=0.032). People that had experienced lecture or mass media about psychiatric illness showed significantly low stigma in un-recoverbility (p=0.045), visibility (p=0.034) and discriminative behaviors (p=0.038).

Conclusion: This pilot study found that stigma of residents living around large mental hospital towards psychiatric patients were highly related to resident period, actual harm experience, proximity and experience not to see psychiatric patients. But experience to lecture or mass media about psychiatric illness showed reduced stigma. Therefore Education about psychiatric illness and communication opportunity will be given to the residents around large mental hospital for reducing stigma.

References:

NR215  Monday, May 21, 12:30 PM - 2:00 PM

Incidence of Internet Addiction and Other Characteristics in Korean Company

Sang-Eun Shin, M.D. Incheon Christian Hospital, Psychiatry, 237, Yul Mok-Dong, Choong-Ku, Incheon, 400-714, 5800, Nam-Seek Kim, M.D., kye-Sung Lee, M.D., Joo-Eon Park

Educational Objectives:

This study is designed to find out the incidence of Internet addiction and to examine the correlation between job-stress and other psychoses at work in Korea. Therefore, participants need to aware that internet over use affects mental health, and to pay enough clinical attention.

Summary:

Objective: This study examined incidence of internet addiction, relationship between internet use and job stress and psychopathology of employees of a company at Incheon Korea.

Methods: Subjects were male employees(n=140) of a company at Incheon Korea. Self rating questionnaires consisted of demographic data, Young's Internet addiction Scale(IAS), the Short form of the Korean Occupational Stress Scale(KOSS-SF) for job stress, Rosenberg Self-Esteem Test, and Symptom Checklist-90-Revision(SCL-90-R). These questionnaires were administered during September 2006.

Results: Incidence was Internet addiction 0, Internet Over use 8.7%(n=12) and Internet non-addiction 91.3%(n=126). For using internet, home was preferred by internet overseuse group than non-addiction group(df=4, p<0.05). Internet use over group showed higher score of total SCL-90-R(n=3.903, p<0.05), somatization(n=3.695, p<0.05), obsession(n=3.957, p<0.05), interpersonal sensitivity(n=3.382 p<0.05), depression(n=4.060, p<0.05), anxiety(n=4.387, p<0.05), hostility(n=3.802, p<0.05), phobia(n=3.125, p<0.05), paranoia(n=3.076, p<0.05), and psychosis(n=3.325, p<0.05). Internet over use showed statistical significance on correlation Rosenberg self esteem(n=1.87, p<0.05), total SCL-90-R(n=0.53, p<0.001), somatization(n=0.50, p<0.001), obsession(n=0.43, p<0.001), interpersonal sensitivity(n=0.43, p<0.001), depression(n=0.50, p<0.001), anxiety(n=0.53, p<0.001), hostility(n=0.48, p<0.001), phobia(n=0.53, p<0.001), paranoia(n=4.59, p<0.001), and psychosis(n=0.49, p<0.001). IAS score showed significance on correlation KOSS-SF(n=0.20, p<0.05)

Conclusion: Internet over use group showed severer psychopathology than Non addiction group. Internet over use correlated psychopathology and total internet addiction score correlated job stress. Internet over use affect mental health. So more detail future study is needed.

References:

NR216  Monday, May 21, 12:30 PM - 2:00 PM

The Influence of Distracting Background Facial Emotion on the Identification of Target Facial Emotion

Sung-Hyouk Park, M.D. Seoul National Hospital, Department of Psychiatry, 51, Neung-dong Ro, Kwanjin-Gu Seoul Korea, Seoul, 143-711, 5800, Jinhun Kim, M.D., Jinhak Kim, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the interaction of background facial emotion and central facial emotion.

Summary:

Purpose: To investigate the effect of the distracting background emotion on the identification of target facial emotion in schizophrenia

Method: 27 schizophrenic patient and 19 controls were tested with a computerized task of rapid identification of target facial emotion(happy, fearful, or neutral faces) with large happy or fearful facial emotion picture or blank as background. The participants were instructed to concentrate on the target emotion and ignore distracting background emotion and to press the right or left button when the target emotion is happy or fearful face. The task con-
sisted of 3 blocks according to distracting background emotion (happy, fearful, or blank). Each block consisted of 96 trials (32 happy, 32 fearful, and 32 neutral). In each trial, after presentation of fixation signal for 200ms, the small target facial emotion picture appeared for 200ms and disappeared for 1600ms while the large background facial emotion or blank background was presented for 1800ms. We measured the number of correct responses according to block and target emotion. We ran independent t-test and repeated measures analysis of variance.

Results: The patient group showed marked poor performances in the happy and fearful background blocks (t=-3.602, p=0.004; t=-3.885, p<0.001 respectively), but not in the blank background block (t=1.634, p>0.05) compared with controls. The interaction effect of background emotion and group was of borderline significance (F=2.6, df=1.6, p=0.087). The effect (F=20.3, df=1.7, p<0.001) of target emotion and interaction effect (F=4.3, df=1.7, p<0.05) of target emotion and group were significant. The interaction effect (F=3.1, df=3.0, p<0.05) of background emotion, task emotion, and group was significant with the poorest performance in the identification of fearful emotion during the fearful emotion background block in the patient group.

Conclusion: These findings suggest that the category of distracting background emotion can influence the identification of the target emotion, especially fearful emotion, in schizophrenia.

References:

NR217 Monday, May 21, 12:30 PM - 2:00 PM Event-Related Potential P300's Follow-Up Study in Schizophrenia Patients
Fenglian Guo First Hospital of Shanxi Medical University, Psychiatry department, No. 85 the south liberates road, Taiyuan, Shanxi, Psychiatry Department, Taiyuan, 030001, 5700

Educational Objectives:
Schizophrenia is an etiologically heterogeneous group of brain disorders, our results suggest that there is variation in Event-related potential P300 with schizophrenic, and the variation is related to schizophrenic itself, not the medications.

Summary:
Objective: To identify the property of Event-related potential P300 in schizophrenic patients.
Methods: The Positive and Negative Syndrome Scale (PANSS) and the Event-related potential P300 of Fz, Cz, Pz were recorded in 43 schizophrenics and 43 normal controls.
Results: 1. In comparison with normal controls, before treating the patients had lower amplitude of P2 and longer latency of P3. During the different periods after treatment, the changes of amplitude and latency in P3 are not significant. The patients had lower amplitude of P2 at Cz. No difference in latency of P2 between normal controls and patients before treated. During the different period of treatment, the changes of amplitude and latency of P2 are not significant at Fz and Cz. The latency of P2 is smaller and the amplitude of P2 is larger when treated for six months than treated before at Pz.
Conclusions: 1. There is variation in Event-related potential P300 with schizophrenic, and the variation is related to schizophrenic itself, not the medications. 2. There is variation in the many process of information processing with schizophrenic. 3. Probably parietal lobe damaged more seriously than frontal lobe and central lobule in schizophrenic. 4. The variation degree of amplitude and latency in P3 is not related to the seriousness of clinical symptoms to some degree. 5. The latency of P3 and amplitude of P3 are probably genetic index of schizophrenic, they may contribute to explore the pathogeny, screen and monitor the high-risk group; 6. It is possible that the Event-related potential P300 should be recorded when the schizophrenic patients are fully recored and stop taking medicine so that the property of P300 can be finally identified.

References:

NR218 Monday, May 21, 12:30 PM - 2:00 PM Event-Related Potential P300's Follow-Up Study in Schizophrenia Patients
Hong Yang The First Hospital of Shanxi Medical University, Psychiatry Department, No. 85 South Liberates Road, Taiyuan, Shanxi, Psychiatry Department, Taiyuan, 030001, 5700

Educational Objectives:
Schizophrenia is an etiologically heterogeneous group of brain disorders, our results suggest that the inter-peak amplitude of P2 - N2 is related to the severity of negative symptom to some degree, they may contribute to explore the pathogeny, screen and monitor the high-risk group and the inter-peak amplitude of N2 - P3 is mainly genetic index, but it is affected by symptoms.

Summary:
Objective: To identify the property of Event-related potential P300 by follow-up studying the variability of Event-related potential P300 in schizophrenic patients.
Methods: The Positive and Negative Syndrome Scale (PANSS) and the Event-related potential P300 of Fz, Pz were recorded in 43 schizophrenics and 43 normal controls.
Results: The patients before treatment had longer inter-peak latency of P2 - N2 and larger inter-peak amplitude of P2 - N2. During the different period of treatment, the changes of inter-peak latency of P2 - N2 is not significant, The inter-peak amplitude of P2 - N2 is significantly smaller when treated for six month than treated before. The patients before treated had smaller inter-peak amplitude of N2 - P3. During the different period of treatment, inter-peak amplitude of N2P3 is still significantly smaller than normal controls. No difference in inter-peak latency of N2-P3 between normal controls and patients before treated. In patients inter-peak amplitude of P2-N2 at Cz and Pz is positively correlated to the negative symptom score. In patients, the inter-peak amplitude of P2-N2 and N2-P3 is smaller at Pz than Fz and Cz.
Conclusions: 1. The inter-peak amplitude of P2 - N2 is related to the severity of negative symptom to some degree, they may contribute to explore the pathogeny, screen and monitor the high-risk group; 2. Inter-peak amplitude of N2 - P3 is mainly genetic index, but it is affected by symptoms. It is possible that the Event-related potential P300 should be recorded when the schizophrenic patients are fully recored and stop taking medicine so that the property of P300 can be finally identified.

References:

**NR219**  Monday, May 21, 12:30 PM - 2:00 PM

A Tracing Study of Contrasting the P300 of Negative and Positive Schizophrenic Patients

Huijun Duan First Hospital of Shanxi Medical University, Psychiatry Department, No. 86 South Liberates Road, Taiyuan, Shanxi, Psychiatry Department, Taiyuan Shanxi, 030001, 5700, Hong Yang

**Educational Objectives:**

Schizophrenia is an etiologically heterogeneous group of brain disorders, our results suggest that both patients had worse P300 after being treated 1 month, negative schizophrenia has higher P2-N2 interpeak amplitude in CZ and positive schizophrenia has lower P3 amplitude in FZ.

**Summary:**

**Object:** To investigate the heterology of P300 in negative and positive schizophrenia tracing and contrasting the P300 in FZ, CZ, and PZ of negative and positive schizophrenia patients without medicine.

**Method:** We adopt case control study, chose 35 positive schizophrenia and 36 negative schizophrenia consistent with DSM-IV and 36 controls from same region. Nicolet Bravo were used to detect P300 in FZ, CZ, and PZ recording P3 latency, P2-N2, N2-P3 interpeak latency, P3 amplitude, P2-N2, N2-P3 interpeak amplitude. Recheck these indexes after being treated by Risperdal 1, 3, 6 month.

**Result:** 1. In comparison with positive schizophrenia, negative schizophrenia had lower amplitude of P3 in FZ before treating (P = 0.05), longer P2-N2 interpeak latency in CZ after being treated 6 months and shorter N2-P3 interpeak latency in CZ, PZ (P < 0.05).

2. In the group of negative schizophrenia the P2-N2 interpeak amplitudes in CZ were different (P < 0.05) during different period; the N2-P3 interpeak latency in PZ was the longest after being treated 6 months. 3. In the group of positive schizophrenia the P3 amplitude of P3 in CZ was higher before being treated than after being treated 1 month.

**Conclusion:** 1. There're differences in P300 between positive and negative schizophrenias. The abnormality in positive schizophrenia was mainly in FZ, CZ, and the abnormality in negative schizophrenia was mainly in CZ, PZ. 2. Both patients had worse P300 after being treated 1 month, negative schizophrenia has higher P2-N2 interpeak amplitude in CZ and positive schizophrenia has lower P3 amplitude in FZ.

**References:**

1. Williams LM, Gordon E, Wright J, et al. Late component ERPs are associated with three.


**NR220**  Monday, May 21, 12:30 PM - 2:00 PM

Association of the Long Allele of the 5-HTTLPR Polymorphism With Compulsive Craving in Alcohol Dependence

Stefan Bleich, M.D. Friedrich-Alexander-University, Psychiatry and Psychotherapy, Schwabacheranlage 6, Erlangen, 91054, 4280, Johannes Rauh, M.D., Thomas Hillemacher, M.D.

**Educational Objectives:**

To learn about the role of genetics in alcoholism and new research in the field of candidate genes

**Summary:**

Various studies have reported a role of the serotonin transporter linked polymorphic region (5-HTTLPR) in alcohol dependence. Aim of the present study was to investigate an association of this polymorphism with obsessive-compulsive alcohol craving.

We included 124 male patients suffering from alcohol dependence who were admitted for detoxification treatment. We found significantly higher compulsive craving in male patients with the long allele of the 5-HTTLPR polymorphism (ANOVA: F = 3.48, p = 0.034). General linear models confirmed these findings (F = 3.92, p = 0.023). Our results suggest that the long variant of the 5-HTTLPR polymorphism is associated with higher compulsive alcohol craving. These findings are in line with recent studies describing a positive effect of serotonin reuptake inhibitors on craving and relapse.

**References:**


**NR221**  Monday, May 21, 12:30 PM - 2:00 PM

Evaluation of White Matter Lesions in Late-Onset Major Depression Using Advanced MRI

Rikke B. Dalby Centre for Psychiatric Research, Aarhus Psychiatric University Hospital, Skovagervej 2, Risskov, DK-8240, 4099, Jamila Ahdidan, Elisabeth Tehran!, Leif Sørensen, Leif Østergaard, Raben Rosenberg, Poul Videbech

**Educational Objectives:**

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

1. Understand the implications of white matter lesions in relation to vascular risk factors and late-onset major depression.

2. Describe the localization of white matter lesions in the normal brain versus the brain in late-onset major depression.

3. Demonstrate the use of advanced MRI techniques when describing the possible impact of white matter lesions on brain tissue integrity.

**Summary:**

**Background:** White matter lesions (WMLs) in magnetic resonance imaging (MRI) are associated with poor treatment response in major depression. They increase with age and correlate with vascular risk factors. WMLs in certain brain areas are believed to affect cognitive function. Advanced MRI techniques, such as diffusion tensor imaging (DTI) and magnetization transfer imaging (MTI), may reveal the impact of WMLs on brain tissue integrity and functionality.

**Purpose:** We aim to describe the localization and possible impact of WMLs in late-onset major depression using advanced MRI techniques.

**Methodology:** We examined 15 unselected, consecutive patients with late-onset major depression and 11 matched controls with an advanced MRI protocol on a 3.0 Tesla MRI scanner. WMLs were assessed by an experienced neuroradiologist and localized to anatomical brain areas in Talairach space. From DTI images we calculated the fractional anisotropy (FA) index for each group. Finally, we calculated the mean arterial pressure (MAP) to describe the effect of blood pressure.
Results: Preliminary results show no difference in the WML load or localization between patients and controls. The WMLs were primarily located in the frontal lobes and sub-lobar nuclei. The number of WMLs showed a linear correlation with MAP, reflecting a possible role of hypertension. The FA was lower for controls in primarily located in the frontal lobes and sub-lobar nuclei. The depression. We await further DTI and MTI data on more subjects.

Perspectives: Advanced MRI techniques such as DTI and MTI may contribute to our further understanding of depressive disease by describing the possible impact of WMLs on the brain microstructure.

References:

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that the functional polymorphism in the MAO-A VNTR gene and its association with anger-related traits in Korean females.

Summary:
Anger is a subjective emotional state that may give rise to aggression, which might manifest as verbal or physical acts of violence. Neurobiological studies have suggested that serotonergic neurotransmission is associated with aggression-related behavior, and that allelic variations in serotonergic genes contribute to the expression of aggressive and impulsive behavior or disorders. The monoamine oxidase-A (MAO-A) are the key enzymes involved in serotonin pathways that regulate the levels of serotonin. The present study investigated the association of functional MAO-A variable number of tandem repeats (VNTR) polymorphisms with anger-related traits. MAO-A VNTR polymorphisms were examined for associations with State-Trait Anger Expression Inventory (STAXI) scores in 211 normal Korean females. All subjects were assessed using the STAXI and genotyped for MAO-A VNTR. The scores on the STAXI subscales differ significantly between the genotypes for the MAO-A VNTR (high activity and low activity) polymorphism on anger expression-out (AX-Out) score (t = -2.942, p = 0.004). Subjects in high-activity MAO-A VNTR scored significantly higher on an AX-Out. MAO-A VNTR polymorphism may contribute, in part, to expression of anger. These findings support the hypothesis that this functional polymorphism in the MAO-A gene is associated with anger-related traits in Korean females.

References:

Clinical Profiles of Obsessive Compulsive Symptoms in Schizophrenic Patients
Jin-Yong Jun, M.D. Kwandong University, College of Medicine, Psychiatry, Kwandong University, Myong-Ji Hospital, 697-24, Hwajeong-Dong, Koyang-shi, Kyonggi, Korea, Koyang, 412-738, 5800, Min-Seong Koo, M.D., Yoon-Seop So, M.D., Chan-Hyung Kim, Ho-Suk Suh, Hong-Schick Lee

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the obsessive compulsive symptoms of schizophrenia.
Summary:
We investigated the prevalence of obsessive compulsive disorder (OCD) among patients with schizophrenia. We also investigated the differences in the psychotic symptoms and suicidality between patients with schizophrenia who did or did not have OCD. Seventy-one subjects with the DSM-IV diagnosis of schizophrenia were evaluated by the Structured Clinical Interview for DSM-IV Axis I disorders, the Yale-Brown Obsessive-compulsive Scale and the Positive and Negative Syndrome Scale. The OCD patients with schizophrenia were 20 (28.2%) among 71 subjects. The 20 subjects with OCD had significantly more severe negative and total psychotic symptoms evaluated with PANSS than subjects without OCD. The schizophrenia with OCD had significant higher recent suicidal attempt rate than the subjects without OCD. The results of this study suggest the possibility that OCD symptoms in schizophrenia may be related to negative symptoms and the OC symptoms may be related to the impulsivity expressed as suicidal attempts.

References:

NR225 Monday, May 21, 12:30 PM - 2:00 PM
State Effect of Traumatic Experience on Personality Structure in a Sample of Korean Adolescents
Sang-Kyu Lee, M.D. Hallym University Medical Center, Psychiatry, 153 Kyo-dong Chuncheon Sacred Heart Hospital, Chuncheon, 200-704, 5800, Hong-Seok Lee, M.D., Heung-Pyo Lee, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that 1) the structural change of personality associated with traumatic experience, 2) the structural reorganization of personality shown in this study refutes the orthodox concept of "invariant universal taxonomy" of personality, and 3) while Cloninger's seven-factor model of personality was appropriate in the non-traumatized Korean adolescents, the structure of the traumatized personality accords with the tripartite model proposed by the field of existential and meaning psychology, philosophy, and religion.

Summary:
Purpose: Personality is enduring, stable but it could vary in different types or points of internal and external situations. This study was undertaken to explore the state effect of traumatic experience on personality structure.

Subjects and Methods: This study was conducted under cross-sectional, naturalistic, and case-control conditions on two data sets: a traumatized adolescent sample (N=71) and a control sample (N=296). We compared the factor structure of the TCI extracted from its 25 lower ordered personality dimensions between two samples and exploratory scale-level factor analyses were carried out for each sample.

Results: In the control group, evaluation of the scree plot suggested a five-factor solution, accounting for 54.0% of the total variance and each of the five factors explained 19.2%, 11.5%, 9.9%, 7.4%, and 5.9%, respectively. For the traumatized sample, on the contrary, a 3-factor solution accounted for 67.8% of the total percentage of variance that emerged and the rotated components accounted for 51.5%, 9.6%, and 6.7%, respectively. The Pearson intercorrelations between all of the TCI scales of the traumatized group were quite a bit higher than the corresponding correlations in the control group, and all seven scales were highly intercorrelated with each other.

Conclusion: The traumatized group showed a somewhat different three-factor structure representing a BAS/BIS Factor, a Social Factor, and an Existential Factor compared to the five factor structure in the normative group. This down regulation of personality factor structure in the traumatized sample may be caused by the strengthening of the correlations among personality subscales having a common function as a response to the trauma, indicating an enhanced synergistic interaction between the functionally related personality factors. This is a key to understanding causal mechanisms of the reorganization of personality dimensions through some cognitive-emotional-behavioral restructuring mechanism as a response to situations.

References:

NR226 Monday, May 21, 12:30 PM - 2:00 PM
Change in Body Weight in Commercially-Insured Patients Treated with Antipsychotic Agents
Thomas Delate, Ph.D. Kaiser Permanente Colorado, Pharmacy, 18601 E. Centreftech Pkwy, Aurora, CO, 80011, 9000, Daniel J. Dugan, Pharm.D., Douglas Vanderburg, M.D., Michael C. Deminski, M.S., Brian J. Cuffel, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that variability exists between second generation antipsychotics in their manifestation of adverse metabolic effects among commercially-insured patients with primarily non-psychotic conditions. In addition, the participant should be able to appreciate that routine metabolic monitoring is warranted with second generation antipsychotic use in this patient population.

Summary:
Background: Little information is available on antipsychotic-related body weight change among commercially-insured persons in usual care settings with primarily non-psychotic mental health disorders. The purpose of this investigation was to compare one-year changes in body-weight, by newly-initiated index antipsychotic, among commercially-insured patients.

Methods: This retrospective analysis was performed at Kaiser Permanente Colorado, a health maintenance organization with approximately 410,000 commercially-insured members. All commercially-insured members ≥18 years of age, newly initiated between 01/01/00 and 12/31/03 on a non-clozapine SGA or haloperidol were included if they had a minimum of one additional claim for the index medication within 90 days of their initial dispense date and both a baseline and one-year follow-up weight measurement. Pre-to post-period changes of >7% weight increase were identified. Multivariate logistic regression was utilized to compare proportions with a >7% weight increase between antipsychotics while adjusting for potentially confounding variables.

Results: A total of 801 newly-initiated regimens were included. Primary mental health conditions included anxiety (7%), dementia (29%), affective (47%), and psychotic (15%) disorders and were comparably represented across groups. Mean duration of treatment exposure (range 195 - 248 days) was similar for the antipsychotic agents studied. At one-year follow-up, >7% weight increases were: olanzapine (n=129), 26%, risperidone (n=400), 21%, quetiapine (n=178), 16%, haloperidol (n=64), 13%, and zi-
Clinical relevant weight gain occurred frequently over a one-year period in antipsychotic-treated, commercially-insured patients (adjusted $P=0.09$). In addition, there was a trend toward an increased likelihood of >7% weight increase in risperidone compared to ziprasidone (n=30), 7% (unadjusted $P=0.03$ across cohorts). Additionally, there was a trend toward increased likelihood of >7% weight increase in risperidone compared to ziprasidone (adjusted $P=0.09$).

**Conclusions:** Clinically relevant weight gain occurred frequently over a one-year period in antipsychotic-treated, commercially-insured patients in usual care. Antipsychotic agents differed in frequency of weight gain with the lowest rates associated with ziprasidone.

**References:**


**NR227**

**Factors Associated With Perceived Need and Use of Child Mental Health Service in 9 to 12 Year Old Korean Children**

Hyun-Chung Kim, M.D. Ajou University Hospital, Department of psychiatry, San 5, Wonchon-dong, Yeongtong-gu, Suwon, 443-721, 5800, Yun-Mi Shin, M.D., Sunmi Cho, Ph.D., Byung Eun An, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to recognize that there is a large gap between perceived need and actual use of child mental health services in Korea. The participant should be able to recognize that child psychopathology associated with arousing parental need for child mental health services, such as behavioral problems, does not necessarily lead to utilization of the services in Korea. The participant should be able to realize that educating the parents about child psychopathology might help give early intervention to children in need of treatment.

**Summary:**

This study examined the degree of perceived need and actual use of child mental health services in Korea and the factors associated with the perceived need and use of the child mental health services in Korea. The sample consisted of 1058 children aged 10 to 13 years. The parents completed the sociodemographic data, the Korean version of the Child Behavior Checklist (K-CBCL). Also, Children's Depression Inventory (CDI), a self-rated depression scale, was completed by the children. Univariate and multivariate logistic regression analysis were used for the statistical analysis.

For the results, 11.4% of the parents demonstrated perceived need for mental health services for their children, and 2.7% utilized child mental health services. Factors associated with the perceived need for child mental health services included father’s education level, CDI, attention problems, and aggressive behavior, withdrawn, internalizing problems, CBCL total problem scores. Factors associated with the actual use of child mental health services included mother’s education level, attention problems.

Whether or not a child receives mental health care is influenced by the child’s psychopathology, especially when attention problems exist. This study helps clarify the important factors associated with arousing parental concern and driving the help seeking behavior from just perceiving a child’s disorder to utilizing mental health services.

**References:**


**NR228**

**Prevalence and Impact of Apathy in Late Life Schizophrenia**

Ipsit Vahia, M.D. SUNY Downstate Medical Center, Psychiatry, 49 Willow Street #1F, Brooklyn, NY, 11201, 9000, Shilpa P. Diwan, M.D., Azziza O. Bankole, M.D., Pia Natalya Reyes, M.D., Mamta Sapra, M.D., Paul M. Ramirez, Ph.D., Carl I. Cohen, M.D.

**Educational Objectives:**

At the end of this presentation, attendees should be able to appreciate apathy as a separate clinical syndrome in older schizophrenia patients and identify social, demographic and clinical predictors of apathy and understand its impact on outcome and functioning on this population.

**Summary:**

**Introduction:** Apathy is commonly seen in older persons with neuro-psychiatric illness. Apathy has not been studied in detail in the older population with schizophrenia. This study aims to:

a) Establish existance of apathy as an independent clinical entity in this population, and distinguish it from other symptoms with similar clinical presentations.

b) Study demographic, social and clinical correlates of apathy in an older schizophrenia population and its impact on functional outcomes.

**Methods:** The schizophrenia group consisted of 178 community dwelling persons age 55+ who developed schizophrenia before age 45. Apathy was measured using the passive-apathetic-social withdrawal subscale of the PANSS. Scores of 3 or above were considered as indicative of apathy. Logistic Regression Analyses were performed to assess correlation of apathy with 16 demographic and social variables, Depression, IADLs, Cognitive Functioning, Physical Illness, Positive symptoms and Neuroleptic-induced Akinesia.

**Results:** Overall 25% of the sample was found to have apathy. On logistic regression, Apathy correlated significantly with Race (White) (OR 0.52, df=1, $p=0.022$), Total Network Size (OR 0.06, df=1, $p=0.00$), and Emotional Intimacy (OR 1.53, df=1, $p=0.035$). Interestingly apathy scores did not correlate with depression, akinesia, or cognitive functioning. Higher apathy scores did not bear correlation with physical illness, history of psychological trauma, positive symptoms, QOL, Level of Education.

**Discussion:** Our study is consistent with other studies that establish existence of apathy in schizophrenia as a clinical syndrome that exists independently from depression, akinesia and cognitive symptoms. Contrary to other studies done in younger populations, we found that presence of apathy in older schizophrenia patients does not correlate with positive symptoms and QOL. It appears that apathy in the older population affects functionality more than psychopathology, and merits further investigation to ascertain whether it may be an effective target for therapeutic interventions to improve functioning.

**References:**


NR229
Monday, May 21, 12:30 PM - 2:00 PM
Differential Profile in the Use of Long-Acting Injectable Antipsychotics.
Samuel Leopoldo Romero Guillena Hospital Virgen Macarena, E.S.M.D Macarena Centro, forqueta@terra.es, Seville, 41008, 4700, Juan Luis velez Noguera, Raul Fernandez Villamor Ortiz

Educational Objectives:
At the conclusion of this presentation, the participant should be able to demonstrate quantitative and qualitative differences in the quality of life and evolution of schizophrenic patients receiving treatment with conventional neuroleptics or atypical antipsychotics and should be able to show a differential profile with respect of the use of different long-acting injectable antipsychotics

Summary:

Background and Aims: The expectations of obtaining a better therapeutic adherence due to an improved medication compliance in schizophrenia has been greater in patients in treatment with long-acting injectable antipsychotics. Nevertheless, there are reasons for thinking of quantitative and qualitative differences in the quality of life and evolution of schizophrenic patients receiving treatment with conventional neuroleptics or atypical antipsychotics. The aim of this project is to show a differential profile with respect of the use of different long-acting injectable antipsychotics.

Methods: 242 patients with psychotic disorders and diagnosed according to the ICD 10 (International Classification of Diseases) were assigned to 3 different treatments: 1) long-acting Injectable Risperidone (LAI Risperidone), 2) Flufenacine decanoate or 3) Zuclopentixole dacanote.

6-years period medical records were reviewed for both before and after the start of the treatment. Subanalysis of 46 schizophrenic patients during 2 years were conducted.

Remission Criteria (Andreasen et al., 2005), Global Clinical Impression (CGI-I) and Global Activities Evaluation (EEAG) scales were measured.

Results: Patients treated with LAI Risperidone experienced a statistically significant decrease in the rate of re-hospitalisation (p<0.01) and the duration of the hospitalization (p<0.01) and an increase in the rate of remissions (p=0.05) and the rate of patients under a monotherapy treatment (p<0.01) all compared to the group of patients who received the conventional depot either Flufenazine decanoate or Zuclopentixole decanoate.

Conventional depots were associated with a larger number of discontinuation of the medication because of side effects related to intolerance.

After a 24-months treatment with LAI Risperidone patients experienced a decrease in 1.07 CGI-I scores and an increase in 15.71 EEAG scores.

Conclusions: It is believed that the circumstances described above with LAI Risperidone may lead to an improvement in patient compliance to the antipsychotic treatment and therefore a better quality of life and evolution of the disease.

References:

NR231
Monday, May 21, 12:30 PM - 2:00 PM
Challenges of Electroconvulsive Therapy in Psychiatric Patient in Medically Induced Coma. Case Report
Szymon R. Hyzak, M.D. Maimonides Medical Center, Psychiatry, 950 49th St Apt 2E, Brooklyn, NY, 11219, 9000, Howard Berkowitz, M.D., Sudharam Idupuganti, M.D., Milton Kramer, M.D.

Educational Objectives:
To recognize special and unique circumstances of the Electroconvulsive Therapy in Psychiatric Patient in medically induced coma. To provide suggestions of management of acutely psychotic patient with a diagnosis of Neuroleptic Malignant Syndrome who in order to safely control agitation have to be put in medically induced coma. To demonstrate the use of Caffeine as an agent prolonging the duration of seizures during ECT in a patient in hypnotics and benzodiazepines induced coma. To demonstrate complexity of psychiatric and medical care in Medical Intensive Care Unit settings.

Summary:

Objective: To describe a case of 27-year old female admitted to Psychiatric unit with a diagnosis of Bipolar Disorder Mixed Episode who was treated with Lithium and Risperdal and subsequently diagnosed with Neuroleptic Malignant Syndrome and transferred to Medicine. While in Medicine, on the third day into admission, her agitation was such that it could not be controlled with high doses of IV benzodiazepines and benzodiazepines induced coma. Patient was transferred to Medical Intensive Care Unit, intubated and put in medically induced coma (using Propofol and Versed drips) solely for a purpose of controlling agitation. Any attempt to lessen sedation would result in recurrence of severe uncontrollable agitation. While remaining in coma for about two weeks patient underwent series of ECTs after the consent was obtained from family. Initial 4 shock treatments were shorter than recommended 20-25 seconds despite maximum energy used (170V Medcraft) and patient did not improved clinically. The same drugs used to control her agitation (Propofol and Versed) were at the same time increasing seizure threshold. Patient was subsequently given Caffeine 500 and 750mg with a prolonging effect on seizures durations during ECT. After 3 adequate ECT treatments patient improved dramatically.

Conclusion: ECT is safe and effective treatment for several psychiatric emergencies. For patients who for psychiatric/medical reasons require heavy sedation with medications increasing seizure threshold Caffeine may be used in order to obtain adequate duration of seizures during ECT.

References:
NR232 Monday, May 21, 12:30 PM - 2:00 PM

Imagery Rehearsal Therapy (IRT) for Treatment of Frequent Nightmares in Veterans with Posttraumatic Stress Disorder (PTSD)

Mary Lu, M.D. Portland VA Medical Center, Psychiatry, 2908 NW Thurman St., Portland, OR, 97210, 9000, Amy Wagner, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss a potential role for imagery rehearsal therapy in treating the symptom of frequent nightmares in veterans with posttraumatic stress disorder.

Summary:

Purpose: To describe the treatment of frequent nightmares in veterans with PTSD with imagery rehearsal therapy (IRT).

Content: We present a case series to illustrate IRT implementation and outcome in a pilot group of four veterans.

Methodology:

In IRT, patients receive psychoeducation about nightmares and sleep, as well as training in relaxation and imagery practices, including making changes to a nightmare and mentally rehearsing the new dream.

Results: Two out of 4 veterans in this pilot group reported a considerable decrease in nightmare frequency and distress. This result was confirmed by answers to the following self report measures: the Nightmare Frequency Questionnaire (NFQ), the PTSD Checklist (PCL) and Beck Depression Inventory (BDI II).

Importance: Due to combat-related trauma, veterans receiving care from the VA include a significant number who have developed PTSD. Over half of PTSD patients report frequent nightmares. Like other PTSD symptoms, nightmares often become chronic or recur after a latent period. Among veterans, frequent nightmares are specific to PTSD diagnosis and correlated with combat exposure. Given the prevalence and chronicity of nightmares in veterans with PTSD, specifically treating frequent nightmares may have a unique role in PTSD treatment.

Conclusion: Among psychotherapy approaches to treating recurrent nightmares, imagery rehearsal therapy (IRT) currently has the broadest evidence base. We anticipate that IRT will be used more frequently with veterans in the near future and deserves more systematic study. To this end, we have implemented a pilot group at the VA in order to offer this treatment to veterans and to help assess the efficacy of IRT in the U.S. veteran population.

References:


NR233 Monday, May 21, 12:30 PM - 2:00 PM

Why Do Patients Continue on Their Antipsychotic Medication After the Initial First-Episode of Schizophrenia?

Mamta Sapra SUNY Downstate Med Ctr, Psychiatry, 7212 Narrows Ave 2nd Floor Apt, Brooklyn, NY, 11209, 9000, Abdelouahed Elmouchtari, Nazlim Hagman, AYA Sunakawa, Peter J. Weiden, Stephen M. Goldfinger

Educational Objectives:

At the conclusion of this presentation, the participants should be able to recognize that major obstacle in effective psychoeducation of patients recovering from a first acute episode of schizophrenia is the lack of understanding of the association between medication and relapse prevention. This presentation will present new data on psychoeducation modified for this patient group, including specific techniques and correlates of likelihood of acceptance.

Summary:

Overview: Patients recovering from a first treatment episode of schizophrenia usually do not stay on medication for very long, and often go on to relapse. The connection between maintenance medication and relapse prevention has not been established on a personal level.

Methods: We are presenting the results of the psychoeducation component of a prospective effectiveness study comparing first-episode schizophrenia patients randomized to a recommendation of maintenance long-acting vs oral atypical antipsychotic. Those meeting key diagnostic and treatment criteria for maintenance antipsychotic therapy also received a brief (3-session) individualized psychoeducation program tailored for first-episode patients and their families. Sessions utilized life-goal motivational approaches, with the maintenance antipsychotic recommendation tailored to the specific life issues elicited.

For factors influencing adherence of medications, we did retrospective evaluation for 38 patients based on a scale being piloted to assess reasons for staying in the study and for subjects leaving early. Using the Primary Reasons for Medication Adherence ("PRIMA") scale, we did an exploratory analysis of relationship between individual's current adherence and factors influencing acceptance of medications.

Results: As rated by the PRIMA, patient life goals were: resume education (50%), resume work (30%), premorbid self (20%). Patient treatment goals were: stay on medications (66%), go off medications (10%), reduce side effects (24%). Families' life goals (for their relative) were: return to premorbid self (20%), resume education or work (40%). Families' treatment goals were stay on antipsychotics (79%), reduce side effects (21%). The clinicians rated therapeutic alliance (71%) as the most common and salient factor in influencing medication continuation.

Conclusion: Clinicians rate therapeutic alliance as the single most important determinant of continued adherence with antipsychotic medication. While further research is needed to address reasons why this pilot study supports the hypothesis that doctor-patient relationship is particularly important in guiding acceptance of ongoing medication among first-episode schizophrenia patients.

References:


NR234 Monday, May 21, 12:30 PM - 2:00 PM

Adrenal Insufficiency Disguised and Quetiapine: A Culprit

Violeta Ong Tan, M.D. Stanford University School of Medicine, Psychiatry, 1170 Welch Road #724, Palo Alto, CA, 94304, 9000, Natalie L. Rason, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that the clinical presentation of adrenal insufficiency is ambiguous and that psychotropic medications, such as...
quétiapine, can be a potential cause for this disorder. While atypical antipsychotics have been shown to reduce cortisol levels with consequent improvement in psychopathology, the extent of the cortisol reduction may be detrimental. Understanding the relationship of antipsychotics on the hypothalamic pituitary adrenal axis and recognizing the variable presentations of adrenal insufficiency can be key in accurate diagnoses and management.

Summary:

Adrenal sufficiency oftentimes presents ambiguously. Psychotropic medications are less recognized as causative factors, contributing to this diagnostic challenge.

A 54-year-old male with history of depression was re-admitted to the hospital with chief complaint of malaise. Previous admission 9 days prior was for a UTI treated with Ciprofloxazin. Patient was re-admitted for fatigue, warmth, chills, and loose stools. Physical exam was benign except for noted lethargy and tenderness to palpation in the area of the clavicle at his 5th rib. During the first admission, his psychotropic medications, quetiapine and bupropion, were restarted since he had discontinued them 6-8 months prior.

Work-up for infectious, malignant, and rheumatologic etiologies was negative. In examining endocrine causes, AM cortisol level was low at 2.5ug/mL. Cosyntropin stimulation test was performed with cortisol increasing from 4.2ug/mL to 20.4ug/mL, making primary adrenal insufficiency unlikely. Brain MRI showed no evidence of pituitary microadenoma, and testosterone, prolactin, and IGF concentrations were within normal limits. However, ACTH level was <5pg/mL, suggesting secondary or tertiary adrenal insufficiency. In reviewing the patient's medications, the potential for quetiapine to reduce ACTH and cortisol secretion was found. Prednisone 20mg qam/10mg qhs was initiated after which the patient's condition improved markedly. He was discharged on this dose and instructed to follow-up with an endocrinologist and his psychiatrist.

This case highlights the potential effects of antipsychotics on the hypothalamic-pituitary-adrenal (HPA) axis with potentially dangerous decreases in cortisol secretion. Psychiatric disorders are more often associated with hypersecretion of cortisol and reduction in cortisol levels is commonly associated with improvement in psychopathology. Acute administration of quetiapine may contribute to marked reduction of ACTH and cortisol secretion, and recognizing this phenomenon can be critical in diagnosing and managing a potentially grave condition.

References:


NR235 Monday, May 21, 12:30 PM - 2:00 PM
First in Class GABA Enhanced Antipsychotic: Results of Phase I, Double Blind Placebo Controlled Study
Michael Davidson, M.D. Sheba Medical Center, Psychiatry, 19 Hartun Street, PO Box 45158 Har Hotzvim, Jerusalem, 91450, 5081, Yona Geffen, Ph.D., Abraham Weizman, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize that the new BL-1020 molecule can bring GABA into the Brain and recognize the safety and efficacy profile of the molecule.

Summary:

Introduction: Indirect evidence implicates Dopamine (DA), NMDA and GABA (Gamma-aminobutyric acid) in the pathophysiology of schizophrenia. GABA activity has also been implicated in antipsychotic induced extrapyramidal symptoms (EPS) as well as in anxiety and cognitive impairment. Unfortunately the effects of increasing brain GABA activity by administering exogenous GABA could not be investigated due to its inability to cross the BBB. BL-1020 is a conjugate of the D2 antagonist Perphenazine and GABA.

Pharmacokinetics studies demonstrate that BL-1020 provides effective transport of GABA into the brain. Receptor binding studies indicate that BL-1020 has a high affinity to dopamine with specific GABA-A agonist activity. In animal models predictive of EPS side effects, BL-1020 have shown relatively minimal catalepsy compared to Perphenazine.

Methods: This single dose escalating, double blind, placebo controlled trial consisted of six cohorts, each of 8 subjects, 6 treated with BL-1020 and 2 with placebo. Subjects were hospitalized for 24h after administration and monitored for occurrence of adverse events, vital signs, cardiac, psychological and neurological events.

Results: BL-1020 was well tolerated at all dosing levels. One out of 48 subjects experiences facial twitching lasting for a few minutes and sleepiness both 24 hours after administration of a single dose of 40 mg of BL-1020 (equimolar to 20 mg Perphenazine), BL-1020 caused no anxiety, depression, Parkinsonism, or akathisia or any laboratory or ECG abnormalities. A dose dependent elevation in serum Prolactin was seen with BL-1020

Conclusion: Even if the brief and transient twitching and sleepiness which appeared in 1/48 subjects 24 hours after administration of 40mg BL-1020 (equimolar to 20mg Perphenazine) represents EPS and sedation the data strongly indicates that BL-1020 has a very wide therapeutic window. The results are consistent with the idea that BL-1020 could be a safe, well tolerated and effective antipsychotic with the added benefits of GABA agonism.

References:


NR236 Monday, May 21, 12:30 PM - 2:00 PM
Association Between Platelet Serotonin Transporter Availability, Prolactin Response to Meta-Chlorophenylpiperazine and Treatment Outcome in Cocaine Dependence
Ashwin A. Patkar, M.D. Duke University, Psychiatry, 2213 Elba St, Durham, NC, 27710, Paolo Mannelli, M.D., Kathleen Pelindi, Ph.D., Tong Lee, M.D., Kevin P. Hill, Cynthia Kuhn, Ph.D., Everett Ellinwood, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the relationship of biological markers to the effects of drugs of abuse and their treatment

Summary:

Introduction: While chronic cocaine exposure alters platelet serotonin transporter (5-HTT) availability, and prolactin (PRL) response to meta-Chlorophenylpiperazine (m-CPP), their relationship and their clinical implications are not fully studied.

Objective: We examined the relationship between 5-HTT availability, a presynaptic 5-HT measure, and PRL response to m-
CPP, a marker of postsynaptic 5-HT activity in cocaine dependent individuals and investigated their association with measures of treatment-outcome. **Methods:** Platelet [3H] paroxetine binding sites were assayed and m-CPP challenge performed in 35 African American cocaine dependents at admission to outpatient treatment program and 33 controls. Outcomes included negative urine drug screens and treatment retention.

**Results:** Cocaine subjects showed reduced Bmax of [3H] paroxetine (t=4.67, p <0.01) and blunted PRL response to m-CPP (F=21.86, p <0.01) compared to controls. There was a significant positive correlation between Bmax and delta PRL[peak - baseline PRL] only in drug addicts (r =0.47, p<0.01). Only a main effect of Bmax on treatment retention was observed (p <0.01).

**Conclusions:** It appears that pre and postsynaptic alterations in 5-HT activity may be associated in cocaine dependence. Although the combined influence of the two 5-HT measures on treatment-outcome was not observed, in view of the small sample size, this issue deserves further study.

**References:**

**NR237**

**Monday, May 21, 12:30 PM - 2:00 PM**

**Racial and Gender Differences Among Substance Abusing Individuals With Co-Morbid Mental Illness: Participants in the Telephone Enhancement Procedure (TELE) Study**

Leslie L. Bronner, M.D., Duke University, Psychiatry, 4303 McQueen Drive, Durham, NC, 27705, 9000, Ashwin A. Patkar, M.D., Kathleen Peindl, Ph.D., Lillian Robinson, Lauren Durant, Ph.D., Robert Hubbard, Ph.D.

**Educational Objectives:**
- At the conclusion of this presentation, the participant should be able to recognize the complex relationship between substance abuse and comorbid disorders and the methodologies applied to their evaluation.

**Summary:**
- **Objective:** We investigated whether racial and gender differences exist among substance abusing individuals with co-morbid mental illnesses. We hypothesized that racial and gender differences would exist among substance abusing individuals with co-morbid mental illnesses.
- **Method:** 339 patients from four short term residential substance abuse treatment programs from three states participated in Telephone Enhancement Procedure (TELE) study (U10 DA13711-01) conducted to evaluate whether a post discharge phone intervention was feasible and effective in publicly funded programs. The Addiction Severity Index (ASI) questionnaire was administered at baseline and 13 weeks post treatment.
- **Results:** At baseline, there was statistically significant difference between gender and ethnic groups (African Americans vs. Caucasian) with respect to the frequency of the following variables: ever depressed, ever anxious, suicide attempts, outpatient treatment and medication use. Interestingly, there were generally higher rates of psychiatric symptoms and treatment exposure among Caucasians as compared to African Americans. For example, anxiety was highest among Caucasian females (84%), followed by Caucasian Males (75%), African American females (69%) and African American males (54%). Medication use was significantly higher among Caucasian men than African-Americans. At follow up, the psychiatric symptoms differed more by gender than by race although the differences were not always statistically significant.

**Conclusions:** There is clearly a complex relationship between substance use and co-morbid psychiatric symptomatology by gender and race. A better understanding of this relationship may lead to better evaluation and treatment in this population.

**References:**

**NR238**

**Monday, May 21, 12:30 PM - 2:00 PM**

**Rapid Treatment and Assessment of Post-Traumatic Stress Disorder (PTSD) Using Virtual-Reality-Assisted Exposure Therapy**


**Educational Objectives:**
- This presentation will provide the participant an introduction to Virtual Reality Exposure Therapy as a therapeutic modality in the treatment of Post-Traumatic Stress Disorder.

**Summary:**
- **Introduction:** Military psychiatrists need methods to both rapidly treat PTSD, and assess if and when a patient is able to return to duty. Virtual-reality-based treatments have previously been shown to be effective for the treatment of PTSD. We report an individual treated with Virtual Reality assisted Exposure Therapy (VRET) before being returned to service with his unit.
- **Case:** The patient is a U.S. Marine who was deployed to Iraq for seven months. Upon returning, he suffered from PTSD for approximately six months. After a suicide attempt, the patient was psychiatrically hospitalized, diagnosed with Chronic PTSD, and placed in a limited duty status that prevented him from returning to his unit's combat engineers.
- **Discussion:** The patient was fit for full duty and he was returned for duty with his previous unit. One month after the completion of treatment, a repeat evaluation was performed which showed ongoing remission of PTSD symptoms, and that the patient was functioning well in his previous military duties.

**References:**

NR239 Monday, May 21, 12:30 PM - 2:00 PM

Increased Plasma Levels of Proinflammatory Cytokines (Tumor Necrosis Factor-Alpha and Interleukin-6) in Obsessive Compulsive Disorder

Numan Konuk, Sr., M.D. Zonguldak Karaelmas University Faculty of Medicine, Department of Psychiatry, Zonguldak Karaelmas University Tip Fakultesi, Paşıyadi AD Kozlu 67600, Zonguldak, 67600, 4890, Ishak Özel Tekin, Ulkem Ozturk III, M.D., Levent Atik, Nuray Atasoy, Sibel Bektas, Ayten Erdogan

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize altered production of the proinflammatory cytokines in obsessive compulsive disorder may help to elucidate the role of inflammation or autoimmunity in the pathogenesis of that disease.

Summary:
Aim: Recent research implicated place of an immune mechanisms in the pathophysiology of obsessive-compulsive disorder (OCD). Despite increasing evidence involvement of cytokine release in OCD, results of the studies are inconsistent. The aim of this study was to evaluate the plasma levels of the cytokines; tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6) in OCD patients.

Methods: Plasma concentrations of TNF-α and IL-6 were measured in 31 drug-free outpatients with OCD, and 31 age and sex-matched healthy controls. At the initial assessment, the study group was evaluated by psychiatrists using the Structured Clinical Interview for DSM-IV, Clinical Version (SCID-I/CV) Subjects were excluded if they had evidence of using psychotropic agents and/or analgesics within the last 3 month and they had any primary disease interfering with immune functions. The severity of symptoms was also assessed with Y-BOCS, HAM-D and HAM-A Scales.

ELISA analyses were performed by the immunologists, who were blind to the condition of the samples. IL-6 and TNF-α kits were purchased by Biosource International Inc.(Camarillo, California, USA)

Patients and controls test scores were compared by the Mann Whitney U test as the data not distributed normally. In addition Spearman correlation test were performed in order to test intercorrelations between clinical findings and cytokine levels in OCD group.

Results: Both TNF-α and IL-6 levels showed statistically significant increases in OCD patients compared to controls (p<0.000; p<0.001 respectively). The age of onset was negatively correlated with TNF-α level (r = -0.402, p = 0.025) and duration of illness was weakly correlated with IL-6 levels (r = 0.357; p = 0.048) in patient group.

Conclusion: OCD patients showed increases in TNF-α and IL-6 levels compared the healthy controls. This study provides evidence for alterations in the proinflammatory cytokines which suggest the involvement of the immune system in the pathophysiology of OCD.

References:


NR240 Monday, May 21, 12:30 PM - 2:00 PM

Neuropsychological Correlates of Remission-Focused Treatment with Venlafaxine XR

Jakub Z. Konarski University of Toronto, Institute of Medical Science, 399 Bathurst Street, Toronto, ON, M5T2S8, 1220, Sidney H. Kennedy, M.D., Zindel V. Segal, Roger S. McIntyre, Helen S. Mayberg

Educational Objectives:
To appreciate role of neuroimaging investigations in psychiatry
To observe changes in brain metabolism associated with exposure to antidepressant therapy.
To discover metabolic brain changes associated with remission-focused treatment.

Summary:
Background: Previous neuroimaging investigations have reported on changes in glucose metabolism (18-fluoro-deoxyglucose positron emission tomography - 18FDG-PET) associated with response to primarily serotonergic antidepressants. Herein, we report changes in 18FDG-PET following treatment of a major depressive episode to remission with venlafaxine XR.

Methods: Fourteen patients (7 men and 7 women) meeting DSM IV criteria for major depressive episode in the context of a major depressive disorder were recruited. Subjects scored 20 or greater on the Hamilton Rating Scale for Depression - 17 item version (HRSD-17), were medication-free for the preceding 2 weeks and in good physical health. Regional cerebral glucose metabolism readings were obtained at baseline and again following 16-weeks of treatment with venlafaxine XR (75mg-225mg). All subjects were evaluated bi-weekly using the HRSD-17 and were classified as remitters based on the criteria of an endpoint HRSD-17 score <7.

Results: Treatment with venlafaxine XR was associated with a significant decrease in mean HDRS-17 scores from 20.3 ± 3.0 at baseline to 7.3 ± 4.9 at endpoint, with a mean symptom reduction of 64% (t = 8.19, df=11, p<0.001). At endpoint, 8/12 subjects met criteria for symptomatic remission (mean HDRS-17 score: 4.1 ± 1.1). Treatment with venlafaxine XR treatment was associated with bilateral decreases in glucose metabolism in the orbitofrontal cortices. Remission was additionally accompanied by increases in anterior cingulate metabolism and decreases in the dorsal thalamus and hippocampus.

Conclusions: Symptomatic remission is the optimal outcome in depression. Consistent with earlier reports, successful antidepressant treatment was associated with a reciprocal modulation of cortical-limbic connectivity. Treatment to remission with venlafaxine also engaged additional clinically-salient regions previously unobserved by neuroimaging investigations evaluating primarily serotonergic antidepressants.

References:

NR241  Monday, May 21, 12:30 PM - 2:00 PM
Personal Mastery, or Sense of Control, Is Associated with Reduced Sympathoadrenomedullary (SAM) Arousal in Stressed Alzheimer’s Caregivers
Susan K. Roepke, B.A. University of California, San Diego, Psychiatry, 3409 Waco Street, Apt. 4, San Diego, CA, 92117, 9000, Brent T. Mausbach, Ph.D., Kirlin Aschbacher, M.S., Thomas L. Patterson, Ph.D., Igor Grant, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize psychosocial coping techniques that may reduce cardiovascular disease risk by inhibiting sympathoadrenomedullary response to acute stress.

Summary:
Background: Stress associated with caring for a loved-one with Alzheimer’s Disease (AD) has been associated with increased mortality and cardiovascular disease (CVD) risk. A possible mechanistic explanation for increased CVD in caregivers is heightened sympathoadrenomedullary (SAM) response to acute stressors.

Mastery, the belief that one is capable of handling one’s problems, may reduce psychological responsiveness to an acute stressor, thus reducing SAM arousal.

Methods: 70 spousal caregivers of AD patients above age 55 underwent an acute stress task designed to induce SAM arousal. Specifically, participants were instructed to deliver a brief speech in response to a vignette depicting a stressful situation. Heart rate and blood pressure were measured at several points in the stress task and blood draws were collected before and after the speech in order to assess NE reactivity. Caregiver health (physical and psychological) and care recipient dementia severity data were also assessed.

Results: Multiple regression analyses revealed that mastery was significantly associated with NE reactivity (β = -9.29, t(62) = -2.18, p = .033), such that participants endorsing greater mastery experienced less reactivity in response to an acutely stressful event, independent of resting NE, age, sex, care recipient dementia rating, body mass index, and systolic blood pressure reactivity. The final prediction model including mastery in addition to the aforementioned covariates accounted for 42.4% of the total variance in NE reactivity (F(7, 62) = 6.52; p < .001).

Conclusions: Caregivers with higher mastery experienced reduced NE reactivity to the stress task suggesting that mastery may protect against the physiological effects of acute stress. This study may provide support for psychosocial interventions that increase mastery, which may further reduce CVD risk among dementia caregivers.

References:

NR242  Monday, May 21, 12:30 PM - 2:00 PM
Relationship between Regional Brain Metabolism Disease Severity and Age in Depressed Subjects
Jakub Z. Konarski University of Toronto, Institute of Medical Science, 399 Bathurst Street, Toronto, ON, M5T 2S8, 1220, Sidney H. Kennedy, Roger S. McIntyre, Joanna Soczynska, Helen S. Mayberg

Educational Objectives:
To appreciate role of neuroimaging investigations in psychiatry
To observe changes in brain metabolism associated with ageing in depression.
To discover metabolic brain changes associated with different degrees of depression severity.

Summary:
Objective: We sought to examine the effects of age, disease chronicity, and treatment resistance on glucose metabolism in a large well-characterized sample of depressed men and a never-depressed control group.

Methods: The subjects were unmedicated, symptomatic, right-handed males (n=66) who met DSM-IV criteria for a major depressive episodes as part of a Major Depressive Disorder (MDD, n=66) and right-handed male never depressed control subjects (n=24). Statistical parametric mapping (SPM) was used to analyze age-dependent changes in cerebral glucose metabolism (18-Fluorodeoxyglucose positron emission tomography) in relation to depressive illness severity.

Results: Metabolic activity in the rostral and dorsal anterior cingulate cortex was negatively correlated with age in MDD, but not in HC (p<0.001). Nonresponse to treatment and previous depressive episodes were associated with a higher degree of age-dependent hypometabolism in the rostral and anterior cingulate cortex.

Conclusions: There are regionally-specific syndrome and age effects on brain function in depressed individuals. The age-dependent changes documented herein may subserve the distinct clinical presentation and treatment response described in older-age depression.

References:

NR243  Monday, May 21, 12:30 PM - 2:00 PM
Regional Cerebral Gray Matter Density Changes Associated with Creativity in Healthy Volunteers
Julie C. Bonner, M.D. Stanford University, Psychiatry, 401 Quarry Rd, Stanford, CA, 94305, 9000, Terence Ketter, M.D., Po W. Wang, M.D., Margarita Garcia-Amador, M.D., John O. Brooks III, M.D., Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that increased paralimbic gray matter density coupled with decreased frontal gray matter density may be related to greater creativity in healthy volunteers.

Summary:
Objective: Few studies have assessed relationships between creativity and neurobiology. We explored relationships between regional cerebral gray matter density and creativity as measured by the Barron-Welsh Art Scale (BWAS).

Method: 25 healthy volunteers (mean age 36.4 years, 60% female), with no history of psychiatric, substance use, or major medical disorders, received 1.5T cerebral Magnetic Resonance Image (MRI) scans and completed the BWAS. MRI images were stereotactically normalized and segmented into gray matter using
Statistical Parametric Mapping (SPM5). Voxel-based morphometry (VBM) was used to assess relationships (p < 0.001, not corrected for multiple comparisons) between total BWAS scores and regional cerebral gray matter density. As BWAS inversely correlated with age (r = -.27, p < 0.05), age was a covariate in all VBM analyses.

**Results:** Higher total BWAS scores were associated with increased gray matter density in bilateral precuneus (BA7), right middle temporal gyrus (BA21), right claustrum/insula, and left fusiform gyrus (BA18). Higher total BWAS scores were associated with decreased gray matter density in right middle frontal gyrus (BA11), left middle frontal gyrus (BA6), left post-central gyrus (BA2), and right posterior middle temporal gyrus (BA39).

**Conclusion:** Our data suggest that increased paralimbic gray matter density coupled with decreased frontal gray matter density may be related to greater creativity in healthy volunteers. This is consistent with there being both affective (paralimbic) and cognitive (prefrontal) components to creativity. Previous work has revealed associations between creativity and cerebral metabolism in regions overlapping those found in this structural study, such as precuneus, right frontal, right insula, and posterior temporal gyri. Our findings are also consistent with our observations in bipolar disorder patients of not only increased creativity, but also structural and metabolic changes in frontal and paralimbic regions.

**Supported by National Alliance for Research in Schizophrenia and Depression, and Stanley Foundation Research Awards Program.**

**References:**

**NR245 WITHDRAWN**

**NR246 Monday, May 21, 12:30 PM - 2:00 PM**

**Melperone, An Atypical Antipsychotic Drug, Which Does Not Increase Weight Or BMI, In Patients With Schizophrenia: Comparison With Clozapine and Olanzapine**

Herbert Y. Meltzer Vanderbilt University, Psychiatry, 1601 23rd Avenue South, Suite 306, Nashville, TN, 37212-8645, 9000, William V. Bobo, M.D.

**Educational Objectives:**
- Describe the comparative weight and BMI profile of melperone as compared with clozapine and olanzapine.

**Summary:**
The major tolerability issue concerning atypical antipsychotic drugs which are more potent serotonin than dopamine antagonists, e.g. clozapine and olanzapine, is their propensity to cause metabolic side effects, including weight gain, glucose dysregulation and increased plasma lipids. Melperone, a butyrophenone, which is also a serotonin-dopamine antagonist has been reported to be efficacious in both non-treatment and treatment resistant patients with schizophrenia (1, 2). We report here the lack of effect of melperone on weight and BMI after 6 weeks and 3 months of treatment. Weight and BMI were determined in 30 patients treated with melperone. Baseline weight and BMI were 170.9±(SD)41.6 lbs and 25.9±5.3, respectively. At six weeks, weight and BMI were 171.5±43.6, and 25.8±3.2, respectively. Both weight and BMI were decreased at 3 months, but only one quarter of the sample was still taking melperone. No lipid or glucose data were available from this study. Comparison of these changes with clozapine and olanzapine will be presented. Further study with melperone to determine if it has any adverse effects on glucose and lipids are indicated. If these prove negative, melperone, which is available in Europe, should be further studied as an alternative to atypical antipsychotic drugs which do worsen metabolic status.

(HYM is a consultant to and grantee of Ovation Pharmaceuticals which is developing melperone in the United States).

**References:**

**NR247 Monday, May 21, 12:30 PM - 2:00 PM**

**Predicting Response Based on Gray Matter Content: Results from the FORM Study**

Jakub Z. Konarski University of Toronto, Institute of Medical Science, 399 Bathurst Street, Toronto, ON, M5T 2S8, 1220,
NR249  Monday, May 21, 12:30 PM - 2:00 PM

Relationship Between Val66Met Polymorphism of the Brain-Derived Neurotrophic Factor Gene and Prefrontal Function in Korean Schizophrenic Patients

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Educational Objectives:

- Brain-derived neurotrophic factor (BDNF) involves in facilitating neuronal growth and in the synthesis, metabolism, and release of neurotransmitter. It also involves in memory and learning. Cognitive function of schizophrenic patients, especially those with chronic course, declines as the disease progresses. Many articles regarding to the relationship between BDNF polymorphism and its role in the development of schizophrenia have been published, but the results have been controversial. In addition, the negative results mostly came from Asians. This paper is to test any possible association between the Val66Met polymorphism of the BDNF gene and prefrontal function.

Summary:

- Objective: This study investigates any associations between the Val66Met polymorphism of the brain-derived neurotrophic factor (BDNF) gene and prefrontal function in Korean schizophrenic patients.

Method: One hundred six patients with schizophrenia, 42 female and 64 male, aged between 19 and 65, and 95 controls have participated in this study. Cognitive tests to check prefrontal function included word color test and trail making test. Polymerase chain reaction method was used to genotype for Val66Met BDNF polymorphism.

Results: No significant differences between the patients group and the control group were found in Val66Met BDNF polymorphism. No relationship between Val66Met polymorphism of the BDNF gene and the results of the prefrontal function test was observed.

Conclusion: Val66Met polymorphism of the BDNF gene does not influence on the cognitive function in Korean schizophrenic patients

References:


NR248  Monday, May 21, 12:30 PM - 2:00 PM

A Follow-Up Study of P300 Subcomponents of Schizophrenias

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Educational Objectives:

- Schizophrenia is an etiologically heterogeneous group of brain disorders, our results suggests that the variations of P300 subcomponents amplitude are the trait marker of schizophrenia.

Summary:

- Purpose: To investigate the variation of event-related potentials P300 subcomponents of schizophrenic patients in episodic and remitted state.

Method: 25 consecutive schizophrenic patients of schizophrenia and 25 normal volunteers served as the control group matched for schizophrenic at sex, age and marrige. All patients and normal controls were right-handed. P300 subcomponents (Target P3a,P3b latencies and P3a,P3b amplitudes ) at four electrode (C3,C4,Cz,Pz) was collected during auditory “oddball” target detection task with a USA Nicolet Brovo instrument from 25 schizophrenic patients before and after 4 weeks under risperidone. The SPSS V10.0 for windows statistical package was used throughout.

Results: In the episodic patients, P300 subcomponents amplitude was significantly decreased at four electrode (C3,C4,Cz,Pz), as compared with normal control. For P300 subcomponents latency no significant group differences were observed. For the whole sample subcomponent amplitudes did not change over 4 weeks despite clinical improvement.

Conclusion: It is suggested that the variations of P300 subcomponents amplitude are the trait marker of schizophrenia.

References:


NR250  Monday, May 21, 12:30 PM - 2:00 PM

An MRI Study of Panic Disorder: Anterior Cingulate Gyrus Hyper Activation and Left Amygdala Compression by Arachnoid Cyst

Valfrido L. de-Melo-Neto  Federal University of Rio de Janeiro, Laboratory of Panic and Respiration, Av. Venceslau Brás, 71 Fundos, IPUB, Residênci Méd, Rio de Janeiro, 22290-140, 3510, Fabiana L. Lopes, Alexandre M. Valenca, Isabella Nascimento, Fabio Vargas Magalhães, Antonio E. Nardi

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the possible altered mechanisms that may lead to, or be related with, Panic Disorder, according to Gorman's Neuroanatomical Hypothesis. The participant should also realize that temporal abnormalities may be related to Panic Disorder. Finally, the participant should be able to identify neuromaging signals of hyper activation of anterior cingulate cortex caused by the visualization of anxyogenic pictures.

Summary:

Objectives: To discuss the possible relationship between Panic Disorder and functional and anatomical abnormalities of temporal structures and pre-frontal regions.

Discussion: Anterior cingulate gyrus hyper activation is seen on high trait anxiety subjects when submitted to decision making tasks and is related to erroneous processing. This structure may be critical on anticipatory anxiety or may be related to increased attention to fear relevant stimuli. Amygdala is proposed to be an important structure related to pathophysiology of Panic Disorder (PD). Some findings suggest that amygdalar volumes are smaller in PD patients compared to controls. Amygdala may be abnormally sensitive in PD patients and it's increased activity may result in automatic, behavioral and neuroendocrine response.

Case Report: A 31-year-old male, afro-american patient, with a recent history of PD (six months) and without any medication for the last six weeks, was examined by fMRI and submitted to visual stimuli (panic, aversive but not-panic and neutral pictures). The image examined exhibited an arachnoid cyst in the left temporal fossa. This finding compresses amygdala and near-by structures of the same side. fMRI showed an hyper activation of the anterior cingulate gyrus, specially when exposed to panericogenic pictures.

Conclusion: This case is unique by the presence of an arachnoid cyst compressing the left amygdala in a PD patient. Although this compression doesn't allow amygdalar examination, the anterior cingulate gyrus hyper activation caused by anxiety stimuli may show how different structures involved with the Gorman's neuroanatomical hypothesis for PD are compromised in a high-trait anxiety patient.

References:


NR252  Monday, May 21, 12:30 PM - 2:00 PM

Clinical Remission in a Multi-ethnic Urban Population of Older Adults with Schizophrenia

Azziza O. Bankole, M.D. SUNY Downstate Medical Centre, Psychiatry, 515 Ovington Avenue #2F, Brooklyn, NY, 11209, 9000, Carl I. Cohen, Ipsit Vahia, M.D., Shilpa P. Diwan, M.D., Azziza O. Bankole, M.D., Paul M. Ramirez, Ph.D., Carl I. Cohen, M.D.

Educational Objectives:

At the end of this presentation, attendees should be able to appreciate the division of factors influencing medication adherence into therapist, patient and family factors. They should also be able to appreciate how patients can be profiled based on their clinical presentation to help determine which factors are more likely to influence their adherence and subsequently their clinical outcome.

Summary:

Introduction: Nonadherence to antipsychotic medications is a major cause of relapse in schizophrenia patients and is affected by attitudes of patients towards treatment. This study evaluates patient attitudes towards antipsychotic medication and predictors/ reasons of medication adherence in older schizophrenia patients. Based on a literature review, we assessed factors that influenced patients' medication adherence.

Methods: The sample consisted of a stratified convenience sample of 196 community-dwelling schizophrenic persons aged 55+ in residential and non-residential settings. We used the Rating of Medication Influences (ROMI) scale to assess patient's attitudes and how they influence adherence. We created three subscales using factor analysis with varimax rotation: (1) 'Therapist factors' (2) 'Patient Factors' (3) 'Family factors'. We identified independent variables using the Illness Behavior Model.

Results: Therapist factors were significantly correlated with lower PANSS positive scores (t=2.09, df=188.3, p=.038), the Conceptualization subscale of the Dementia Rating Scale (DRS) (t=2.21, df=181.8, p=.028). Patient factors were significantly correlated with PANSS Insight score (t=2.59, df=165.7, p=.010), Initiation and Perseveration DRS subscale (t=-2.13, df=182.9, p=.035) and Conceptualization DRS subscale (t=-2.13, df=171.7, p=.034). Family factors were significantly correlated with higher PANSS negative scores (t=-2.02, df=108, p=.030), total DRS scores (t=-3.29, df=80.6, p=.001), lower IADL scores (t=2.43, df=24.9, p=.023), fewer non-kin supports (t=-2.23, df=108, p=.027).

Discussion: Therapists' role is prominent in older schizophrenia patients with fewer positive symptoms and better ability to abstract and conceptualize. Patients own understanding is more prominent in patients with more insight and better cognition. Role of family is more prominent is patients with more negative symptoms, less cognitive impairment, lower functioning, and a smaller support structure outside of family. Our data suggest that older schizophrenic patients may be profiled based on overall clinical status to determine factors most likely to impact adherence. Individualized treatment plans based on this may promote medication adherence.

References:

Educational Objectives:
At the conclusion of this presentation, the participant should understand and bring to the clinical session the importance of remission. As the field of schizophrenia advances, patients as well as their relatives and advocates are questioning mental health professionals about recovery. It is a concept that we need to keep in mind.

Summary:
Objective: This study aims to determine the prevalence of clinical remission in older adults with schizophrenia.
Methods: The Schizophrenia Group consisted of 198 persons aged 55* living in the community who developed schizophrenia before age 45. We established criteria for clinical remission based on a comprehensive literature review. PANSS, Dementia Rating Scale (DRS), Center for Epidemiologic Studies Scale for Depression (CES-D) and history of hospitalization were used to determine criteria. Scores of 2 or below on all 30 subscales of PANSS, 129 or below on the DRS, 7 or above on CESD and no hospitalizations within the previous year were criteria for remission. Summed scores based on all these criteria determined remission rates.
Results: 34.3% of patients met criteria for PANSS scores below 3 on all subscales. 36.9% of patients had CESD scores below 7. 58% of patients had DRS scores of 130 or above and 83.4% of patients had no history of hospitalization within the last years. Upon summation of scores, 8.1% of our sample met our clinical criteria for remission. Using bivariate analysis, remission correlated with a small network of contacts but a greater degree of intimacy especially with non-kin individuals. It also correlated with higher IADL, religiousness, a greater aptness to resort to prayer in conflicts, and greater amount of time spent with others. These individuals compared themselves favourably with others. The type of residence, use of mental health services, and medication were not found to correlate with remission. No demographic variables correlated with remission.
Conclusions: Remission rates based on our data were consistent with rates reported in the literature. Our findings suggest that clinical remission is an attainable goal. Factors that influence clinical remission merit closer study, and development of treatment models based on these studies may augments outcomes in the older population with schizophrenia.

References:

NR254 Monday, May 21, 12:30 PM - 2:00 PM
Internal Consistency of the Scale Pediatric Symptom Checklist - PSC in Young Victims of the Winter Disaster of 2005 in Girón, Colombia
Heidi C. Oviedo, M.D. Universidad Javeriana, Psychiatry, Transv 5 45-30 apto 301 Bloque 3 Edificio CRAMER45, Bogotá, 00000, 3010, Adalberto Campo-Arias, M.D., MSc., Esperanza Acevedo, Psy.D., David A. Rincón, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the utility of Pediatric Symptom checklist at in high-risk child and adolescent population.

Summary:
Background: The prevalence of psychosocial problems is high among children victims of disaster. The Pediatric Symptom Checklist is used to identifying quickly child and adolescent common mental disorders. However, the internal consistency of its four subscales has not reported properly in Colombian children.
Objective: To compute the internal consistency of the sub-scale of the Pediatric Symptom Checklist in displacement children victims of the winter disaster of 2005 in Girón, Colombia
Method: One-hundred one mothers of children and adolescents were selected from the primary school of an alberge. Theirs children and adolescents were aged between 6 and 16 years (Mean = 10.6; SD = 1.7), 54.5% were girls, and scholarship between one and six years (Mean = 3.9; SD = 1.1). Mothers were ask for completing the Pediatric Symptom Checklist. This scale is a 35-item psychosocial screening questionnaire with four sub-scales designed to alert pediatricians to which school-aged children are in need of a more substantial mental health evaluation. Cronbach alpha coefficients were calculated for the subscales (attention deficit and hyperactivity, depressive, conduct and anxiety disorders).

NR253 Monday, May 21, 12:30 PM - 2:00 PM
Partial Evidence of an Association between Epidermal Growth Factor A61G Polymorphism and Age at Onset in Male Schizophrenia
DongChung Jung, M.D. Seoul National University College of Medicine, Department of Psychiatry, 28 YEONGEON-DONG JONGNO-GU, SEOUL NATL UNIV. HOSPITAL Neuropsychiatry dept., Seoul, 110-744, 5800, Kyu Young Lee, M.D., Sung Chan Kim, M.D., Eun-Jeong Joo, M.D., Yong Sik Kim, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize whether A61G plays a role in predisposition to schizophrenia and its effects on AAO.

Summary:
Epidermal growth factor (EGF) is a well-known neurotrophic factor regulating the development of various neuronal cells, including dopaminergic neurons, and dysfunction of EGF signals has been demonstrated as a risk factor for schizophrenia. Recently, several researchers have investigated associations including age at onset (AAO) with EGF A61G functional polymorphism, but the results of these studies have been controversial. Thus, we investigated whether A61G plays a role in predisposition to schizophrenia and its effects on AAO. Our subjects included 190 patients with schizophrenia and 347 controls. We assessed three different points of AAO: age at first occurrence of positive psychotic symptoms, medication, and hospitalization as a patient with schizophrenia. We found no differences in allele and genotype frequencies between patients and controls or associations between A61G and AAOs across stratified points in the entire sample and in each gender. However, we found significant gender differences in patients with the AA genotype in all stratified points of AAOs. Subset analyses of G allele distribution between clinical subsets with an AAO cutoff of 20 years revealed that male patients with early onset schizophrenia were more likely to exhibit the common AA homozygote than male patients with adulthood onset schizophrenia. In conclusion, although we were unable to support an association between EGF A61G and schizophrenia, the AA genotype might play a disease-modifying role differentially according to gender.

References:
NR255  Monday, May 21, 12:30 PM - 2:00 PM
A 8-year Alcohol Related Mortality in An Isolated Mountainous Rural Community in korea
Kim Tae Hui Yonsei University Wonju College of Medicine, psychiatry, Yonsei University Wonju College of Medicine, Wonju, 200-701, 5800, Min Seongho, Shin Jongho

Educational Objectives:
The aim of this study was to demonstrate the effects of alcohol intake and alcohol dependency on mortality over eight years in an isolated mountainous rural community in South Korea.

Summary:
Of 1,058 men and women in a rural community who reported their alcohol use in 1998, 150 men and women died during eight years of follow-up. We performed the descriptive analyses of the dead with basic data, daily alcohol consumption, and Severe Alcohol Dependence Questionnaire (SADQ). In order to determine odds ratios (OR) for alcohol related mortality, we control for various confounding factors using binary logistic regression. Those who are above 16 of SADQ were significantly higher in mortality and showed an odds ratios (OR) of 2.50 [95% confidence interval(CI)=1.18-5.28]. Those who had 12g of daily alcohol consumption showed lower mortality than never drinker and drinker of above 12g per day. It revealed the U-shaped relation between alcohol intake and mortality as in many western countries.

References:

NR256  Monday, May 21, 12:30 PM - 2:00 PM
Innovative Approaches to Designing Culturally Competent Interventions for Pacific Islander Victims of Domestic Violence: Collaborations in Research and Service Provision to Assess Patient Needs
Sophia Haeri New School for Social Research, Psychology, 110 Greenwich St, Apt 6F, New York, NY, 10006, 9000, Doris Chang

Educational Objectives:
At the conclusion of this session, the participant should be able to: (1) Identify reasons why API women may be less likely to seek help from mainstream agencies; (2) evaluate the possible implementation of an innovative model for collaboration between investigative research teams and domestic violence advocacy centers; and (3) Identify unique patient needs and potential barriers to help-seeking among API victims of domestic violence.

Summary:
Background: Due to particular stresses associated with acculturation, poverty, and gender inequality, mainstream “family violence” or “feminist” approaches to domestic violence intervention may not adequately address needs of more collectivistic, or interdependently oriented, Asian and Pacific Islander (API) women.

Method: In order to assess ethnic-specific service needs and utilization patterns, an intake and follow-up protocol was developed in collaboration with a community-based domestic violence center targeting API victims of domestic violence. Instruments were translated from English into Chinese, Vietnamese, and Cambodian. A relational database was constructed to make results available to researchers and clinic staff. Pilot data involving both Asian and non-Asian women seeking domestic violence services was analyzed for this study.

Results: Asian respondents reported significantly less symptom distress and better interpersonal role functioning than non-Asians. Though the Asian respondents were also showed more interdependent self-construal, 95% of women interviewed stated that they wished to leave or had left their abusers. Women’s subjective ratings of the severity of abuse bore no statistical relationship to the actual number of incidents of physical, psychological, or emotional abuse they reported having experienced.

Conclusions: Further investigation into the relationship between collectivistic orientation, level of acculturation, and willingness to leave the abuser is necessary to determine how best to service the needs of this population; however, identification of adaptive functioning that specific to women in the API community provides a promising avenue for further research in the development of culturally competent interventions. Study method also presents an innovative model of collaboration between investigative research teams and domestic violence advocacy centers to enhance parity and access to care for traditionally underserved ethnic populations.

References:
Methods: The subject of this study was 1,019 students of Korean high school. Young’s internet addiction was used to find out the internet subgroups. And 6 psychiatric scales (Spheres-of-Control Battery Item, Computer self-efficacy and outcome expectancy scale, Sensory seeking scale (SSS), State-trait anger expression inventory (STAXI), Maudsley Obsessive-Compulsive Inventory (MOCI), and Barratt Impulsiveness Scale (BIS)) were used to figure out some psychological characteristics of subgroups.

Results: In Young’s internet subgroups there was a difference in gender. Male students are shown to be most addicted to a computer game, while female students are shown to be most addicted to a cyber relationship.

Psychological characteristics of Young’s internet subgroups are followings: Cyber-relationship addiction is related to Computer self-efficacy and outcome expectancy scale, SSS, and MOCI. And information overload is related to STAXI, net compulsion is concerned with SSS. Computer game addiction is related to Computer self-efficacy and outcome expectancy scale, SSS, and BIS. Cyber-sexual addiction is concerned with Computer self-efficacy and outcome expectancy scale, STAXI.

Conclusion: Each internet addiction subgroups have psychologically different characteristics. Therefore each internet addiction subgroups need the therapeutically different approaches.

References:

NR258 Monday, May 21, 12:30 PM - 2:00 PM
Relationships Between Brain Structure and Cognitive Function in Development: The Impact of Socio-cultural Factors

Marc J. Dubin, M.D., Ph.D. Well Cornell Medical College, Sackler Institute for Developmental Psychobiology in the Department of Psychiatry, 435 East 70th St., Apt 27C, New York, NY, 10021, 9000, Sumit N. Niogi, M.S., Kimberly G. Noble, Ph.D., Bruce D. McCandless, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should have an understanding of the connection between phonological processing and the development of reading ability. The participant should be able to understand the neuroimaging technique of diffusion tensor imaging, its utility for imaging white matter tracts in the brain and the concept of fractional anisotropy as a measure of white matter tract integrity. The participant should have an appreciation for how cerebral white matter tract integrity may be related to phonological processing and reading ability and how this relationship may be affected by sociocultural factors.

Summary:
Phonological processing abilities represent critical aspects of language skill that also hold a strong predictive and causal relationship with reading development in children (Torgeson and Davis, 1996). We previously reported findings that two aspects of phonological processing in children were separately correlated with integrity measures of two distinct white matter tracts measured through Diffusion Tensor Imaging (DTI) (Dubin et al., 2007). Specifically, a) short term memory performance (CTOPP Memory for Digits) correlated with a measure of white matter tract integrity in a frontal lobe structure (bilateral regions of the anterior corona radiata (ACR)), and b) phonological awareness (CTOPP Elision) correlated with white matter tract integrity in a left anterior parietal region (left superior corona radiata (left SCR)). The current study investigates the extent to which these reported structure-function correlations in children are representative across different socio-economic status (SES) contexts. To examine this, a sample of 42 children were divided into higher and lower SES groups, as characterized by family education, occupation, and income. Both structure-function relationships were found to be significant within the higher SES subgroup (N=20, average age=8.1 years) and a multivariate analysis demonstrated a form of double dissociation of correlations. In contrast, results within the lower SES group (N=22, average age=8.3 years) demonstrated no significant correlations between either phonological measure and the corresponding white matter tract structures. We hypothesize that such SES effects may reflect differences in access to resources that might impact phonological development. For example, if lower SES children are exposed to a wider range of differences in access to educational resources, this might overshadow brain behavior relationships evident in the higher SES group.

References:

NR259 Monday, May 21, 12:30 PM - 2:00 PM
Medical Care for Older Schizophrenia Patients: Comparing Primary Care Providers and Psychiatrists

Ipsit Vahia, M.D. SUNY Downstate Medical Center, Psychiatry, 372 State Street #1, Brooklyn, NY, 11217, 9000, Sarah Jones, M.D., Azziza O. Bankole, M.D., Shilpa P. Diwan, M.D., Nikhil Palekar, M.D., Carl I. Cohen, M.D.

Educational Objectives:
At the end of this presentation, attendees will be able to appreciate factors that impact care provision of primary care to older schizophrenia patients by PCPs and psychiatrists. They will also be able to appreciate need for improved communication between treating physicians for this patient population.

Summary:
Introduction: Medical illness is the chief cause of morbidity and mortality in older adults with schizophrenia. Earlier work at our site suggested that older schizophrenia patients have access to medical care, but the adequacy of this care seems to be lacking. In order to address some of these issues, we tested the following hypotheses: (1) This disparity may be attributed to the attitude of Primary Care Providers (PCPs) towards older schizophrenia patients, (2) Poor communication between psychiatrists and PCPs (3) Physician behavior is influenced by patients’ symptom presentation.

Method: We administered a semi-structured 20-item questionnaire to a stratified convenience sample of 24 PCPs and 27 psychiatrists working in the New York area. We assessed beliefs, experiences, and procedures in treating medical illnesses in older persons with schizophrenia. Attitude was measured using a 13 item summed scale, We assessed communication using a 4-item summed score of percentage of time materials were sent and percentage of time they were received. We designed clinical vignettes to test physicians’ attitudes towards presenting symptoms.

Results: The mean summed score for Attitude for PCPs and Psychiatrists were 27.2 and 28.5. These scores indicated that both specialties showed little stigma toward older persons with schizophrenia. We found that PCP to psychiatrist communication scores indicated no significant discordance, but psychiatrist to PCP scores demonstrated a statistically significant discordance.

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At the conclusion of this presentation, to evaluate the influence of depression, anxiety and auditory hallucination on quality of life in Korean schizophrenic patients.

Summary:

Objective: To evaluate the influence of depression, anxiety and auditory hallucination on quality of life in schizophrenic patients

Methods: One hundred and nine schizophrenic patients were included. Psychotic symptoms were evaluated using the Positive and Negative Syndrome Scale (PANSS) and Psychotic Symptom Rating Scale (PSYRATS). Depression was evaluated using Beck Depression Inventory (BDI) and anxiety symptom with Beck Anxiety Inventory (BAI). The quality of life was evaluated using the Quality of Life Scale (SQLS).

Results: The PANSS total, PANSS general psychopathology subscale, PSYRATS total, PSYRATS hallucination subscale, BDI and BAI were negatively correlated with quality of life scale in schizophrenia. SQLS were significantly lower in depressed and anxious patients and slightly lower in hallucinatory patients.

Conclusion: Because of strong association to their quality of life, we should pay attention to depressive and anxious symptoms in schizophrenic patients.

References:
Conclusion and Importance: In this population-based sample, the existence of the sasonality of violence might be evidence-based.

References:

NR263 Monday, May 21, 3:00 PM - 5:00 PM
The Effects of Symptoms and Type of Psychopharmacological Treatment on The Cognitive Impairment of Patients With Major Depression: A Longitudinal Analysis

Karel J. Frasch, M.D. BKH Guenzburg, Dept. Psychiatry II of the Uni Ulm, Ludwig-Heilmeyer-Strasse 2, Guenzburg, 89312, 4280, Reinhold H. Killian, Ph.D., Norbert U. Neumann, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
- know about the importance of cognitive symptoms within the course of affective disorders
- understand that the loss of cognitive ability due to depression might be reversible by effective antidepressant (drug) treatment (state marker) and that on the other hand the extent of that reversibility may be limited by individual characteristics (trait marker)
- consider other effects than the reduction of the depressive symptoms that may work to improve cognition in depressive patients

Summary:
Objective: Major depressive disorders (MDD) are often accompanied by cognitive impairment which is associated with functioning level and treatment response. The exact nature of cognitive impairment in MDD remains unclear. This study aims to examine the influence of depressive symptoms and type of psychopharmacological treatment on cognitive performance in patients with major depression over a period of two years.

Methods: 107 in- and outpatients with MDD ranging from remitted to severely depressed were included in an open prospective observational study with three measurement points and tested with three different computerized cognitive performance tests (VAT, CAT, WRT). Psychotropic medication was classified by subclass and dose by two consultant psychiatrists. Statistical analysis was performed by random-effects regression models.

Results: Information processing speed was found to improve on the VAT and CAT. Depressive symptoms affected processing speed on the VAT and WRT. The quality of performance improved only on the WRT. The quality of performance was affected by depressive symptoms only on the CAT. Psychiatric treatment setting, psychotropic medication and gender had no relevant effect on cognitive performance. Age was negatively associated with the processing speed on the CAT and WRT. Education correlated positively with the processing speed on the VAT and CAT and with positive outcome on all tests.

Conclusions: Improvement of two processing speed variables during the study period and their negative relation with depression indicate that the loss of cognitive ability due to depression might be reversible by effective antidepressant treatment; on the other hand, the negative effect of age and the positive effect of education suggest that the extent of that reversibility may be limited by individual characteristics. Results in all tests improved over time suggesting that effects other than reduction of depressive symptoms (e.g. learning effects) may work to improve cognition.

References:

NR264 Monday, May 21, 3:00 PM - 5:00 PM
Mirtazapine Versus Venlafaxine in the Treatment of Major Depression

Nitin Dharwadkar, M.D. Monash University, Dept of Psychological Medicine, Dept of Psychological Medicine, Monash Medical Centre, 246 Clayton Road, Clayton, Victoria, 3150, 6021, Michelle Gopold, M.A., Mary Samuhel, M.A.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that the results obtained showed that like previous research in inpatient settings, both mirtazapine and venlafaxine can be used to treat major depression with melancholic features in outpatient settings. However there was demonstrated greater efficacy and tolerability for the mirtazapine group than individuals using venlafaxine.

Summary:
The study investigated whether previous results of the comparable efficacy and tolerability of mirtazapine and venlafaxine in severe depression in inpatients were transferable to an Australian naturalistic outpatient population of individuals with severe depression with melancholic features.

Twenty-six people suffering from major depressive disorder with melancholic features as assessed on DSM-IV, who attended Pine Lodge Clinic (a private Psychiatric Clinic in suburban Melbourne, Australia) as outpatients, from 1st September 2004 to 30th June 2005, were included in this study.

All participants were randomly allocated to two treatment groups. Twelve of the participants were randomly allocated to taking venlafaxine and fourteen participants took mirtazapine, over the 8 week trial period. Scores were obtained at baseline, and then at 1, 2, 4, 6 & 8 weeks post baseline. The investigation was focused on the tolerability and efficacy of these medications.

There has been a large-scale study looking at these variables but this was done on an inpatient hospital sample (Guefl, et al, 2001). This is the first study comparing these antidepressants in an outpatient setting.

Efficacy was assessed on total scores of the Montgomery-Asberg Depression Rating Scale (MADRAS), Hamilton Rating Scale for Depression (HAM-D -17), Clinical Global Impression Scale (CGI), Patient Rated Quality of Life (PRQL). Tolerability was measured by looking at side-effect profiles and the number of completers in the study groups and and The Sexual Dysfunction Scale (SDS).

The results demonstrated that 58% of Mirtazapine group and 33% of the Venlafaxine group completed the study. The Mirtazapine group showed overall greater tolerability. Both groups showed efficacy on the outcome measures, however the Mirtazapine group showed greater efficacy than the Venlafaxine participants on outcome measures. Some treatment gains were evident from one week onwards in both sample groups. There was no significant weight gain evident on either of the medications in this sample group.
NR265  Monday, May 21, 3:00 PM - 5:00 PM
Deep Brain Stimulation in Treatment Refractory Major Depressive Disorder: A Crossover Study
Loes Gabriels, Ph.D. University of Antwerpen (UA), Collaborative Antwerp Psychiatric Research Institute (CAPRI), Koninklijklaan #34, Berchem, B-2600, 4231, Paul Cosyns, Ph.D., Bart Nuttin, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize patients with treatment refractory major depressive disorder (MDD) for whom deep brain stimulation (DBS) might be a treatment option, and to understand inclusion and exclusion criteria for this treatment. The participant should be able to provide clinical guidance to a patient undergoing DBS. The participant will understand characteristics of therapeutic benefits and side effects of DBS in MDD.

Summary:
Deep Brain Stimulation (DBS) is a neuromodulation technique that involves the implantation of electrodes into specific parts of the brain. DBS is reversible, nondestructive, and can be modified after implantation. Since 1998 we investigate DBS as a therapeutic option for severe, treatment-refractory obsessive-compulsive disorder (OCD). DBS in the anterior limbs of the internal capsules induced clinically significant therapeutic benefit in this patient group. Besides OCD symptoms, mood scores improved as well.

Objective: Despite advances in biological treatment and psychotherapy for major depressive disorder (MDD), a substantial number of patients fail to improve or frequently relapse. Based on the results of DBS in OCD, this study investigates the effectiveness, safety, and tolerability of DBS in the same target for treatment-refractory MDD.

Methods: Randomized, double blind crossover study in three patients with a longstanding history of severe MDD who fulfilled stringent criteria for treatment refractoriness. Bilateral DBS leads were implanted in the ventral part of anterior limb of the internal capsule. Participants underwent standardized and detailed psychiatric assessments on a regularly scheduled basis, at baseline before surgery, and under continuous DBS. After six months of DBS, they entered a crossover trial with 1-week of no DBS, 1-week active DBS.

Results: At baseline, the mean Montgomery-Asberg Depression Rating Scale (MADRS) score was 41 (SD 7.2). After six months of chronic DBS, all three patients showed a clinically significant reduction in depression severity, and MADRS score dropped by a mean of 67% (SD 12%). Two of the three patients were in remission. In the blinded crossover, mean MADRS was 35 (SD 2.9) after 1 week of no DBS, 12 (SD 7.2) after 1 week of active DBS. No unacceptable side effects were noted.

Conclusions: Further research is warranted, but patients with severe, longstanding, treatment-refractory MDD may benefit from DBS.

References:
Cognitive Impairment in Bipolar Disorder: Analyzing the Influence of Psychotic Symptoms

Guillermo Lahera, M.D. Principe de Asturias University Hospital, Madrid, Spain, Psychiatry, Conde de Aranda, 3, 4B, MADRID, 28001, 4700, Jose Manuel Montes, M.D., Adolfo Benito, Elena Medina, Isabel Mirapeix, Maria Valdivia, Jeronimo Saiz-Ruiz

Educational Objectives:

At the conclusion of this presentation, the participant should be able to analyze the influence of a prior history of psychosis in the performance of cognitive tasks, in stable bipolar patients.

Summary:

Introduction: Several recent studies have confirmed the presence of cognitive deficits in stable bipolar patients - specially in attention and executive function - but the influence of a prior history of psychotic symptoms remains unclear.

Objective: To compare the performance in sustained attention and executive function of two groups of euthymic bipolar patients with and without a history of psychotic symptoms.

Methods: 75 patients meeting DSM-IV criteria for Bipolar Disorder type I were recruited from three outpatient clinics. They were described as euthymic by their consultants, but Hamilton Rating Scale and Young Mania Rating Scale were used in order to confirm it. Schizoaffective disorder was excluded. The sample was divided in two groups: 33 of the 75 patients had a positive history of psychotic symptoms, after been assessed with the Schedule for Affective Disorders and Schizophrenia -Lifetime Version (SADS-L), and 42 had not. They all had had three or more affective relapses. Patients were assessed with the Asarnov Continuous Performance and the Wisconsin Card Sorting Test.

Results: Mean ages of patients were 51.2 (9.85) and 45.8 (12.61). Both groups did not differ in education level, number of episodes, age of first episode and medication regime (t<0.05; C1, 1 - test: p = n.s.). No main effect for group was observed in sustained attention nor executive function (t - test; p = 0.98; 0.58.). Attention were negatively correlated with progression of illness in both groups (Pearson; p = 0.00).

Conclusion: Our results suggest that a prior history of psychotic symptoms in BD-I may not be associated with a more severe impairment of sustained attention and executive function. These findings partially refute the hypothesis of the existence of a subgroup of psychotic bipolar patients with specific psychometric characteristics.

References:


NR267 Monday, May 21, 3:00 PM - 5:00 PM

Correlates of Suicidality Among Patients With Psychotic Depression: Results From the STOP-PD Trial

Ayal Schaffer, M.D. Sunnybrook Health Sciences Centre, Psychiatry, 2075 Bayview Avenue, Room FG29, Toronto, ON, M4N 3M5, 1220, Alastair J. Flint, M.D., Eric Smith, M.D., Anthony J. Rothschild, M.D., Benoit H. Mulsant, M.D., Katalin Szanto, M.D., Barnett S. Meyers, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the correlates of suicidal ideation and attempts in patients with psychotic depression.

Summary:

Objective: Patients with psychotic depression are at high risk of suicide. The purpose of this study was to examine the independent association of age and other factors with suicidal ideation and suicide attempts in patients with unipolar psychotic depression.

Method: Data were obtained from baseline assessments of the first 183 subjects participating in the NIMH-sponsored Study of the Pharmacotherapy of Psychotic Depression (STOP-PD). Intensity of current suicidality and lifetime history of suicide attempts were determined. The independent association of age and other variables with intensity of suicidality at index assessment and with lifetime suicide attempts was examined using hierarchical regression analyses.

Results: Thirty-eight (20.8%) subjects had attempted suicide during the current depressive episode and 71 (38.8%) subjects had current suicidal ideation but had not made a suicide attempt during the current episode. Older age was associated with lower intensity of current suicidality, but this association was not statistically significant when controlling for other factors. Male gender, Hispanic background, history of past suicide attempt, greater severity of current depressive symptoms, and higher cognitive scores were each significantly associated with greater intensity of current suicidality. Older age was associated with a lower likelihood of a lifetime suicide attempt, and this association remained significant when controlling for other factors.

Conclusions: Subjects with psychotic depression have high rates of suicidal ideation and attempts. Age is inversely correlated with risk of a lifetime suicide attempt, while other sociodemographic and clinical variables are correlated with greater intensity of current suicidality in patients with psychotic depression.

References:


NR269 Monday, May 21, 3:00 PM - 5:00 PM

Frequency of Depression in Patients With Bipolar Disorder Using Self-Reported data

Michael Bauer, M.D. Technische Universitaet Dresden, Universitaetsklinikum Carl Gustav Carus, Psychiatry and Psychotherapy, Universitaetsklinikum Carl Gustav Carus, Fetscherstr. 74, Dresden, 01307, 4280, Paul Grof, Tasha Glenn, Natalie L. Raasgon, Johanna Sasse, Peter C. Whybrow

Educational Objectives:

The viewer should understand that brief depressive episodes occur frequently in patients with bipolar disorder, and that severe symptoms may occur during these brief episodes.

Summary:

Objective: We studied how changing the length requirement to that typical of recurrent brief depression (2-4 days) would impact the number of depressed episodes in patients with bipolar disorder.

Method: 203 patients with bipolar disorder according to DSM-IV criteria (135 bipolar I; 68 bipolar II) recorded mood daily (30,348 total days; mean 149 days) using ChronoRecord software on a
home computer. Episodes of depression and days of depression outside of episodes were determined. Symptom intensity (mild versus moderate or severe) within and outside of episodes was also analyzed.

Results: Decreasing the minimum duration criterion to 2 days increased the number of patients with a depressed episode two and a half times (52 to 131), and quadrupled both the number of depressed episodes per patient (0.62 to 2.60) and the number of depressed outcomes for all patients (125 to 584). With a 2-day episode length, 34% of days of depression remained outside an episode. The ratio of days with severe symptoms within episodes remained consistent (about 25%) in spite of decreasing the episode length to 2 days. Considering only days with severe symptoms, about 25% remained outside of episodes even with a 2-day length. None of the results distinguished bipolar I from bipolar II disorder.

Conclusion: Brief depressive episodes occur frequently in both bipolar I and bipolar II disorder. Moderate or severe symptoms occur during brief episodes at a ratio similar to that for episodes that meet the DSM-IV criteria.

References:

NR270  Monday, May 21, 3:00 PM - 5:00 PM
The Productivity Loss Among Korean Workers with Depression
Jong-Min Woo, M.D. Inje University Seoul Paik Hospital, Neuropsychiatry, Inje University Seoul Paik, Hospital Jurdong-2 ga Jung-gu, Seoul, 100-032, 5800, Won Kim, Tae- Yeon Hwang, Se-Joo Kim, Joon- Seok Lee, Byoung-Ju Ham, Chang- Soo Lee

Educational Objectives:
Attendants can understand how depression contributes to the socioeconomic burden of working peoples, And effective treatment can reduce the burden to the significant degree.

Summary:
Objective: The authors tried to calculate lost productive time among workers with and without depression. And we also tried to estimate how much benefit was obtained after 8 weeks treatment.
Methods: Patient group were recruited from workers visiting psychiatric outpatient clinic who had depressive disorders without physical illness and other mental disorders (N=62). Age and sex matched healthy control group were also recruited from advertisement through website (M=101). WHO Health and Work performance Questionnaire (HPQ) was applied to measure lost productive time and HAM-D was rated at initial visit. Patients were treated with antidepressant for 8 weeks and were measured for HPQ and HAM-D at 4 weeks and 8 weeks time point.
Result: The number of absence (1.01/day/month vs. 0.14-day/month, p=0.019) and the number of early leaving (1.70/day/month vs. 0.21-day/month, p=0.001) is significantly high in the patient group. The score of HAM-D of two groups were 23.78(±5.72) and 6.85(±5.72) respectively. The patient group evaluated their performance level lower than normal control group with significant value (7.51 vs. 5.24, p<0.001). Especially, patient group estimated their performance level during recent 4 weeks much lower than during past 1-year (6.69 vs. 5.24, p<0.001).
Among 62 patients, 37 completed the treatment. After 8 weeks medication, HAM-D score (23.63 vs. 7.69, p<0.001) and the number of early leaving (1.77-day/month vs 0.09-day/month, p=0.025) were decreased significantly. Moreover, self-rated score of average performance level for recent 4 weeks increased significantly after 8 weeks medication (5.16 vs. 6.53, p<0.001). 26 of 32 patients reported that their recent performance were better than 8 weeks ago (p=0.002).

Conclusion: Depression contributed to loss productive time among workers and thus increased socioeconomic burden. It was interesting that the "presenteeism" was prominent than the "absenteeism". Proper treatment of depression can reduce the loss productive time and contribute to economic gain.

References:

NR271  Monday, May 21, 3:00 PM - 5:00 PM
Biomarkers for Rapid Identification of Treatment Effectiveness in Major Depression (BRITE-MD): A Prospective Evaluation of an EEG Biomarker
Andrew F. Leuchter, M.D. Semel Institute for Neuroscience and Human Behavior at UCLA, Psychiatry, 760 Westwood Plaza, Room 37-426, Los Angeles, CA, 90024, 9000, Lauren B. Marangell, M.D., Karl S. Burgoyne, M.D., Jeff Sigl, Ph.D., Rakesh Jain, M.D., M.P.H., Sidney Zisook, M.D., Maurizio Fava, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize a simple-to-use frontal quantitative electroencephalographic (fEEG) biomarker of treatment response (ATR) may predict the therapeutic benefit of antidepressant treatment with escitalopram in patients with Major Depressive Disorder (MDD).

Summary:
Objective: To prospectively evaluate the role of frontal quantitative electroencephalography (fEEG) as an early predictor of subsequent clinical response in major depressive disorder (MDD).
Method: 40 subjects (age: 42 ± 11; 62% female) meeting DSM-IV criteria for MDD entered prospective treatment with a fixed dose of escitalopram (10 mg/day) for 7 weeks in one limb of an ongoing study (www.BRITE-MD.org). At each study visit we assessed severity of depression with the Hamilton Depression Rating Scale (HAM-D-17), and we recorded 4-channel fEEG (At1-Fpz, At2-Fpz, A1-Fpz, A2-Fpz). An EEG Index (Antidepressant Treatment Response [ATR, rev 0.4]) previously developed to predict clinical response (0 to 100, low to high probability of response) was tested prospectively using fEEG assessed at baseline and week 1. Clinicians were also asked to predict likelihood of response or remission based on overall clinical judgment at the week 1 assessment. Response to treatment was defined as a reduction from baseline symptom burden at week 7 of ≥ 50% (i.e., predicted HAM-D change of <50% vs. >50%).
Results: 24 (60 %) subjects responded to treatment. ATR was higher in responders than non-responders (52 ± 13 vs. 43 ± 12, p=0.045) and correlated with % change in HAM-D from baseline to week 7 (r=-0.312, p=0.05). ATR correctly predicted response in 28 subjects (p=0.041). Clinician's prediction of response was not significantly better than chance. EEG predictions were numerically greater than clinician predictions.
Discussion: EEG response to initial dosing was predictive of clinical response and numerically more accurate than clinician prediction.

Conclusions: This prospective evaluation confirmed that an EEG biomarker can be used to predict treatment efficacy after one week of escitalopram treatment. Future studies are needed to evaluate the utility of this EEG predictor in helping to guide antidepressant treatment decisions.

References:

NR272 Monday, May 21, 3:00 PM - 5:00 PM
Atypical Antipsychotics: Now the Treatment of Choice for Bipolar Disorder?
Annette M. Matthews Oregon Health Science, Psychiatry, Portland VA Medical Center, 3710 Southwest U.S. Veterans Hospital Road, Portland, OR, 97207, 9000, Robert Socherman, Ph.D., Alex Linke, Peter Hauser, M.D.

Educational Objectives:
At the conclusion of this presentation the participant should be able to identify changes in the prescribing practices in the treatment of bipolar disorder since the introduction of atypical antipsychotics.

Summary:
Objective: To examine prescribing practices since the introduction of atypical antipsychotics (between 2000 and 2006) in the treatment of bipolar disorder.

Methods: We collected data on 2,682 bipolar patients in the Veterans Administration VISN 20 region between January 2000 and December 2005. Of these 771 patients were followed for the entire study period and constitute the sample of our study.

Results: 672 (87%) of the patients were male, and 582 (75%) of the 618 patients we had information of race were Caucasian. 241 (31%) of the total group had at least one inpatient mental health stay during the study period. For those who had any inpatient admission, the average number of admissions was 2.2 hospitalizations during the 6 year study period.

Between January 2000 and December 2005, the percentage of patients on any atypical antipsychotic increased from 192 (25%) to 307 (40%) and the percentage of patients on any typical antipsychotic decreased from 54 (7%) to (24) 3%. The use of more “traditional” (non antipsychotic) mood stabilizers decreased from 459 (60%) to 407 (53%). Specifically, lithium use decreased from 335 (43%) to 251 (33%). The number of patients who were on antidepressants remained relatively unchanged at 312 (40%) and bipolar I disorder (n = 45) were assessed cross-sectionally by highly trained raters using semi-structured interviews and self-reports. All participants were in a major depressive episode. The groups were compared on a series of indicators of psychosocial functioning.

Results: Both bipolar I and II disorder were associated with high rates of absenteeism from work due to psychopathology, as well as high rates of hospitalization and suicide attempts. Bipolar II disorder had fewer hospitalization than bipolar I disorder which may have led to slightly less severe work impairment. Both conditions had similar rates of serious suicide attempts.

Conclusion: Bipolar II disorder is associated with serious work impairment and high suicide attempts. The level of impairment is similar to that seen with bipolar I disorder. It would be a mistake for clinicians to presume that the “softer” bipolar spectrum is less impairing than bipolar I disorder.

References:

NR274 Monday, May 21, 3:00 PM - 5:00 PM
Antidepressant Prescribing Practices of Primary Care Physicians
Marijo B. Tamburrino, M.D. University of Toledo, Psychiatry, 3000 Arlington Ave., Stop # 1193, Toledo, OH, 43614, 9000, Denis Lynch, Ph.D., Rollin Nagel, Ph.D.

Objective: Significant research has looked at the psychosocial impairment associated with bipolar I disorder and major depressive disorder. Far less is known about the impact of bipolar II disorder. The present study sought to assess the social and work functioning impairment associated with bipolar II disorder and whether these are more or less severe than those associated with bipolar I disorder.

Method: Psychiatric outpatient with bipolar II disorder (n = 89) and bipolar I disorder (n = 45) were assessed cross-sectionally by highly trained raters using semi-structured interviews and self-reports. All participants were in a major depressive episode. The groups were compared on a series of indicators of psychosocial functioning.

Results: Both bipolar I and II disorder were associated with high rates of absenteeism from work due to psychopathology, as well as high rates of hospitalization and suicide attempts. Bipolar II disorder had fewer hospitalization than bipolar I disorder which may have led to slightly less severe work impairment. Both conditions had similar rates of serious suicide attempts.

Conclusion: Bipolar II disorder is associated with serious work impairment and high suicide attempts. The level of impairment is similar to that seen with bipolar I disorder. It would be a mistake for clinicians to presume that the “softer” bipolar spectrum is less impairing than bipolar I disorder.

References:
**Educational Objectives:**

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

1. List tools used to diagnose depression in primary care settings.
2. Outline the prevalence of depressive disorders in primary care populations.

**Summary:**

The majority of prescriptions for antidepressant medications are written by primary care physicians (PCPs). Concerns about the effectiveness of their prescribing practices have been raised. The purpose of the present study was to explore whether primary care patients with continuing depression symptoms have their medications changed. Subjects were 128 patients from a primary care research network attending either a family medicine or internal medicine clinic, who reported being on an antidepressant for at least one month. Subjects were recruited through notices placed in the waiting room and exam rooms, and through invitations extended by nursing personnel. Participants completed the Beck Depression Inventory (BDI), the Patient Health Questionnaire (PHQ) and the 36-item Short-Form Health Survey (SF-36). Patients' medical charts were later examined to review any changes in antidepressants made by the PCP either 6 weeks before or after their study entry date. It was hypothesized that the majority of patients who were still symptomatic would not have changes in their medication. PHQ depression diagnoses were dysthymia (N=8), major depressive disorder (N=33) and both dysthymia and major depressive disorder (N=32). Medication changes were reported for only 33% of those with dysthymia, 24% of those with major depressive disorder and 33% of those with both diagnoses. The average score on the BDI for subjects whose medications had not been changed was 20.6. BDI scores were significantly inversely related to the SF-36 general health (r = -.486, p<.0001) and mental health (r = -.819, p<.0001) scores. In spite of the presence of significant symptoms of depression and reduced quality of life, PCPs did not make any changes to subjects' medications. This study confirms concerns about the adequacy of depression treatment by PCPs and suggests that closer follow-up of patients is indicated.

**References:**


**NR276**

**Monday, May 21, 3:00 PM - 5:00 PM**

**Predictors of Bipolar Disorder in Patients Diagnosed with Major Depression in a Privately Insured Population**

Siddhesh A. Kamat, M.S. HealthCore, Inc., Health Economics, 800 Delaware Ave, 5th Floor, Wilmington, DE, 19801, 9000, Krishika Rajagopalan, Ph.D., Ned Pethick, M.B.A., Vincent Willey, Pharm.D.

**Educational Objectives:**

At the conclusion of this session, the participants should be able to recognize the potential for missing diagnosis in patients with bipolar disorder and to identify misdiagnosed patients based on characteristic predictors.

**Summary:**

**Hypothesis:** Patients with bipolar disorder (BD) who are misdiagnosed with major depressive disorder (MDD) can be identified through claims data-based predictor variables.

**Methods:** Administrative claims data from 3 US health plans were used to identify patients diagnosed with MDD between 1/1/2000 through 3/31/2004. An age-, gender-, and region-stratified random sample of patients with ≥2 medical claims for MDD and none for BD was surveyed via telephone to complete the Mood Disorder Questionnaire (MDQ), a tool used to screen patients for BD symptoms. Univariate logistic regression, followed by multivariate techniques, was used to identify predictors of BD. Baseline

sured by the Montgomery-Åsberg Depression Rating Scale total score (MADRS) (study period I [SPI]), and the maintenance of response with OFC or olanzapine monotherapy (OLZ) (study period II [SPII]).

**Method:** Puerto Rican outpatients received open-label OFC at doses of 12 mg/25 mg (range 6/12.5-25 mg) for 7 weeks in SPI and responders were then randomized to OFC at their last dose from SPI or OLZ 10 mg (range 5-20 mg) for an additional 12 weeks in SPII. Secondary measures included Clinical Global Impressions of Severity of Depression (CGI-S-D), the Medical Outcomes Study 12-item Short Form Health Survey (SF-12) and safety parameters. 

**Result:** SPI: n=161; SPII entered/completed: OFC n=57/44, OLZ n=57/39. MADRS improved for OFC during SPI (-20, p<.001), improved slightly for the OFC and worsened for OLZ group (-4 vs 8.2 respectively, p<0.001) during SPII. Almost 70% and 60% patients met response and remission criteria, respectively in SPI. More patients in the OFC group vs the OLZ group met response criteria (p=0.047) and remission criteria (p=0.002) in SPII. Drug compliance rates were 86% (SPI) and 77% (SPII). Most frequently reported treatment-emergent adverse events in SPI and SPIII were increased appetite, weight increased, somnolence, anxiety, insomnia, and depressed mood. There were statistically significant changes for some laboratory analytes in both study periods (cholesterol, triglycerides, LDL, and some hepatic enzymes).

**Conclusion:** Acute treatment of BD patients with OFC at a starting dose of 12/25 mg/day resulted in significant improvement for depression and most health outcomes. This study suggests that acute treatment gains and safety in BD patients on OFC are maintained for up to 19 weeks with OFC therapy, but switching to OLZ monotherapy may result in worsening in efficacy. The safety profiles for both treatments were fairly similar.

**References:**

variables with a univariate p-value < 0.10 were entered into the “best-fit” multivariable model with acceptable predictive validity for final predictor variable selection.

Results: From a sampling frame of 41,738 patients diagnosed with MDD, based on sample size calculations, surveys were administered until a target sample of 1360 patients was screened. Screened BD positive patients (n=94, 6.9%) were considered likely to be inaccurately diagnosed. A higher percentage of males screened positive compared to females (6.6% vs 6.1% respectively, P=0.092) and patients aged 18-35 were 3 times more likely to screen positive than patients 56 years and above (P<0.01). Rates of inpatient or ER visits related to mental health conditions were higher in patients screening positive compared to patients screening negative for BD (40.4% vs 21.3%, P<0.01). The final model indicated that age, gender, rate of inpatient or ER visits related to mental health conditions, substance abuse, concomitant use of anticonvulsants, antidepressants, antipsychotic medications, and anxiolytic agents are useful predictors in identifying BD patients who are diagnosed inaccurately with MDD.

Conclusions: These claims data-based predictor variables, after necessary validation and reliability checks, can be used by health plans in identifying patients at high risk of missed BD diagnosis. Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

NR277  Monday, May 21, 3:00 PM - 5:00 PM
Prevalence of Potential Missed Diagnoses of Bipolar Disorder in Patients Diagnosed with Major Depressive Disorder in a Commercially Insured Population
Siddhesh A. Kamat, M.S. HealthCore, Inc., Health Economics, 800 Delaware Ave, 5th Floor, Wilmington, DE, 19801, 9000, Krithika Rajagopalan, Ph.D., Ned Pethick, M.B.A., Vincent Willey, Pharm.D.

Educational Objectives:
At the conclusion of this session, the participants should be able to discuss (1) the potential and extent of missed diagnoses of bipolar disorder in patients diagnosed with major depressive disorder, (2) features that assist in identifying the subpopulation of patients with most prevalent misdiagnosis, and (3) the adverse effect of misdiagnosis for the patient and healthcare system.

Summary:
Introduction: Patients with bipolar disorder (BD) spend more time in the depressed than the manic state. The objective of this study was to evaluate the prevalence of potential missed diagnoses of BD in patients diagnosed with major depressive disorder (MDD).

Methods: Claims data (1/1/2000 through 3/31/2004) from patients diagnosed with MDD were evaluated. An age-, gender-, and region-stratified random sample of patients with ≥2 medical claims for MDD (none for BD) were targeted for a telephone survey, which included demographic and comorbidity questions, the Mood Disorder Questionnaire (MDQ), the Medical Outcomes 12-item Short Form, and the Sheehan Disability Scale.

Results: In a survey of 1360 patients screened using the MDQ, 94 patients (6.9%) screened positive for BD. Prevalence of these screen positives was highest in males aged 18-35 years (12.3%) compared with females (7.1%). More patients screening positive reported obsessive-compulsive disorder (24% vs 8%), psychotic disorders or hallucinations (9% vs 2%), suicidal ideation (61% vs 29%), and drug abuse (34% vs 11%) compared with patients screening negative (all p<0.05). Patients screening positive had a lower overall mental health-related quality of life and a higher proportion had impaired work, social and family function compared with patients screening negative (all p<0.05). The annualized per patient overall cost in patients screening BD positive was approximately USD $9314 versus $4356 for patients actually diagnosed with BD (p<0.05).

Conclusions: In this study of patients diagnosed with MDD, approximately 7% were likely to be bipolar. The prevalence of misdiagnosis was highest among young males (12.3%). These findings may benefit interventions for appropriate screening, diagnosis and management.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

NR278  Monday, May 21, 3:00 PM - 5:00 PM
Health Behaviors in Bipolar Patients
Nancy C. Maruyama, M.D. Beth Israel Medical Center, Psychiatry, 317 East 17th Street, Suite 5F09, New York, NY, 10003, 9000, Avivit Fuchs, M.D., Clarisa Atencio, M.D., Samantha Yard, B.A., Susan Tross, Ph.D., Igor I. Galynker, M.D.

Educational Objectives:
At the end of this presentation participants should understand that bipolar patients carry an excess burden of medical illness, and that these medical illnesses might be modifiable by health behavior change.

Summary:
Objectives: We assessed health behaviors in bipolar patients who are known to have higher rates of medical illness and earlier death.

Methods: In a cross-sectional study, 18 male and female bipolar I and II outpatients followed at a tertiary care clinic, filled out validated self-report measures of physical activity, diet, smoking, and health screening behaviors.

Results: Mean age was 43.7. Most were female, single or divorced, with annual income of less than $20,000. 70% had had more than five episodes of mania/ hypomania or depression. Compared to the US general population, our bipolar subjects were more likely to be smokers (39% vs 21%) and physically inactive (44% vs 24%). They had higher rates of heart disease and diabetes (11% vs 7%), despite their relatively young age. Bipolar subjects were equally likely to be obese/ overweight than the general population. Mammography, Pap smear, PSA, and serum cholesterol screening were performed at rates equivalent to US general population. Colonoscopy and stool for occult blood testing were done at higher rates than the US prevalence. Subjects reported feeling more concerned with their health since bipolar diagnosis (51%) and a large percentage reported attempting health behavior changes (50% to 100%). The great majority (94%) of bipolar subjects felt health behavior change might help mood, and 72% felt it might influence bipolar disorder course.

Conclusions: Bipolar patients are more likely than other members of the general population to engage in unhealthy behaviors such as smoking and sedentary life-style that carry risk of chronic physical illnesses. While these patients appear to perform health screening behaviors and have knowledge of health behaviors they do not appear to be able to translate this into health behavior.
change. There is a need for interventions aimed at improving behavior change.

References:

NR279 Monday, May 21, 3:00 PM - 5:00 PM
Similarities and Differences of Depression in Bipolar I, Bipolar II and Unipolar Patients
Sermin Kesebir V, M.D. Yuksek Ihtisas Hospital, Psychiatry, Kirikkale Yuksek Ihtisas Hospital, Psychiatry, Department, Turkey, Kirikkale, 71100, 4890, Yasemin Simsek, Ph.D.

Educational Objectives:
Clinical characteristics between bipolar depression (BD) and unipolar depression (UD) have been studied for years with controversial results. Bipolar disorder is often misdiagnosed as unipolar disorder when exploration of symptoms is not adequate enough. The objective of this study was to investigate a number of variables which could differentiate bipolar I (BPI), bipolar II (BP2) and unipolar (UP) patients depressions.

Summary:
All the patients were assessed with Hamilton Depression Rating Scale (HDRS-17) and Montgomery and Asberg Depression Scale (MADRS). The current sample consisted of 180 patients: 110 UP, 42 BPI, 28 BPII.

We found that the mean age of onset for the first depressive episode lifetime was earlier in BPI (22.53, sd= 9.1) and BPII (20.18, sd= 7.8) than in UP (27.61, sd= 14.2) (p= 0.025). We also found that differences in recurrence of depressive episodes (mean number of episodes) 6.3, sd= 2.4 in BPI; 8.4, sd= 3.2 in BPII and 5.1, sd= 2.8 in UP (p= 0.001). There was a difference in the severity of the depressive episode for those patients who were depressed at baseline interview, a severe depressive episode was observed in 86.4% in BPI, 60.2% in BPII and 54.7% in UP (p= 0.001). BP patients were more melancholic: 72.6% in BPI, 82.2% in BPII and 44.4% in UP (p= 0.001) and more psychotic: 57.8% in BPI, 28% in BPII and 18.7% in UP (p= 0.001). 56.4% of UP had a score > 12 months (n=23). The main demographic and clinical variables were compared in the two groups using t-tests and chi-square tests. Results: The group with a DUI<12 months presented a greater prevalence of males (x^2 4.005, p=0.045). With respect to clinical variables, significant differences were found between the two groups; patients with a DUI<12 months presented an earlier onset (t=2.515, p=0.014), a longer duration of illness (t= -2.483, p= 0.016), a higher number of recurrences (t= -2.262, p<0.027) and had more frequently comorbid Axis I disorders with onset later than MDD (x^2 5.595, p=0.05).

Conclusions: These preliminary findings seem to suggest that a longer DUI can negatively influence the long-term outcome of MDD.

References:

NR281 Monday, May 21, 3:00 PM - 5:00 PM
Clinical Characteristics and Response to Mood Stabilizers in Late Onset Bipolar Disorder
Carlo Alfredo Altamura, M.D. University of Milan, Dept. of Psychiatry, Dept. of Clinical Sciences, via GB Grassi 74, Milan, 20157, 4759, Silvia Zanoni, M.D., Nazzaro D'Urso, M.D., Massimiliano Buoli, M.D., Sara Pozzoli, M.D., Roberta Bassetti, M.D., Bernardo Dell'Ossio, M.D., Emanuela Mundo, M.D.

Educational Objectives:
At the conclusion of this presentation the participants should be able to recognize the clinical features of later onset Bipolar Disorder (BD) and the characteristics of the response to long-term mood stabilizer treatment.

Summary:
Objective: The aim of this study was to investigate for differences in the clinical characteristics and response to mood stabilizers between patients with earlier (< 45 years) or later (>45 years) onset Bipolar Disorder (BD)

NR280 Monday, May 21, 3:00 PM - 5:00 PM
Does the Duration of Untreated Illness Influence the Long-Term Outcome of Major Depressive Disorder?
Carlo Alfredo Altamura Dept. of Psychiatry, University of Milan, Dept. of Psychiatry, Department of Clinical Sciences, via GB Grassi 74, Milan, 20157, 4759, Bernardo Dell'Ossio, M.D., Emanuela Mundo, M.D., Massimilano Buoli, M.D., Liliana Dell'Ossio, M.D.

Educational Objectives:
At the conclusion of this presentation, the participants should be able to recognize the role of the duration of untreated illness (DUI), defined as the time elapsed between the onset of Major Depressive Disorder (MDD) and the first adequate antidepressant treatment, on the long-term outcome of MDD.

Summary:
Objective: The role of the duration of untreated illness (DUI) as predictor of outcome in Major Depressive Disorder (MDD) has not been systematically investigated yet, with most studies in the field focusing on psychotic disorders and anxiety disorders. The present naturalistic study was aimed to evaluate the predictive value of the DUI on the long-term outcome of a group of patients with MDD.

Methods: Sixty-eight patients with MDD, according to the DSM-IV-TR criteria, were selected and interviewed. The DUI was defined as the interval between the onset of the first depressive episode and the first antidepressant treatment. The sample was divided in two groups according to a DUI < 12 months (n=45) and > 12 months (n=23). The main demographic and clinical variables were compared in the two groups using t-tests and chi-square tests.

Results: The group with a DUI<12 months presented a greater prevalence of males (x^2 4.005, p=0.045). With respect to clinical variables, significant differences were found between the two groups; patients with a DUI<12 months presented an earlier onset (t=2.515, p=0.014), a longer duration of illness (t=-2.483, p= 0.016), a higher number of recurrences (t=-2.262, p<0.027) and had more frequently comorbid Axis I disorders with onset later than MDD (x^2 5.595, p=0.05).

Conclusions: These preliminary findings seem to suggest that a longer DUI can negatively influence the long-term outcome of MDD.

References:

NR279 Monday, May 21, 3:00 PM - 5:00 PM
Similarities and Differences of Depression in Bipolar I, Bipolar II and Unipolar Patients
Sermin Kesebir V, M.D. Yuksek Ihtisas Hospital, Psychiatry, Kirikkale Yuksek Ihtisas Hospital, Psychiatry, Department, Turkey, Kirikkale, 71100, 4890, Yasemin Simsek, Ph.D.
Methods: 103 patients with DSM-IV-TR BD I or II diagnosis, were selected. All patients gave their informed consent to participate in the study. Patients were subdivided in two groups according to the age at onset (> 45 years or < 45 years). The main demographic and clinical variables were collected by clinical interviews (SCID-I) or review of the clinical charts by expert psychiatrists, and then compared between the two groups (Student’s t-test and chi-square tests). Response to mood stabilizers was assessed by computing the number of major mood episodes occurring during the 24 months before and after the start of mood stabilizers (t-tests for paired data).

Results: 13.8% of patients had an age at onset > 45 years. Patients with later onset BD had a shorter duration of untreated illness (DUI) (t=4.652, p<0.04), and a lower number of mixed episodes occurring before mood stabilizer treatment (t=3.498, p<0.001) than patients with earlier onset. Patients were treated with lithium, valproate, or atypical antipsychotics as mood stabilizers and followed up for 24 months. In earlier onset BD mood stabilizers were effective in reducing manic (t=3.749, p<0.001) and depressive (t=3.323, p<0.001) recurrences, while in later onset BD mood stabilizers were effective only in reducing manic recurrences (t=2.876, p=0.01) but not depressive ones (t=0.001, p<0.9).

Conclusions: Patients with later onset BD may have significant clinical differences from patients with earlier onset BD. In addition, the lack of efficacy of mood stabilizers in preventing depressive recurrences in later onset BD suggests that depressive episodes in this sub-group of BD patients may need a specific clinical and pharmacological management.

References:

NR282 Monday, May 21, 3:00 PM - 5:00 PM
Addiction in Bipolar Disorders: The Mediating Role of Cyclothymic Temperament
Sermin Kesinbek II, M.D. Yuksek Ihtisas Hospital, Psychiatry, Kirikkale Yuksek Ihtisas Hospital, Psychiatry, Department, Turkey, Kirikkale, 71100, 4890, Yasemin Simsek, Ph.D.

Educational Objectives:
Bipolar spectrum disorders and addiction often co-occur and constitute reciprocal risk factors that the authors believe are best considered under a unitary perspective. Cyclothymic and hyperthymic substrates are at increased risk for substance use, possibly moving towards addiction through exposure to intrinsically dependence-producing substances. The contribution of bipolar spectrum disorders to the addictive process is often clinically missed because attenuated and subclinical expressions of such mood disorders as bipolar II and cyclothymia are not adequately appreciated by our current formal diagnostic system.

Summary:
We evaluated 100 outpatients with bipolar I or II disorder using SCID-I, TEMPS-A (Temperament evaluation Memphis, Pisa and San Diego- Autoquestionnaire) and clinician administered and self-rated questionnaires to determine affective disorders and substance use disorders. 36 of the patients (36%) with bipolar disorder also met DSM-IV criteria for at least one comorbid lifetime substance use disorder. There were no differences in comorbidity between patients with bipolar I and II disorder. Both lifetime and current comorbidity were associated with cyclothymic temperament (p= 0.001 and p= 0.03), earlier age at onset of affective symptoms and syndromal bipolar disorder (p= 0.045 and p= 0.042), switch (p= 0.028 and p= 0.035) and suicide attempt (p= 0.045 and p= 0.05). Total numbers of episodes and duration of manic episodes were higher in comorbid patients (p= 0.027 and p= 0.035). Cyclothymic temperament was associated with positive family history for bipolar disorder and substance use disorder but there were no differences in family history between bipolar patients with or without substance use disorder. This findings suggest the hypothesis of a common familial genetic diathesis for a subtype of bipolar disorder and substance abuse.

References:

NR283 Monday, May 21, 3:00 PM - 5:00 PM
Aripiprazole as Adjunctive Therapy in Major Depressive Disorder With and Without Chronic Features
Edward Kim, M.D. Bristol-Myers Squibb Company, Neuroscience Medical Strategy, 777 Scudders Mill Road, Plainsboro, NJ, 08536, 9000, Robert M. Berman, M.D., Ronald N. Marcus, M.D., Rene Swanink, Robert D. McQuade, Ph.D., Andrei A. Pikalov III, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the role of aripiprazole augmentation in patients with both chronic and non-chronic depression that has not responded adequately to antidepressant monotherapy.

Summary:
Objective: To assess the efficacy of adjunctive aripiprazole or placebo with standard antidepressant therapy (ADT) in patients with major depressive disorder with and without chronic features who showed an incomplete response to at least one historical treatment and one prospective treatment. This was a subanalysis of a Phase III prospective clinical trial (CN138-139).

Methods: Patients experiencing a major depressive episode (HAM-D17 Total score ≥18) received open label escitalopram, fluoxetine, paroxetine CR, sertraline or venlaftaxine XR plus single-blind, adjunctive placebo. Patients with an incomplete response after 8 weeks were randomized to a 6-week double-blind phase of either: continued adjunctive placebo or adjunctive aripiprazole (2-20 mg/day). The primary efficacy endpoint was the mean change from end of open label ADT treatment to end of double-blind adjunctive treatment (Week 14, LOCF) in the MADRS Total score. Patients with durations of current episode of greater than or equal to 24 months were classified as chronic, while those with durations of less than 24 months deemed non-chronic.

Results: In the efficacy sample of 353 patients, the median duration of the current episode was 21.5 months, with a mean duration of 40.9 months (range 1.7-474.0 months). 187 (53%) patients were chronic and 166 (47%) were non-chronic. Overall, the mean change in MADRS Total score was significantly greater in those receiving adjunctive aripiprazole than adjunctive placebo (-3.0; p < 0.001). In both chronic and non-chronic patients, the mean change in MADRS Total score was significantly greater in those receiving adjunctive aripiprazole than placebo (-3.04, 95% CI - 5.50, -0.58 and -2.88, 95% CI -5.12, -0.64, respectively). The
interaction test with subgroup-by-treatment as interaction effect was non-significant (p=0.922).

Conclusions: Adjunctive aripiprazole is efficacious in patients with major depressive disorder and without chronic features who demonstrate an incomplete antidepressant response. The interaction between subgroup and treatment response was not significant.

References:

NR284 Monday, May 21, 3:00 PM - 5:00 PM
Can EEG-guided Antidepressant Selection Improve Response Rates? Insights from the BRITE-MD Trial
Andrew F. Leuchter, M.D. Semel Institute for Neuroscience and Human Behavior at UCLA, Psychiatry, 760 Westwood Plaza, Room 37-426, Los Angeles, CA, 900954-8300, 9006, Ian A. Cook, M.D., William S. Gilmer, M.D., Scott D. Greenwald, Ph.D., Robert H. Howland, M.D., Madhukar H. Trivedi, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that: 1) the BRITE-MD study (www.BRITE-MD.com) was designed to assess the accuracy of an frontal quantitative electroencephalographic (fqEEG) biomarker (ATR) in predicting clinical response to escitalopram treatment using EEGs assessed at baseline and 1 week after treatment; 2) interim results suggest that using an EEG biomarker of early (Day 7) response to escitalopram may help guide antidepressant selection. Patients whose ATR predicts response do best when continued on treatment, while others may benefit from alternate regimens.

Summary:
Objective: The BRITE-MD study (www.BRITE-MD.com) was designed to assess the accuracy of a frontal quantitative electroencephalographic (fqEEG) biomarker in predicting response to escitalopram (ESC) treatment. This analysis compares the response rate between subjects who received treatment consistent with the biomarker prediction vs. other subjects.

Method: 111 subjects (age: 42 ± 14; 59% female) meeting DSM-IV criteria for MDD began treatment with escitalopram (ESC; 10 mg/day) and were randomly assigned after 1 week to either: 1) continue ESC (10 mg/day; n=40); 2) augment with bupropion XL (AUG; 300 mg/day; n=36); or, 3) switch to bupropion XL (BUP; 300 mg/day; n=35) for 7 weeks of treatment. At each visit severity of depression was assessed with the Hamilton Depression Rating Scale (HAM-D-17) and 4-channel fqEEG was recorded. Clinical response was defined as a reduction in HAM-D at week 7 ≥ 50% from baseline. A previously developed index to predict probability of clinical response (0 to 100) using baseline and week 1 EEGs (Antidepressant Treatment Response ATR rev 0.4) was evaluated. Treatment consistent with ATR included subjects continued on ESC when ATR>THRESHOLD or switched to alternate treatment when ATR< THRESHOLD. All other subjects received treatment inconsistent with ATR.

Discussion: For subjects remaining on the initial treatment (ESC), the response rate was higher with ATR-consistent treatment vs. ATR-inconsistent treatment (73% vs. 36%, p=0.025). For all subjects, the response rate was higher with ATR-consistent treatment than with ATR-inconsistent treatment (65% vs. 41%, p=0.008), and higher than the pooled response rate (65% vs. 51%, p=0.043).

Conclusions: Using a fqEEG biomarker at week 1 of ESC treatment may help guide antidepressant selection. Subjects whose ATR predicts response do better when continued on ESC, while subjects whose ATR predicts non-response may benefit from alternate regimens.

References:

NR285 Monday, May 21, 3:00 PM - 5:00 PM
Cortisol, CD19, and CD56 Cell in Patients with Major Depressive Disorder
Yang-Whan Jeon Our Lady of Mercy Hospital, The Catholic University of Korea, Department of Psychiatry, 665 Bupyeong Dong, Bupyeong-gu, Incheon, 403-720, 5800, E-Jin Park, Sang-Ick Han

Educational Objectives:
In depressive illness, a wide variety of disturbances in endocrine systems and immunologic parameters have been reported. In this study, we investigated the relationship among the endocrine, immune system and clinical symptoms in patients with unmediated major depressive disorder (MDD) in acute state, we measured the clinical symptom and plasma ACTH, cortisol and peripheral lymphocyte parameters were examined.

Summary:
44 patients with MDD from outpatient clinic were recruited. To investigate depressive symptom, we administered Hamilton Depression Rating Scale (HDRS) for the subjects. 17-items of HDRS were factorized using the confirmatory factor analysis and three factors were obtained: depression factor (Fd), anxiety factor (Fa), insomnia factor (Fi). Plasma ACTH, cortisol and peripheral lymphocyte or NK cell measures (CD3, CD4, CD8, CD 19 or CD56) was obtained. We calculated Pearson's correlation coefficients and used the "STATISTICA" program for statistical analyses. There was a significant negative correlation between Fd and CD56 cell number (r = -0.31, P < 0.05). There was a significant positive correlation between Fi and cortisol level (r = 0.33, P < 0.05). Number of CD 56 (NK T) cells was negatively correlated with depression factor. Decreased CD 56 cells in acute, major depressed patients may reflect the core symptoms in acute major depression and suggest the possible involvement of an immune suppression in depression. Also our data showed influences of anxiety factor on CD 19 (B) cell distribution and influences insomnia factor on cortisol level in major depression in acute state. In this study, endocrinological and immunological change in patients with major depressive disorder may reflect various factors of depression respectively.

References:
Lamotrigine As Add-On to Lithium in Bipolar Depression
Marc van der Loos, M.D., Isala Klinieken, Psychiatry, Dr. van Heesweg 2, Zwolle, 8000 Gk, 4210, Willem Nolen, M.D.

Educational Objectives:
At the conclusion of this poster readers will have a new treatment option in the treatment of the bipolar depression.

Summary:
Introduction: Lamotrigine is one of the pharmacological options in bipolar depression, but has been studied in RCT’s so far only as monotherapy. In an 8 week, double-blind study we compared the acute effects of lamotrigine (maximum dose 200 mg/d) and placebo as add-on therapy to ongoing treatment with lithium in patients with bipolar depression.

Method: Inclusion criteria: age ≥18 years, bipolar I or II disorder, depressive episode, MADRS >18 or CGI-BP severity of depression ≥4, lithium levels between 0.6 and 1.2 mmol/l.

Exclusion criteria: Psychotic features, rapid cycling course with ≥10 episodes/year, alcohol or substance abuse, severe personality problems, severe somatic illness, current use of antidepressants, antipsychotics or benzodiazepines ≥2 mg lorazepam equivalent.

Outcome measures: MADRS and CGI-BP.

Results: In total 124 patients (68% BP-I, 32% BP-II) were included (Netherlands: 112, Spain: 12). 64 patients received lamotrigine, 60 placebo. Change on the MADRS from baseline (primary outcome criterium) was 15.38 points with lamotrigine and 11.03 points with placebo (p=0.024). Significantly more patients responded to lamotrigine (n=33, 51.6%) than to placebo (n=19, 31.7%) on the MADRS (p=0.030), but not on the CGI-BP (p=0.103) or MADRS and CGI-BP combined (p=0.069).

Switch to (hypo)mania occurred in 5 patients (7.8%) on lamotrigine and 2 patients (3.3%) on placebo (p=0.441).

Conclusion: Lamotrigine was found effective as add-on to lithium in the acute treatment of bipolar depression.

References:

Affective Temperaments in 119 Consecutively Admitted Patients to An Affective Ward
Ketil J. Oedegaard, Sr., M.D., M.P.H., University of Bergen, Psychiatry, Haukeland University Hospital, Bergen, 5021, 4039, Vigsid E.G Syrstad, Jr., M.D., Dag Neckelmann, Sr., M.D., M.P.H., Ole Bernt Fasmer, Sr., M.D., M.P.H.

Educational Objectives:
The purpose of the presentation is to show that characterizing affective temperaments in patients with mood disorders attending an affective ward may give clinically valuable information regarding these patients, possibly delineating a distinct group of patients with mood disorders with a particular presentation of affective symptoms and psychiatric and somatic co-morbidity. The educational purpose is to demonstrate that the correct recognition of affective temperaments may be helpful in establishing the correct diagnosis and treatment of patients with mood disorders.

Summary:
Objective: Bipolar disorder is associated with impairments in cognitive functioning, yet the longitudinal course of bipolar disorder associated with those deficits has not been explored. This study investigates the association between the course of bipolar disorder and cognitive functioning.

Methods: Study participants were 53 patients with DSM-IV bipolar disorder (BP-I, n=35 and BP-II, n=18). Subjects completed the Affective Disorders Evaluation (ADE), Hamilton Rating Scale for Depression (HAMD) and Young Mania Rating Scale (YMRS). Patients also completed a battery of neuropsychological tests.
including the Wechsler Test of Adult Reading (WTAR; estimated IQ), the California Verbal Learning Test (CVLT-II), the Letter Number Sequencing subset from the Wechsler Memory Scale (WMS-III), as well as tests from the Cambridge Automated Neuropsychological Battery (CANTAB) such as the Rapid Visual Information Processing (RVP), Spatial Working Memory (SWM) and the Matching to Sample Test (DMS).

Results: Correlation analysis indicated that subjects with more lifetime depressive episodes had more difficulties in the RVP attention task as indicated by more responses to distractors (r=-.45, p<.05) and made more errors in the Spatial Working Memory Task (SWM; r=+.18, p<.05). Earlier onset of bipolar disorder was associated with overall lower estimated IQ (r=-.39, p<.05). Subjects with earlier onset made more errors in the delayed matching to sample task (r=-.29, p<.05). Subjects with more depressive symptoms at the time of testing (HAM-D) performed worse in the letter number sequencing working memory task (r=-.29, p<.05). More depressive (HAMD; r=-.41, p<.05) and more manic (YMRS; r=-.33, p<.05) symptoms were associated with more errors in the SWM working memory task.

Conclusions: A more chronic course of illness in bipolar disorder was associated with attentional and working memory dysfunctions, but not with learning and memory impairments. These findings are consistent with structural and functional abnormalities found in prefrontal cortex and hippocampus in bipolar disorder.

References:

NR289  Monday, May 21, 3:00 PM - 5:00 PM
Predictors of First Episodes of Clinical Depression in Midlife Women
Joyce Bromberger, Ph.D. university of pittsburgh, Epidemiology, Psychiatry, 3811 O'Hara St, pittsburgh, PA, 15232, 9000, Howard M. Kravitz, M.P.H., Karen A. Matthews, Ph.D., Ada Youk, Ph.D., Charlotte Brown, Ph.D., Wentao Fang, M.S.

Educational Objectives:
At the conclusion of this presentation, the participant should understand better (1) the multiple risk factors for a first episode of clinical depression among midlife women, (2) that symptomatic markers (i.e., frequent vasomotor symptoms) of the menopausal transition and early postmenopause are also risk factors for first episodes, and (3) the role of reproductive hormones and status (typically defined as bleeding patterns) in the development of first episodes remains unclear. Importantly, participants should recognize that a substantial number of women experience their first episode of major or minor depression during midlife.

Summary:
Objective: Little is known about factors that predict first episodes of clinical depression in women during midlife and whether the menopausal transition is a risk factor for first episodes. We evaluated longitudinally the contribution of menopausal status indicators, health-related factors, and life stress to onset of a first episode of clinical depression.
Method: We conducted the Structured Clinical Interview for DSM-IV with 443 premenopausal or early perimenopausal women, aged 42-52 at study entry. 99 African American and 169 White women had no history of major depression initially and at least one annual follow up assessment over 7 years. Women annually provided information on menstrual characteristics, psychosocial and health related factors. Blood samples for assay of reproductive hormones were obtained on days 2-5 of the follicular phase when possible. Menopausal status indicators included bleeding patterns that typically define perimenopause and postmenopause, vasomotor symptoms (hot flushes/night sweats), and hormone levels. Cox proportional hazard models were used to calculate hazard ratios of incident depression in univariate and multivariate models.

Results: Over 7 years of follow up, 81 (30.2%) women met criteria for a first diagnosis of past year and/or current major or minor depression. After simultaneous adjustment for multiple predictors in Cox Proportional Hazards analyses, social functioning (Hazard Ratio (HR)=1.85, p=.03) and lifetime history of an anxiety disorder (HR=2.31, p=.001) at baseline, and vasomotor symptoms (HR=1.80, p=.04) and a stressful life event (HR=1.63, p=.04) prior to depression onset predicted a first episode.

Conclusions: The menopausal transition as indicated by frequent vasomotor symptoms, but not bleeding patterns, may carry an increased risk for a first episode of clinical depression. Also, earlier, e.g., history of anxiety disorders, and more proximal factors, e.g., life stress, contribute to a first episode of depression during midlife.

References:
point decrease in patients with baseline item >1) or scale/sub-scales (20 % decrease) from baseline to 2 weeks were determined along with associated positive predictive values (PPVs) and negative predictive values (NPVs).

Results: Two week HAMD item improvement for depressed mood, work, psychological anxiety, and general somatic symptoms significantly predicted remission for both treatments; however, guilt, suicidality, late insomnia, and psychomotor retardation predicted remission for duloxetine but not escitalopram while the opposite was true for early insomnia, middle insomnia and somatic anxiety. Changes in remaining items were not predictive of remission. Statistically significant individual item ORs ranged 1.9-7.1, NPVs 65%-88%, and PPVs 44%-53 %. Related values were determined for the HAMD and its subscales with Maier subscale NPVs of 87.5% for duloxetine and 73.5% for escitalopram.

Conclusion: Lack of early response in depression symptoms was predictive of lack of sustained remission during an 8-month treatment period. Symptom changes were specific to drug treatment.

References:
2. Wade A, Andersen HF. The onset of effect for escitalopram was predictive of lack of sustained remission during an 8-month treatment period. Symptom changes were specific to drug treatment.

NR291 Monday, May 21, 3:00 PM - 5:00 PM
Risperidone Augmentation and Psychosocial Variables In Patients With Difficult-To-Treat Depression
Christine E. Ryan, Ph.D. Rhode Island Hospital, Mood Disorders Program, 593 Eddy Street, Potter 3, Providence, RI 02903, 9000, Steven J. Garlow, M.D., Gabor I. Keitner, M.D., David Arthur Solomon, M.D., Charles B. Nemeroff, M.D., Martin B. Keller, M.D.

Educational Objectives:
Educational Objective: At the conclusion of this presentation the participant should recognize that augmenting an antipsychotic medication may help patients with difficult-to-treat nonpsychotic unipolar depression by decreasing their depression and increasing some areas of their psychosocial functioning.

Summary:
Objective: To examine psychosocial variables and functioning in patients treated with risperidone augmentation for difficult-to-treat depression.
Methods: 97 patients with unipolar, nonpsychotic major depression who failed to respond or only partially responded to at least 5-weeks of open label antipsychotic monotherapy were continued on their antipsychotic medication and randomized to receive adjunctive risperidone (n=64) or placebo (n=33) for an additional 4-week double-blind treatment trial. Outcome measures were administered at baseline, and after two and four weeks of receiving study medication and included clinician and patient Clinical Global Impressions (CGI), the Social Adjustment Scale (SAS), the Range of Impaired Functioning (LIFE-RIFT) scale, and the Quality-of-Life (Q-LES-Q). Chi-square analysis, repeated measures analysis of covariance, and slopes analysis were used to examine rates of change in functioning and patient response.

Results: After two weeks on study medication clinician CGI improvement ratings were significantly better for patients in the risperidone augmentation group (2.6 ± .98) compared to patients in the placebo augmentation group (3.3 ± 1.1, higher-worse) (F(1,88)=9.85, p=.002). By 4 weeks improvement in the two patient groups had converged (risperidone = 2.4 ± 1.0 vs placebo = 2.7 ± 1.1) (F(1,77)=1.50, p=.22). Patient CGI ratings were similar: early response after 2 weeks on medication followed by convergence after 4 weeks. Married patients were more likely to remit than non-married (56% vs. 35%, Fisher's exact p = .055). Risperidone augmentation had a greater effect than placebo on SAS-social/leisure, SAS-family, LIFE-total, LIFE-satisfaction, and Q-LES-Q total, Q-LES-Q medication satisfaction, and Q-LES-Q overall satisfaction after 2 weeks (all p-values < .05) and in SAS-marital, LIFE-interpersonal, LIFE-satisfaction, Q-LES-Q total, and Q-LES-Q medication satisfaction after 4 weeks of treatment (all p-values <.05).

Discussion: For many patients with difficult-to-treat depression, augmenting an antidepressant with risperidone has a rapid and significant impact in many areas of psychosocial functioning.

References:

NR292 Monday, May 21, 3:00 PM - 5:00 PM
The Impact of Gender, Age and Depressed State on Patients’ Perspectives of Remission
Joseph McQuinney, Ph.D. Brown University, Dept. of Psychiatry and Human Behavior, 235 Plain St., Suite 501, Providence, RI 02905, 9000, Mark Zimmerman, Michael A. Posternak, Michael Friedman, Naureen Attilullah, M.D., Daniela Borescu

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize potentially important variables mediating perceptions of remission in major depressive disorder (MDD), and to be able to think more critically about the issue of defining remission in treating depressed patients.

Summary:
Objective: Current standards for treatment outcome from major depression assess remission solely from the vantage point of symptom resolution. Recent evidence, however, suggests that depressed patients consider factors beyond symptom resolution as important for defining remission. The goal of this study was to examine the influence of three predictors on patients’ views of factors important for achieving remission: gender, age, and current depressed state (i.e., remitted or depressed).

Methods: Five hundred and sixty-two depressed psychiatric outpatients completed a survey assessing the importance of 16 remission factors. Depressed state was assessed by the St abbreviated Clinical Outcome Rating scale for Depression (SCOR-D), a clinician rated scale that is based on the number of DSM-IV criteria for a major depressive episode and level of psychosocial impairment present during the past week.

Results: Relative to male patients, females showed a greater likelihood for rating remission factors related to emotional stabilization (e.g., achieving emotional control, being able to cope with normal stress) as very important. Relative to younger cohorts, the oldest depressed patients endorsed a greater number of remission factors as very important and emphasized positive mental health.
states (e.g., feeling satisfied, having a general sense of well-being) more. There were no significant differences between remitted and depressed patients in rating the remission factors’ importance.

Conclusions: Perspectives on remission may be differentially perceived by women versus men and by older versus younger depressed patients.

References:

NR293 Monday, May 21, 3:00 PM - 5:00 PM
Larks and Owls in Psychiatric Patients
Iwona Chelmsinski, Ph.D. Rhode Island Hospital, Psychiatry, 235 Plain Street Suite 501, Providence, RI, 02905, 9000, Mark Zimmerman, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should have a better understanding of the prevalence of diurnal preferences in psychiatric patients, and their association with the types of psychopathology.

Summary:
- Mood disorders involve not just mood alterations but also disruption of circadian features (e.g., sleep, body temperature, TSH).
- Some researchers proposed a phase-shift hypothesis to explain the etiology of these disorders. Although circadian rhythms tend to be fairly consistent across individuals, significant differences in those rhythms have been observed, referred to as the “morningness-eveningness” dimension (MED). One small study found significantly more eveningness in depressed individuals than in matched controls. Overall, though, scarce data exists on the association between depression and the MED. The purpose of this study was to examine diurnal preferences in a large group of psychiatric outpatients who presented for treatment for various psychiatric problems, and to determine whether eveningness is in fact associated with depression, and whether it is specific to mood disorders.

As a part of the MIDAS project 410 psychiatric outpatients and 230 gastric surgery candidates, who served as a control group, were evaluated with the SCID. In addition, everybody completed the MEQ (Morningness-Eveningness Questionnaire). The prevalence of the circadian types and the total MEQ scores were compared in 5 nonoverlapping groups: 1) controls, 2) depression only, 3) anxiety only, 4) depression and anxiety, 5) disorders other than anxiety or depression.

Overall, the psychiatric group had a stronger tendency toward eveningness than the control group. The depressed groups were associated with the highest degree of eveningness, in terms of the total MEQ, as well as the circadian type distribution (evening type 56% vs. 38%, p<.05). The control and nondepressed-nonanxious groups did not differ significantly.

This is the first large-scale study of the morningness-eveningness dimension in a clinical population. It confirmed earlier suggestions that “eveningness” may be reflecting a risk factor or vulnerability to psychopathology, and particularly to depression. Given the distribution of the morning types one might speculate that to be a “lark” might be protective against depression.

References:

NR294 Monday, May 21, 3:00 PM - 5:00 PM
Exploring a Dimensional Representation of Depression Symptoms with Item Response Modeling
Joseph McGlinchey, Ph.D. Brown University, Dept. of Psychiatry and Human Behavior, 235 Plain St., Suite 501, Providence, RI, 02905, 9000, Mark Zimmerman, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able, through an applied example, to understand how novel psychometric techniques can inform our understanding of the psychometric performance of symptom criteria for Axis I disorders, and also to consider an alternative representation of depression as a dimensional latent construct wherein symptom criteria are weighted according to the information they contribute towards the depression factor.

Summary:
- Objective: The current diagnostic criteria representing common Axis I psychiatric disorders have received little empirical study. The aim of the current study was to apply item response modeling (IRM) to the nine symptom criteria used to diagnose major depressive disorder (MDD). IRM can be used to present depression as a dimensional construct, wherein patients' degrees of depression may be measured according to the specific symptom profile they present.

Methods: The sample consisted of 2,300 psychiatric outpatients who were administered the Structured Clinical Interview for DSM-IV disorders (SCID). The MDD symptom criteria were assessed in each patient. The viability of a single, underlying factor (Depression) for explaining the covariation among the nine symptom criteria was tested. Then, a two-parameter logistic (2PL) item response model was applied to examine how the nine symptom criteria mapped along the depression factor continuum.

Results: A confirmatory factor analysis indicated sufficient evidence for a single factor underlying depression symptoms (chi-square = 183.2; CFI = .98; RMSEA = .05). Sleep disturbance and fatigue represented the most commonly endorsed depression symptoms among outpatients (difficulty parameters < 0), whereas death thoughts/suicide and psychomotor disturbance were the least common (difficulty = 0.68 and 0.72, respectively). Each of the nine symptom criteria were strong discriminators of the depression factor (discrimination parameters > 1.25 for all criteria), with depressed mood and anhedonia contributing the most information and death thoughts/suicide, weight/appetite disturbance, and psychomotor disturbance contributing the least. Eight specific symptom profiles accounted for 34.4% of the outpatient sample.

Conclusions: The current study provides an alternative representation of depression as a dimensional continuum, in which patients’ degrees of depression are weighted according to the specific symptom profile they endorse and how much each symptom criterion contributes towards the latent factor of depression.

References:
NR295  Monday, May 21, 3:00 PM - 5:00 PM
Variations in Prevalence of Substance Use in First Admission Mood Disorder Patients in Quebec, 1980-2005

Javad Moamai, M.D., MSc. Pierre Janet Hospital, Gatineau and
Montreal University Hospital Centre, Montreal, Psychiatry, 1295
Parkhill Circle, Ottawa, ON, K1H 6K2, 1220, Denis Boilevert, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to:
1) be aware of the risk of generalizing statistical data without
looking at age and gender,
2) recognize the importance of assessing substance abuse in first admission mood disorder patients.

Summary:

Background: Although high prevalence of Substance Abuse
(SA), either alcohol or illicit drugs among Inpatients with Mood
Disorder (IMD) is a well-known fact, the pattern of comorbidity
between the two pathologies remains controversial. Use of mixed
samples may partly generate this controversy.

Aims: To assess the variation of prevalence rates of SA among
IMD with consideration for age, gender and diagnostic subgroup.

Method: Rates of SA from 1980 through 2005 were analyzed
using a representative sample of all admissions to a psychiatric
hospital in Quebec. Data (ICD-9 codes: 296.x, 298.0, 298.1, 300.4,
and 311.9) were taken from separation sheets of 2,116 first admis-
sion subjects (13*years). Correlation analysis included analysis
for linear trend in proportions, with specific examination of the
year of admission, age and gender.

Results: Over the 25-year period, annual prevalence rate of SA
averaged 23.5% (alcohol = 18.5%, illicit drug = 10.7%). The rates
varied between 21.7% for dysthyemic disorders and 27.3% for
bipolar disorders. Associations of SA with male gender and
younger age were observed (p<.0001). The crude rates remained
stable for both depressive disorders but increased annually for
bipolar disorders. The pattern of variation changed completely
when age group and gender were considered separately. After
adjustment, an increased rate was seen only for 1) adult female
major depressive disorder patients, 2) young adult male dysthyemic
disorder patients and 3) young adult male bipolar disorder patients.

Conclusions: Our study highlights: 1) A high prevalence of SA
at onset of the disease and 2) A different pattern of correlation
between SA and mood disorders when gender and age are consid-
ered. These findings strongly imply: 1) The increasing rates might
be an artifact of growing substance use rate and its acceptability
in society and 2) Use of prevalence rates in mixed samples in
comorbidity studies can be misleading.

References:
2. Kraemer HC, Willson KA and Hayward C: Lifetime Prevalence
and Pseudocomorbidity in Psychiatric Research. Arc Gen Psy-
chiatry 2006;63:604-608.

NR296  Monday, May 21, 3:00 PM - 5:00 PM
Korean Medication Algorithm for Depressive Disorder 2006(III): Depressive Disorder with
Psychotic Features

Won Kim Seoul Paik Hospital, Inje University, Psychiatry and
stress research institute, 85, Jeodoong-2-ga, Jung-gu, Seoul,
100-032, 5800, Won-Myong Bahk, Jeong Seok Seo, Kyung
Joon Min, Jeong-Ho Seok, Hae-Chul Song, Sang-Yeol Lee

Educational Objectives:

Since there has been a substantial need for the revision due to
rapid progress in the pharmacological management for depressive
disorder, we revised KMAP-MDD to Korean Medication Algorithm
Project for Depressive Disorder (KMAP-DD) in 2006. At the con-
clusion of this presentation, the participant should be able to recog-
nize the Korean expert consensus about medication strategies for
depressive disorders.

Summary:

Objective: Since the publication of Korean Medication Algorithm
Project for Major depressive Disorder(KMAP-MD) in 2002, there
has been a substantial need for the revision due to rapid progress
in the pharmacological management for depressive disorder. We
revised KMAP-MD to Korean Medication Algorithm Project for
Depressive Disorder(KMAP-DD) in 2006.

Methods: The questionnaire consisted of 4 parts; initial treat-
ment of 1) non-psychotic depressive disorder, 2) psychotic de-
pressive disorder, 3) treatment for clinical subtypes and drugs
choice considering adverse effects, and 4) treatment for de-
pressive disorder in women. The questionnaire was completed
by the review committee consisting of 101 experienced Korean
psychiatrists. It is composed of 22 questions, and each question
includes 54 sub-items. We classified the expert opinion to 3 cate-
gories (the first-line, the second-line, or the third-line) by x²-test.

Results: For psychotic depression, most reviewers prefer the
combination of antidepressant and atypical antipsychotics. Elec-
troconvulsive therapy and the combination of antidepressant and
atypical antipsychotics were the second-line treatment. Among anti-
depressant, venlafaxine was most preferred, and SSRI, mirtazap-
ine followed. Among atypical antipsychotics, quetiapine, risperi-
done, olanzapine were preferred in order. In patients non-
responsive with the first-line treatment, a lot of reviewers recom-
mended switching to another antidepressant or adding another
atypical antipsychotics

Conclusion: For severe depressive disorder with psychotic fea-
tures, the combination of antidepressant and atypical antipsy-
chotics was the first-line treatment. These results suggest that the
medication strategies of depressive disorder are rapidly changing
and it reflects the recent studies and clinical experiences.

References:
the treatment of depression: making the right decision at the
2. Trivedi MH, Kleber BA. Using treatment algorithms for the
effective management of treatment-resistant depression. J Clin

NR297  Monday, May 21, 3:00 PM - 5:00 PM
Is the Circadian Phase Delay More Pronounced Among the Depressed Psychiatric Outpatients in the
Winter?

Iwona Chelminski, Ph.D. Rhode Island Hospital, Psychiatry,
235 Plain Street Suite 501, Providence, RI, 02905, 9000,
Mark Zimmerman, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should
have a better understanding of whether the seasonal changes in
mood and behaviors that are often seen in a general population
and have been linked to phase delay of the circadian rhythm
would be reflected in diurnal preferences of depressed outpa-
tients presenting for treatment throughout four seasons of the year.
Objective: The phase-shift hypothesis for mood disorders suggests that depression seen in SAD is a result of a phase delay of the free-running, endogenous circadian rhythm. Shifts toward eveningness on the Morningness-Eveningness Questionnaire (MEQ) indicate a phase delay. The purpose of this study was to determine whether purported seasonal fluctuations would be reflected in diurnal preferences of the depressed outpatients presenting for treatment across four seasons of the year. Specifically, it sought to detect a greater degree of eveningness among the depressed in the fall/winter season relative to the spring/summer season.

Method: As a part of the Rhode Island Methods to Improve Diagnostic and Assessment Services (MIDAS) project 410 depressed outpatients were evaluated with the Structured Clinical Interview for DSM (SCID) and completed the MEQ. The prevalence of the evening circadian types and the total MEQ scores among the clinically depressed patients were compared across two seasons of the year: 1) fall/winter (n=93) and 2) spring/summer (n=181).

Results: The distribution of circadian types among the depressed individuals was almost identical during both seasons (57%/5%/38% vs. 55%/10%/35% for the evening, morning, and neither types, respectively). Likewise, the total MEQ scores among the depressed did not differ across the seasons of the year (50 vs. 51).

Conclusions: Even though existing data suggests a general tendency for people to experience seasonal changes in mood and behaviors it did not extend into our clinical sample population. The degree of eveningness, as well as the distribution of the circadian types among our depressed outpatients remained the same, regardless of the season of the year. As suggested by some, perhaps it is more depressogenic to experience a phase delay relative to one’s own phase in the summer, rather than relative to other people in the winter.

References:

NR299 Monday, May 21, 3:00 PM - 5:00 PM
Efficacy and Tolerability of Ziprasidone Psychotic Major Depression: A 12-week Randomized Double-Blind Study
Frederick Cassidy, M.D. Duke University, Psychiatry, 1003 12th Street, Butner, NC 27509, 9000, George M. Simpson, M.D., K. Ranga R. Krishnan, M.D.

Educational Objectives:
At the conclusion of this session, participants should be able to:
1. Describe the efficacy and safety of desvenlafaxine succinate (DVS) in outpatients with a primary diagnosis of major depressive disorder (MDD).
2. Compare the response of patients receiving DVS and those receiving placebo in clinical evaluations of improvement, functionality, general well being, pain reduction, and remission.

Summary:
Objectives: DVS has demonstrated efficacy and safety in prior studies. In this study, the primary objective was to compare the antidepressant efficacy and safety of DVS and placebo. The secondary objective was to compare overall improvement, functionality, general well being, pain reduction, and remission in both patient groups.

Methods: This phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel-group, flexible-dose study enrolled adult outpatients with MDD age 18. Patients were randomized to receive DVS 200-400 mg (n=117) or placebo (n=118). The

Summary:
Objective: The phase-shift hypothesis for mood disorders suggests that depression seen in SAD is a result of a phase delay of the free-running, endogenous circadian rhythm. Shifts toward eveningness on the Morningness-Eveningness Questionnaire (MEQ) indicate a phase delay. The purpose of this study was to determine whether purported seasonal fluctuations would be reflected in diurnal preferences of the depressed outpatients presenting for treatment across four seasons of the year. Specifically, it sought to detect a greater degree of eveningness among the depressed in the fall/winter season relative to the spring/summer season.

Method: As a part of the Rhode Island Methods to Improve Diagnostic and Assessment Services (MIDAS) project 410 depressed outpatients were evaluated with the Structured Clinical Interview for DSM (SCID) and completed the MEQ. The prevalence of the evening circadian types and the total MEQ scores among the clinically depressed patients were compared across two seasons of the year: 1) fall/winter (n=93) and 2) spring/summer (n=181).

Results: The distribution of circadian types among the depressed individuals was almost identical during both seasons (57%/5%/38% vs. 55%/10%/35% for the evening, morning, and neither types, respectively). Likewise, the total MEQ scores among the depressed did not differ across the seasons of the year (50 vs. 51).

Conclusions: Even though existing data suggests a general tendency for people to experience seasonal changes in mood and behaviors it did not extend into our clinical sample population. The degree of eveningness, as well as the distribution of the circadian types among our depressed outpatients remained the same, regardless of the season of the year. As suggested by some, perhaps it is more depressogenic to experience a phase delay relative to one’s own phase in the summer, rather than relative to other people in the winter.

References:
primary endpoint was change from baseline in the HAM-D_{17} total score at the final evaluation. Secondary efficacy endpoints were the Clinical Global Impressions Scale Improvement (CGI-I) score, change from baseline on the Montgomery and Asberg Depression Rating Scale (MADRS) total score, CGI-S Severity of Illness (CGI-S) ratings, and the visual analog scale-pain intensity (VAS-PI) overall pain score.

Results: At the final evaluation, there was no significant difference between patients treated with placebo and those treated with DVS for change from baseline in the HAM-D_{17} score using the ANCOVA analysis with LOCF data (p=0.078). However, using observed-cases analysis, there was a significant difference at week 8 between treatment groups for change from baseline in the HAM-D_{17} score (p=0.008). DVS was significantly superior to placebo at the final evaluation for CGI-I score, MADRS total score, CGI-S score, HAM-D_{6} total score, and MADRS response rate (both LOCF and observed data). Treatment-emergent adverse events (TEAEs) were consistent with other SNRI drugs and included nausea (36%), dry mouth (31%), insomnia (28%), somnolence (23%), sweating (21%), anorexia (20%), tremor (11%), and impotence (males; 16%).

Conclusion: A flexible dosage of DVS (200 to 400 mg/day) is effective, safe, and well-tolerated in relieving depression in adult patients with MDD. There were significant differences between treatment groups in the observed case analysis and secondary analyses (using both LOCF and observed cases).

References:

NR300 Monday, May 21, 3:00 PM - 5:00 PM
Effects of Gender and Menopausal Status on Response and Remission in Patients With Recurrent Depressive Disorder Treated With Venlafaxine XR or Fluoxetine
Susan G. Kornstein, M.D. Virginia Commonwealth University, Psychiatry, 3805 Cutshaw Avenue, Suite 504, Richmond, VA, 23230, 9000, Tahmina Ferdousi, Ph.D., Peter J. Holland, M.D., Charles B. Nemeroff, M.D., Anthony J. Rothschild, M.D., Michael E. Thase, M.D., Madhukar H. Trivedi, M.D.

Educational Objectives:
At the conclusion of this presentation on the effects of menopausal status on response to treatment with venlafaxine XR or fluoxetine, the participant should be able to:
- Understand the potential role of gender on treatment outcomes with different classes of first-line antidepressant treatment for depression.
- Recognize the potential influence of menopausal status on treatment outcomes in women with different classes of first-line antidepressant treatment for depression.

Summary:
Objective: To evaluate effects of gender and menopausal status on acute- and continuation-phase treatment outcomes in patients with recurrent major depressive disorder (MDD).
Methods: Treatment by gender and menopausal status interactions were evaluated using data from a multiphase, multicenter, double-blind study of adult outpatients with recurrent MDD randomly assigned to venlafaxine XR (75-300 mg/d; n=821) or fluoxetine (20-60 mg/d; n=275) for 10 weeks' acute-phase treatment followed by 6-months' continuation-phase treatment (n=530, venlafaxine XR; n=185, fluoxetine) for those achieving response/remission at the end of the acute phase. Proportions of men and women in each treatment group achieving response (HAM-D_{17} score ≤12 or ≥50% decrease from baseline) and remission (HAM-D_{17} score ≤7) were compared using logistic regression, including assessment of the treatment-by-gender interaction. Effects of menopausal status (using ages 18-39, 40-55, and >55 as proxies for pre-, peri-, and post-menopause respectively) on outcome were evaluated as described above for gender. These results will be compared with those determined based on information regarding actual menopausal status collected at baseline for all female patients.

Results: The ITT population was comprised of 781 patients in the venlafaxine XR group (65% women) and 266 patients in the fluoxetine group (61% women). The proportion of women in the overall population who were premenopausal, perimenopausal, and postmenopausal were 52%, 39%, and <10%, respectively. There were no statistically significant differences between venlafaxine XR and fluoxetine in rates of response or remission at the acute-phase and continuation-phase end points in men or women or in the subgroups of pre-, peri-, and postmenopausal subgroups, nor were there significant interactions of gender or menopausal status with treatment.

Conclusion: In this study of patients with recurrent MDD, treatment outcomes with venlafaxine XR and fluoxetine did not differ on the basis of gender or menopausal status.

References:

NR301 Monday, May 21, 3:00 PM - 5:00 PM
Comparing MMRM and LOCF ANCOVA Analyses in the Quetiapine Mania Trial Database
Charles L. Bowden, M.D. University of Texas Health Science Center at San Antonio, Department of Psychiatry, 7703 Floyd Curl Drive, San Antonio, TX, 78229, 9000, Joseph R. Calabrese, M.D., Robert M.A. Hirschfeld, M.D., Robert Arvekvist, M.S., Anders Carlsson, M.S., Björn Paulsson, M.D.

Educational Objectives:
At the conclusion of this session, the participants should be able to understand differences in sensitivities between MMRM and LOCF ANCOVA models based on analyses of the quetiapine mania trial database.

Summary:
Introduction: The mixed-effects model, repeated measures (MMRM) approach may produce more robust estimates than last-observation-carried-forward analysis of covariance (LOCF ANCOVA) taking into account patient withdrawals. This analysis compared MMRM and LOCF ANCOVA using the quetiapine mania trial database.
Methods: Data were analyzed from two 12-week double-blind, randomized, placebo-controlled trials of quetiapine monotherapy (n=208) versus placebo (n=195) and two 3- and 6-week double-blind, randomized, placebo-controlled trials of quetiapine (n=185) or placebo (n=185) combined with lithium or divalproex.
outcome measures were mean change from baseline to endpoint in Young Mania Rating Scale (YMRS) total score.

Results: In combined adjunctive therapy studies, MMRM and ANCOVA LOCF yielded similar results for YMRS change from baseline. YMRS change at Day 21 was -17.3 for quetiapine (n=137) and -14.5 for placebo (n=117) by MMRM, and -15.3 (n=185) and -12.2 (n=185) respectively by ANCOVA LOCF. In the combined monotherapy studies, MMRM yielded a greater YMRS change from baseline than ANCOVA LOCF. YMRS change at Day 84 was -26.4 for quetiapine (n=129) and -21.9 for placebo (n=77) by MMRM, and -19.0 (n=208) and -9.6 (n=195) respectively by ANCOVA LOCF. Estimated differences between quetiapine and placebo were significant by both models and were smaller with MMRM than ANCOVA LOCF (-2.9 [P=0.025] vs -3.1 [P=0.014] for adjunctive therapy; -4.5 [P<0.001] vs -9.42 [P<0.001] for monotherapy). In general, both models identified significant divergence of quetiapine from placebo at the same point times.

Conclusions: By both MMRM and LOCF ANCOVA analyses, quetiapine was significantly more effective than placebo both as monotherapy and in combination with lithium or divalproex for treating bipolar mania.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

NR302 Monday, May 21, 3:00 PM - 5:00 PM Identifying Frank Neurocognitive Impairment with CNS Vital Signs in Patients with Untreated Depression

Grant L. Iverson, Ph.D., Brian L. Brooks, M.D., Allan H. Young, Allan H. Young, M.D., Ch.B., Lynda G. Johnson, Ph.D., C. Thomas Gualtieri, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to identify neurocognitive deficits commonly associated with untreated depression. Specifically, the participant should have an understanding of how to assess a patient’s neurocognitive abilities using a brief computerized assessment battery, recognize frank neurocognitive impairment that is associated with untreated depression, and interpret test results at the individual level.

Summary:
There is considerable interest in the identification of neurocognitive impairment in patients with depression. The purpose of this study is to illustrate the clinical usefulness of the CNS Vital Signs battery for identifying frank neurocognitive deficits in a subset of adults with depression. This computerized assessment battery takes 30 minutes to administer and is comprised of seven common neuropsychological measures, including verbal and visual memory, finger tapping, symbol digit coding, the Stroop test, a shifting attention test, and a continuous performance test. The battery generates 15 primary scores that are used to calculate five domain scores (Memory, Psychomotor Speed, Reaction Time, Cognitive Flexibility, and Complex Attention) and a summary score (Neurocognition Index). Participants were 33 patients with depression who were not on antidepressants. They were carefully matched on age, gender, and ethnicity to 33 control subjects from the CNS Vital Signs normative database. The univariate ANOVA results revealed significantly worse neuropsychological test scores for those in the depression group on the Cognitive Flexibility Index (d=.65) and Complex Attention Index (d=.72). The groups did not differ on the Memory, Processing Speed, or Reaction Time Indexes. When using two or more scores below the 5th percentile as the cutoff for frank neurocognitive impairment, 33.4% of the depressed sample and 3.0% of the control sample scored in this range (x2[1]=10.2, p=.001; Odds Ratio=16.0, 95% CI=2.4-101.7; Sensitivity=.33, Specificity=.97, Positive Predictive Value=.92, 95% CI=.67-.99, Negative Predictive Value=.59, 95% CI=.54-.61). In this study, patients with depression were 16 times more likely to have two or more index scores that were below the 5th percentile. Based on the results of this preliminary study, the clinician could be 91% confident that having two unusually low index scores reflects neurocognitive impairment and not broadly normal cognitive functioning.

References:

NR303 Monday, May 21, 3:00 PM - 5:00 PM The Influence of Comorbid Metabolic Disorders Upon Treatment Outcome in Patients Hospitalized with Bipolar Disorder.

Dale A. D'Mello, M.D., Michigan State University, Psychiatry, 4805 Canyon Trail, Lansing, MI, 48917, 5000, Supriya Narang, M.D.

Educational Objectives:
Appreciate the high prevalence of comorbid metabolic disorders in patients hospitalized with bipolar mania and mixed states. Understand the possible clinical consequences of disturbed glucose metabolism in patients with bipolar disorder. Explore neuroendocrine, neuroimmune, cerebrovascular and circadian phenomena that convey a shared vulnerability in patients with diabetes and bipolar disorder

Summary:
Patients with bipolar disorder are susceptible to metabolic disorders such as obesity, dyslipidemia and diabetes. While these comorbid conditions increase disease burden and diminish quality of life, their influence upon treatment outcomes remain to be elucidated.

Objectives: The purpose of the present study was to examine the prevalence, and clinical correlates of comorbid metabolic disorders in a cohort of patients hospitalized with bipolar disorder.

Method: We recruited patients with bipolar disorder who were consecutively admitted to the adult psychiatric unit of a general hospital in mid-Michigan during calendar years 2004-2006. We gathered demographic, and health related information from the hospital medical records. We then examined statistical correlations between metabolic variables (body mass index, fasting plasma glucose, lipid parameters, and blood pressure), levels of psychopathology (YMRS: Young Mania Rating Scale) and treatment outcomes (psychotropic use, and length of hospital stay).

Results: Of the 73 patients who were included in the study, 64% were either overweight or obese, 70% had dyslipidemia, 79% were pre-hypertensive or hypertensive, 43% were pre-diabetic or diabetic, and 48% met diagnostic criteria for metabolic syndrome. There was a positive correlation between admission fasting plasma glucose levels and subsequent duration of hospital stay.
(Pearson correlation co-efficient: r=0.553, p=0.002). Patients who met diagnostic criteria for metabolic syndrome had longer lengths of stay than others. Body mass index, lipid and BP parameters did not display a significant impact upon length of stay or admission YMRS scores.

Conclusions: A correlation between glycemic control, and depressive symptom severity is now widely recognized. It is conceivable that the stress of acute mania, dysregulation of neuroendocrine, neuroimmune function, and disrupted circadian rhythms contribute to impaired glucose metabolism. Conversely, the cerebrovascular sequelae of poorly controlled diabetes may impede treatment response.

References:

NR304 Monday, May 21, 3:00 PM - 5:00 PM Aripiprazole Monotherapy in the Treatment of Acute Bipolar I Mania: A Randomized, Placebo- and Lithium-controlled Study (Study CN138-135)
Paul E. Keck Jr. Psychopharmacology Research Program, Department of Psychiatry, University of Cincinnati College of Medicine, and General Clinical Research Center and Mental Health Service Line, Cincinnati Veterans Affairs Medical Center, University of Cincinnati College, Raymond Sanchez, Anne Torbeyns, Ronald N. Marcus, Robert D. McQuade, Andrew Forbes

Educational Objectives:
At the conclusion of this presentation, 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:
Objectives: Evaluate the efficacy and safety of aripiprazole monotherapy as acute and continuation therapy for acute bipolar I mania.

Methods: Patients with acute bipolar I mania (Young Mania Rating Scale [YMRS] ≥20), manic or mixed (with or without psychotic features) who required hospitalization were randomized to double-blind aripiprazole (15-30 mg/day; n=155), placebo (n=165) or lithium (800-1500 mg/day; n=160) (1:1:1) for 3 weeks. Placebo-treated patients then received double-blind aripiprazole for another 9 weeks; while all other patients remained on the same blinded treatment. Outcome measures included the mean change from baseline in YMRS Total score to Week 3 (primary endpoint) and Week 12 (LOCF). Response rate (≥50% improvement in YMRS Total score) was a secondary endpoint.

Results: Completion rates were similar between groups. Aripiprazole demonstrated significantly greater improvement from baseline to Week 3 in mean YMRS Total score than placebo (-12.64 vs. -9.01; p<0.001, LOCF). Significant improvement in YMRS Total score was also seen with lithium versus placebo at Week 3 (-12.03 vs. -9.01; p=0.005, LOCF). Improvements in YMRS Total score were maintained to Week 12 for aripiprazole and lithium (-14.48 and -12.71). Response rates at Week 3 were significantly higher with aripiprazole (46.8%) and lithium (45.8%) than placebo (34.4%; both p<0.05, LOCF); response rate increased to Week 12 with aripiprazole (56.5%) and lithium (49.0%). Most common adverse events with aripiprazole were headache (23.4%), nausea (22.7%), and akathisia (14.9%); with lithium were nausea (23.9%), headache (22.0%) and constipation (12.6%). More aripiprazole-treated patients showed clinically relevant weight gain (14.6%, 6/41) than lithium-treated patients (3.7%, 2/54) (Week 12).

Conclusions: Aripiprazole was superior to placebo for acute treatment and similar to lithium for both acute and continued treatment of patients with bipolar I mania.

References:

NR305 Monday, May 21, 3:00 PM - 5:00 PM Prescription Trends in the Treatment of Bipolar Disorder Inpatients, 2001–2006
Cho D. Hwan, Sr., M.D. Maryknnol general hospital, Neuropsychiatry, Jung-Ku Daecheng-Dong 4-12, Pusan, 600-094, 5800, Cheol-Jung Kang, Jr., M.D., Bogeum Kong, Jr., M.D., Dae-Soo Lee, Sr., M.D.

Educational Objectives:
We examined recent changes in the prescribing patterns for medications to treat bipolar disorder inpatients in the treatment of bipolar disorder inpatients, 2001–2006, especially frequencies of atypical antipsychotics and conventional antipsychotics prescription. At the conclusion of this poster presentation, the participant should be able to recognize that valproic acid is prescribed most commonly and atypical antipsychotics are increasing.

Summary:
Objectives: Purposes of this study are to identify of belows:
1. Prescription frequencies of atypical and conventional antipsychotics on bipolar disorder inpatients
2. Changes of mood stabilizers’ use (Lithium vs Valproic acid)
3. Is diagnosis of bipolar disorders increasing?

This study examined recent 5-year changes in the prescribing patterns for medications to treat bipolar disorder in general hospital based inpatient practice.

Methods: The authors analyzed physician-reported inpatients’ data from two general hospitals and two university hospitals for 2001-2006. Demographic, clinical, and medication prescription characteristics of inpatients were compared to identify changes between the years, 2001, 2002, 2003, 2004, 2005, 2006. x² (Chi-square test) was used to identify trends of medication prescription.

Results: In each survey periods, atypical antipsychotics and conventional antipsychotics were prescribed 50% and 31.25% at 2001, 53.49% and 16.28% at 2002, 64.1% and 23.08% at 2003, 75.81% and 25.81% at 2004, 75% and 9.66% at 2005, 90.32% and 5.97% at 2006. There was an increase in the use of atypical antipsychotics over time, accompanied by a decrease in the use of conventional antipsychotics. And mood stabilizers were prescribed more frequently in the 2001, 2002, 2003, 2004, 2005, 2006 than 2001, 2002. There was a decrease in the use of lithium and an increase in the use of valproic acid over time. In bipolar disorder patients, most frequent cause of admission was poor drug compliance, 62.5%. Inpatient number was increase time to time, 32 inpatients in 2001, 104 inpatients in 2005. It is obvious to diagnose bipolar disorders more frequently.

Conclusion: Despite usefulness of atypical antipsychotics on the bipolar disorder, Lithium and valproic acid are most common and effective treatment of bipolar disorder. But applications of...
atypical antipsychotics were increased and more popular in the 2005-2006 than 2001 and a diagnosis of bipolar disorder is increasing.

References:

NR306 Monday, May 21, 3:00 PM - 5:00 PM
Premorbid Profile of Circadian Activity in Patients Affected by Psychiatric Disorders: Comparison Between Subjects Affected by Depressive and Anxiety Disorders.
Giuseppe Bersani La Sapienza University of Rome, Department of Psychiatric Sciences and Psychological Medicine, Viale dell'Universita, 30, Rome, Italy, 00186, 4759, Lucilla Limpido, Daniele Russo, Daniela Marconi

Educational Objectives:
At the conclusion of this presentation, the participant should be able to demonstrate differences between the chronobiological profile of patients affected by depressive and anxiety disorders.

Summary:
Objective: Aim of this study was to investigate the existence of a circadian profile that characterizes patients with depressive and anxiety disorders, and to evaluate the possible "chronobiological" differences between Major Depressive Disorder and Panic Disorder. Moreover, this study proposed to characterize the circadian premorbid profiles, possible expression of a psychiatric vulnerability already present in the youth and adolescence periods.

Methods: 268 subjects were selected: 91 affected by depressive disorders (32 with a Major Depressive Disorder), 89 affected by anxiety disorders (29 with a Panic Disorder), and 88 healthy individuals. All the subjects were asked to fill a questionnaire about the time of awakening, of falling asleep, of maximum appetite, of time of maximum mental focusing, and of maximum energy, and of maximum mental focusing during the adolescence period (12-15 years), the youth period (16-20 years), and the present period. Results from patients and healthy individuals were compared.

Results: In depressed patients time of awakening was anticipated and time of maximum mental focusing was delayed compared to healthy subjects. Comparisons between anxious patients and healthy subjects showed an anticipated time of awakening and of maximum energy, and a delayed time of maximum mental focusing during the present period. Differences between patients with anxiety and depression disorders progressively decreased during the years, emphasizing the presence of a common physiopathologic substrate. Patients with Major Depressive Disorder and Panic Disorder did not show significant differences.

Conclusions: The obtained data, having the character of a preliminary study, encourage the realization of further researches that allow to establish morbid and premorbid factors affecting the chronobiological aspects in psychiatric disorders. Moreover, the study suggests that the analysis of the circadian profile could contribute to characterize profiles of subjects predisposed to develop a psychiatric disorder.

References:

NR307 Monday, May 21, 3:00 PM - 5:00 PM
Substance Use Disorders among Adolescents with Bipolar Spectrum Disorders
Benjamin I. Goldstein, M.D. Western Psychiatric Institute and Clinic, Psychiatry, 100 N. Bellefield Ave., Room 807, Pittsburgh, PA, 15237, 3M5, 9000, Michael Struber, Ph.D., Boris Birmaher, David A. Axelson, M.D., Christianne Espósito-Smythers, Ph.D., Henrietta L. Leonard, Martin B. Keeler, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to: 1. Identify the prevalence of substance use disorders (SUD) among adolescents with bipolar disorders; 2. Recognize putative predictors of SUD; 3. Appreciate the hazards associated with SUD in this population.

Summary:
Objective: Comorbid substance use disorders (SUD) are highly prevalent among adolescents and adults with bipolar disorder (BP). Studies of BP adults report greater illness severity and morbidity among subjects with SUD. However, few studies with small samples have examined SUD among adolescents with BP.

Methods: Subjects were 249 adolescents ages 12 to 17 years old, who fulfilled DSM-IV criteria for BPI (n = 154) or BPII (n = 25), or operationalized criteria for BP not otherwise specified (BP NOS; n = 70) via the K-SADS. As part of the multi-site Course and Outcome of Bipolar Youth study, demographic, clinical, and family history variables were measured via intake clinical interview with the subject and a parent/guardian.

Results: The lifetime prevalence of SUD among adolescents with BP was 16% (40/249). After controlling for age, the prevalence of SUD among child- versus adolescent-onset BP subjects did not differ significantly. In multiple regression analyses, conduct disorder and history of suicide attempt were associated with increased prevalence of SUD, whereas living with both biological parents was associated with significantly lower prevalence of SUD. Subjects with SUD reported significantly greater 12-month prevalence of trouble with police, and females with SUD reported significantly greater 12-month prevalence of pregnancy and abortion. SUD was not significantly associated with the lifetime prevalence of psychosis, mixed episodes, ADHD or anxiety disorders, or with baseline global functioning or symptom severity.

Conclusions: SUD among adolescents with BP is associated with profound hazards including suicide attempts, trouble with police, and teenage pregnancy and abortion.

References:

NR308 Monday, May 21, 3:00 PM - 5:00 PM
Affective Disorders and Solar Activity. 16 Years Follow Up
Fernando Ivanovic-Zuvic, Sr. University of Chile, Psychiatry, Callao 2970-604 Las Condes, Santiago, 7550274, 3370, Rodrigo De la Vega, Sr., Nevenka Ivanovic-Zuvic, Eduardo Correa

Educational Objectives:
The present work discusses the link between solar activity and appearance of affective disorders. Solar activity is reflected by...
the Wolf number which is given by the formula $R = K(10g + f)$, where “$g$” stands for the groups of sunspots and “$f$” is the total number of sunspots.

At the conclusion of this presentation, the participant should be able to know the relationships between solar activity and affective disorders including depressions and manic episodes

Summary:

Introduction: The present work discusses the link between solar activity and appearance of affective disorders. Solar activity is reflected by the Wolf number, which is given by the formula $R = K(10g + f)$, where “$g$” stands for the groups of sunspots and “$f$” is the total number of sunspots.

Methodology: We examined 1862 clinical files at the Clínica Psiquiátrica Universitaria, Santiago de Chile. Patients with major depressions and manic disorders were considered, but only those admitted to the clinic for the first time. We examined the correlation between years of hospitalization and average Wolf numbers for those years, and this for the period 1990-2005, which corresponds to approximately one and half solar cycles of 16 years.

Results: A big number of hospitalizations of depressive patients occurred during years of low solar activity, and there was a slight increase in the number of manic patients during years of high solar activity. Depressive disorders showed a negative correlation with solar activity, the Spearman coefficient being equal to -0.812 ($p=0.000$). Manic disorders showed a positive correlation with the Spearman coefficient, equal to 0.399 ($p=0.063$) close to statistical significance.

Conclusions: Depressive disorders have a significant inverse correlation with solar activity, while manic disorders showed a positive correlation, but without statistical significance.

References:


NR309 Monday, May 21, 3:00 PM - 5:00 PM
Factors Associated with Different Mood Stabilizing Therapies in Bipolar Disorder with Special Regard to Mixed Episodes

Stefan Wilhelm Lilly Deutschland GmbH, Medical, Saalburgstrae 153, Bad Homburg, D-61348, 4280, Hans Peter Hundemer, Alexander Schacht, Anette Minarzyk, Anja Liebeskind, Heinz C. Grunze

Educational Objectives:

At the conclusion of this presentation, the participant will have got a general survey of the anamnestic heterogeneity in bipolar patients with mixed episodes, including comorbidity and special risk factors

Summary:

Background: Since relapse prevention is considered one of the major issues in the treatment of bipolar disorder, this ongoing, 18-months, prospective, multicenter, non-interventional study is targeted to assess treatment maintenance and specific patient features of different mood stabilizing therapies.

Methods: Observational data from 761 outpatients were collected by 150 office or hospital based psychiatrists throughout Germany in the course of standard treatment for bipolar disorder. A baseline analysis was performed, investigating the disposition of patients receiving different mood stabilizer therapies, including a comparison of patients without mixed episodes (0-MX) to those with one (1-MX) and more (>1-MX) mixed episodes.

Results: In this baseline-analysis 26.1% of the patients included received olanzapine monotherapy (OM), 21.2% lithium monotherapy (LM), 30.1% anticonvulsant monotherapy (AM), 6.4% olanzapine/lithium combination therapy (OLC), 9.5% olanzapine/anticonvulsant combination therapy (OAC), 6.7% other combinations of mood stabilizers (OC) and 5.8% no mood stabilizers (NO). At baseline, 36.4% of the patients had been hospitalized within the last 12 months due to psychiatric disorder, 26.8% had a history of suicide attempts, 10.7% were considered rapid cyclers. Within the last 12 months 66.5% of the patients experienced manic episodes, 88.6% depressive episodes and 43.1% mixed episodes. The hospitalization rate was 33.2% for the 0-MX, 36.5% for the 1-MX and 43.4% for the >1-MX group. The 0-MX group had 5.6% rapid cyclers, compared with 11.0% for the 1-MX and 32.8% for the >1-MX group. Regarding treatment, 0-MX mostly received AM (31.1%), 1-MX OM (31.6%) and >1-MX AM (35.3%). Presence of psychiatric comorbidities was associated with less mixed episodes (0-MX: 71.3%, 1-MX: 69.2%, >1-MX: 57.5%).

Conclusion: The present data demonstrate that bipolar patients initiated on maintenance therapy form an exceedingly heterogeneous population. The increased hospitalization rate in patients with mixed episodes suggests that these need particular careful medical monitoring and optimized pharmacotherapy.

References:


NR310 Monday, May 21, 3:00 PM - 5:00 PM
Efficacy And Safety Of Aripiprazole As Adjunctive Therapy In Major Depressive Disorder: A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study (Study CN136-139)


Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the efficacy and safety of aripiprazole as adjunctive therapy in major depressive disorder.

Summary:

Objective: Evaluate the efficacy and safety of adjunctive aripiprazole versus placebo to standard antidepressant therapy (ADT) in patients with major depressive disorder who showed an incomplete response to ≥1 historical ADT and one prospective ADT.

Methods: The study comprised a 7 to 28-day screening phase, an 8-week, prospective treatment phase and a 6-week randomization phase. During prospective treatment, patients experiencing a major depressive episode (HAM-D17 Total score ≥18) received ADT dosed per label guidelines: escitalopram, fluoxetine, paroxetine CR, sertraline or venlafaxine XR, each with single-blind, adjunctive placebo. Patients with an incomplete response were then randomized to either continued adjunctive placebo or adjunctive aripiprazole (2-20 mg/day). Primary efficacy endpoint was the mean change in MADRS Total score from end of prospective treatment to end of randomized treatment (Week 14, LOCF), as-
sessed by ANCOVA, with the end of prospective treatment value as a covariate and treatment and study center as main effects.

Results: 178 patients were randomized to adjunctive placebo and 184 to adjunctive aripiprazole. Baseline demographics were similar between groups (mean MADRS score 26.0). Mean MADRS change was significantly greater with adjunctive aripiprazole versus adjunctive placebo (-8.8 vs. -5.8; p<0.001). Adverse events occurring in ≥10% of patients with either adjunctive placebo or adjunctive aripiprazole groups were: akathisia (4.5 vs. 23.1%); headache (10.6 vs. 6.0%); restlessness (3.4 vs. 14.3%). Incidence rates of adverse events leading to discontinuation were low in patients treated with adjunctive placebo (1.7%) and with adjunctive aripiprazole (2.2%); only one adjunctive aripiprazole-treated patient discontinued due to akathisia. Weight gain ≥7% was seen in 1.2% and 7.1% of adjunctive placebo- and adjunctive aripiprazole-treated patients, respectively.

Conclusions: In patients with major depressive disorder who showed an incomplete response to standard antidepressant therapy, adjunctive aripiprazole is efficacious and well tolerated.

References:

NR311 Monday, May 21, 3:00 PM - 5:00 PM
Two Studies To Evaluate The Safety And Efficacy Of Aripiprazole Monotherapy In Outpatients With Bipolar I Disorder With A Major Depressive Episode Without Psychotic Features (Studies CN138-096 And CN138-146)
Ronald N. Marcus Bristol- Myers Squibb, Wallingford, 5 Research Parkway, Wallingford, CT, 06492, 9000, Randell Owen, Rene Swanink, Robert D. McQuade, Taro Iwamoto

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the efficacy and safety of aripiprazole monotherapy in outpatients with bipolar I disorder experiencing a major depressive episode without psychotic features.

Summary:
Objective: To evaluate the efficacy and safety of aripiprazole monotherapy versus placebo in bipolar depression.
Methods: Two identically designed, 8-week, multicenter, randomized, double-blind, placebo-controlled studies in outpatients aged 18-65 years with bipolar I disorder experiencing a major depressive episode without psychotic features (DSM-IV) were conducted. After a 3 to 28-day screening period, patients were randomized to placebo or aripiprazole (initiated at 10 mg/day, then flexibly-dosed 5-30 mg/day based on clinical effect/tolerability). Patients completing the study could enter a 26-week, open-label extension phase. Anxiolytics or hypnotics were allowed throughout the study only for patients under chronic, stable treatment with these drugs, or between Weeks 1-4 in patients who required them after treatment initiation. All anxiolytics/hypnotics had to be discontinued abruptly at the end of Week 4. The primary efficacy endpoint was mean change from baseline to study-end (Week 8 LOCF) in the MADRS total score.

Results: In total, 186 and 187 patients were randomized to aripiprazole and 188 and 188 to placebo, in Studies 1 and 2, respectively. Baseline demographics were similar between groups (mean MADRS: 28.5-29.1 in Study 1; 29.4-29.6 in Study 2). Aripiprazole did not achieve statistical significance on the MADRS change at endpoint in either study, although statistically significant differences were observed during weeks 1-6. Aripiprazole had a higher incidence of akathisia, insomnia, nausea, fatigue and restlessness versus placebo. More patients discontinued with aripiprazole versus placebo (46.8 vs. 35.1% in Study 1; 41.2 vs. 29.8% in Study 2). The most common reasons for discontinuation in the aripiprazole group were adverse events and loss to follow-up.

Conclusions: Aripiprazole administered as monotherapy in this study design and with the utilized dosing scheme does not have a favorable risk/benefit ratio in bipolar depression.

NR312 Monday, May 21, 3:00 PM - 5:00 PM
Social and occupational functioning in patients with partial or complete remission of a MDD episode
Irene Romera Lilly Spain, Clinical Research Department, romeral@lilly.com, Alcobendas-Madrid, 28270, 4700, Pepa Polavieja, Victor Pérez, Jose Manuel Menchón, Lorena Redondo, Inmaculada Gilaberte

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the differences in social and occupational functioning between patients in partial remission of the major depressive episode (MDD) and patients in complete remission. The participant will recognize the clinical and functional implications associated with the partial remission of a MDD episode.

Summary:
Objective: Evaluation of differences in social and occupational functioning between patients in partial remission of the major depressive episode (MDD) and patients in complete remission.
Methods: This case-control study included 278 patients. One group of 139 patients (cases) in partial remission (HAM-D-17 score >7 and ≤15) of a MDD episode (DSM-IV-TR) matched by age, gender and health-care area with a control group of patients in complete remission (HAM-D-17 score ≤7). Both groups had been on antidepressant treatment for 12 weeks and no longer met criteria for MDD episode. Absence days at work in the previous 3 months for paid for labor patients (141) and self-reported disability days in the previous 30 days for non-paid for labor patients (137) were recorded.

Functioning was assessed by means of the Social and Occupational Functioning Assessment Scale (SOFAS).

Results: Patients' age were 50.5±14.5 years (mean±SD), and 263(77%) were female. HAM-D score at first assessment was 12.0±2.1 for cases and 4.2±1.8 for controls.

There were no differences between groups in number of previous MDD episodes, age at first episode, duration of the current episode, presence of psychological-environmental problems or antidepressant treatment. However patients in partial remission had more history of personality and dysthymic disorders, lower educational level, had been absent from work more days (45.1±35.6 vs 22.1±27.7; p-value < 0.001) and have had more days of self-reported disability if not employed (11.8±12.1 vs 3.2±6.1, p-value < 0.001).

Partial remitters showed statistically significant (p-value<0.001) lower functioning (63.2±12.4) than complete remitters (80.7±10.5). Scores above 80 in the SOFAS describe individuals who besides being without significant psychopathology exhibit normal functioning, while most individuals in psychiatric treatment are rated between 1-70.

Conclusions: Partial remission was associated with a clinically significant functioning impairment whereas patients in complete remission showed a functioning close to normality.
Relationships Between Temperament Dimensions and Life Events in Recovered Bipolar I Disorder and Normal Controls


Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the relationships between temperament dimensions and early or recent life events in patients suffering from Bipolar I Disorder. The participant should be able to recognize that life events influence only anxious and irritable temperament dimensions. Whereas, cyclothymic and depressive temperaments had no relationships with life events.

Summary:

The aim of this study was to investigate how early and recent life events relate to temperament dimensions in Bipolar I Disorder patients and controls.

Methods:

Fifty probans with DSM-IV diagnosis of Bipolar I Disorder were recruited. They had euthymic mood for at least four weeks. Fifty controls subjects, whose age and gender matched the 50 Bipolar I patients, were recruited. Control subjects were interviewed using MINI PLUS and were free from any psychiatric disorder.

Variables, such as early parental loss and life events in the last six months according to Paykel life events scale (PLEs), were examined.

Affective temperament dimensions of patients and controls were evaluated using the Arabic version of TEMPS-A.

Results:

Bipolar I patients showed higher cyclothymic and depressive temperament scores (respectively: 10,16 vs. 5,92; p<0,001 and 11,12 vs. 8,56; p=0,002) and higher PLEs global score (2,16 vs. 1,26; p=0,005) than controls. The mean score of anxious and irritable temperament were higher in BP who had a parental early loss than those who had not (respectively: 15,80 vs 9,09; p=0,014 and 9,20 vs 5,07; p=0,026). A multiple linear regression showed that the PLEs global score was correlated with anxious temperament score in Bipolar I patients (r=0,455, p=0,001) and with irritable temperament score in controls (r=0,438, p=0,001).

Conclusion:

According to our findings, the early parental loss influenced anxious and irritable temperament dimensions in Bipolar I patients. The number of recent life event according to PLEs was correlated to anxious temperament in Bipolar I patients and to irritable temperament in controls. Cyclothymic and depressive temperaments, which had higher mean score in Bipolar I patients than controls, were not related to neither of early and recent life events in Bipolar I patients and controls.

References:

Educational Objectives:

1. Appreciate the prevalence of anxiety disorders in patients with bipolar disorder.
2. Recognize the challenges associated with treating bipolar patients with a co-occurring panic or generalized anxiety disorder.
3. Discuss the limitations of treatments for bipolar patients with a co-occurring anxiety disorder.
4. Evaluate the evidence for the use of atypical antipsychotics in the treatment of patients with bipolar disorder and a co-occurring anxiety disorder.

Summary:

Introduction: Although anxiety disorders are common in patients with bipolar disorder, the anxiolytic effects of pharmacological agents for mania and bipolar disorder have not been well studied. In this study, we investigate the efficacy of risperidone in bipolar patients with a co-occurring panic disorder (PD) or generalized anxiety disorder (GAD).

Methods: 111 outpatients meeting DSM-IV criteria for bipolar disorder and comorbid PD or GAD were randomized 1:1 to 8 weeks of double-blind flexible dose (0.5-4.0 mg/day) treatment with risperidone or placebo. Repeated measures analysis of variance (ANOVA) of the last-observation-carried-forwards scores was used to assess efficacy on the primary outcome measure, the 21-point (-10 to +10) Clinical Global Improvement Scale for Anxiety (CGI-21) and on secondary measures including the Hamilton Anxiety Scale (HAM-A), Sheehan Panic Disorder Scale (SPS), Patient Global Improvement Scale (PGI-21), Young Mania Rating Scale (YMRS), Inventory of Depressive Symptoms (IDS), a 7-point-CGI (CGI-BP) for bipolar symptoms, and the Sheehan Disability Scale (SDS).

Results: Of the 111 randomized patients, 88% had comorbid GAD and 59% had comorbid panic disorder. 104 had at least one post baseline visit and 63 completed the study. Although no significant differences between risperidone and placebo were found on the primary or secondary outcome measures, subgroup analysis indicated that risperidone treated patients without panic disorder had better (LOCF) CGI-21 scores (1.8 vs. 5.2, p < 0.04) and lower LOCF Ham-A scores (11.9 vs. 18.9, p<0.04) than risperidone patients with panic disorder.

Conclusions: Risperidone is widely used as a treatment for acute mania in bipolar disorder. Our results suggest that it is not an effective anxiolytic over 8 weeks of treatment in outpatient bipolar patients with co-occurring anxiety disorders. These results may be due in part to the high rate of comorbid panic disorder in the sample and the lower response rate for this group.

References:


NR316 Monday, May 21, 3:00 PM - 5:00 PM

Safety and Tolerance of TMS in the Treatment of Major Depression: Evidence from Extended Exposure and Reintroduction Treatment

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Educational Objectives:

At the conclusion of this presentation, the participant should understand the safety and tolerability profile of TMS in the treatment of patients with major depression. The participant should be able to describe the common adverse events, their time course, and any potentially clinically significant short and longer term risks of treatment with TMS.

Summary:

Objective: Transcranial magnetic stimulation is effective in the treatment of major depression. However, earlier studies provided limited information regarding the safety of TMS, due to the use of sub-optimal treatment parameters, short duration of acute treatment, and limited follow up. Furthermore, adverse events were rarely reported using standardized terminology. The present report describes the comprehensive safety summary of a recently completed multi-site clinical development program for TMS in the treatment of major depression.

Methods: The program comprised 3 separate clinical protocols (N=301 patients), a 6-week randomized controlled trial of active TMS v sham TMS, a 6-week open-label extension study for non-responders in the first trial, and a 24-week continuation pharmacotherapy maintenance of effect study for responders in either the controlled or the open-label study. The latter study also permitted reintroduction of TMS for symptom worsening, as an add-on treatment. Treatment parameters were optimized in a fixed, maximum feasible dose design. Spontaneous adverse events were collected at each study visit across the clinical program. Air conduction auditory threshold was assessed at fixed treatment intervals in all studies. Cognitive function was also examined.

Results: TMS was well tolerated in both the controlled and open-label acute treatment studies, with an all-cause discontinuation rate of <6% through 4 weeks of acute treatment. Discontinuation rate due to adverse events was less than 5% in both active and sham TMS treatment conditions, and did not differ between treatments. Common adverse events were transient headache and scalp discomfort, largely reported as mild to moderate in severity. There was no evidence of exacerbation of depression or emergent suicidal ideation. Extended and reintroduction treatment showed no evidence of late-appearing adverse events.

Conclusions: TMS can be safely administered in both acute and repeated courses. The adverse event experience is predictable, very well tolerated, and transient.

References:


NR317 Monday, May 21, 3:00 PM - 5:00 PM

Impact of Depression and its Pathways on Work Productivity

Ralph W. Health Outcomes Swindle Eli Lilly and Company, Health Outcomes, Lilly Corporate Center, DC4025, Indianapolis, IN, 46285, 9000, Ronald C. Kessler, Leigh Anne White, Howard G. Birnbaum, Shamim Mondal, Ying Qiu, Yohanne Kidolezi

Educational Objectives:

At the conclusion of this presentation, the participant should be familiar with a survey-based method of measuring employee work productivity. The participant should understand the impact of depression and comorbidities on work productivity, as it was ob-
served in this employee sample. Participants should also recognize differences between survey respondents and nonrespondents, and understand why it is important to adjust for differential survey non-response.

Summary:

Objective: Describe the impact of depression and related conditions on workplace productivity.

Methods: Using a survey of 7,538 employees of a large U.S. firm in conjunction with integrated medical and pharmacy claims data, we examined the comparative effects of depression and strongly related comorbid conditions (anxiety disorder, chronic fatigue, and chronic sleep problems) on absenteeism and work performance (presenteeism). The workplace outcomes were assessed with the WHO Health and Work Performance Questionnaire (HPQ). Regression methods were used to assess the effects of the target health problems on absenteeism and presenteeism controlling for socio-demographics and claims-based measures of utilization in the six-month pre-survey period. Results were weighted to adjust for differential survey non-response.

Results: Among all physical and mental conditions affecting 5 percent or more of the population, depression had the largest adverse effect on overall work performance, followed by fatigue, anxiety, headache, obesity, and chronic sleeping problems. Depression was associated with a 3.2 percentage point reduction in presenteeism and a 2.5 percentage point reduction in overall work performance (absenteeism and presenteeism combined), equivalent to approximately 6-8 workdays per year. Comorbid anxiety, sleep disturbance, and fatigue increased the adverse effect of depression on overall work performance to 4-6 percentage points, but had little direct effect on work performance independent of depression. Depression, in comparison, had significant adverse effects on work performance even in the absence of other comorbid conditions. In this analysis, adjusting for non-response did not affect the results.

Conclusion: Depression is a robust predictor of decrements in work performance loss. It appears to exacerbate the effects of several comorbid conditions that have little effect on work performance in the absence of depression.

References:

NR318 Monday, May 21, 3:00 PM - 5:00 PM

Can the PHQ-9 replace the BDI-II for inpatient depression measurement?


Educational Objectives:
At the conclusion of this presentation the participant should be able to discuss the similarities and differences in using the PHQ-9 and BDI-II for inpatient depression assessment.

Summary:

Purpose: Assessment instruments are useful in screening and tracking the clinical course of depressive symptoms. The BDI-II (Beck Depression Inventory) has been used for decades in both clinical and research studies. The PHQ-9 (Patient Health Questionnaire 9) is newer and free of charge, although mostly used in primary care patient populations. This study investigated whether the PHQ-9 can replace the BDI-II as the main measurement instrument on a specialized inpatient unit.

Methods: We conducted a retrospective study between April and July 2006 on depressed patients treated in our inpatient Mood Disorders Unit. All patients were asked to complete a BDI-II and PHQ-9 on admission and discharge for clinical assessment. Correlations between BDI-II and PHQ-9 for admission and discharge were calculated. Sixteen BDI-II items were deemed mappable to corresponding PHQ-9 items. Weighted Kappas were calculated for each of the 16 pairings to assess strength of agreement.

Results: Ninety-six patients were included. Mean length of stay was 8.8 days. Mean BDI-II scores on admission and discharge were 27.4 and 11.3, respectively. Mean PHQ-9 scores on admission and discharge were 18.7 and 8.6. Correlation between BDI-II and PHQ-9 scores was 0.786 for admission and 0.656 for discharge. For the 16 weighted Kappa scores for admission data, 1 was rated in the “poor” (0.01) category, 12 were “fair” (0.21-0.40), and 3 were in the “moderate” (0.41-0.60) strength category. For the discharge data, 8 were “fair” and 8 were “moderate” strengths.

Conclusions: BDI-II and PHQ-9 scores were strongly correlated, indicating that for a general measure of improvement in depression over a short inpatient stay, the PHQ-9 is a reasonable substitute for the BDI-II. However, when examining individual items, the strength of agreement was mostly in the fair to moderate range, suggesting that direct item comparison may not be valid.

References:

NR319 Monday, May 21, 3:00 PM - 5:00 PM

Patient Acceptability of the Use of Scales to Measure the Outcome of Depression in Clinical Practice

Mark Zimmerman, M.D. Rhode Island Hospital, Psychiatry, 235 Plain Street, Suite 501, Providence, RI, 02905, 9000, Joseph B. McGlinchey, Ph.D.

Educational Objectives:
At the conclusion of this presentation the participant should be able to describe the high level of patient acceptance of completing self-administered questionnaires in outpatient clinical practice.

Summary:

Background: Self-report questionnaires are a cost-effective option to monitor the outcome of clinical care. Even when using self-report scales, consideration should be given to how much time they take to complete and how burdensome they are perceived to be. In the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services project we compare the acceptability of completing two depression scales, the Beck Depression Inventory (BDI) and the Clinically Useful Depression Outcome Scale (CUDOS).

Methods: In the first study, 50 depressed psychiatric outpatients completed the CUDOS and a questionnaire assessing how burdensome it was to complete the scale during the visit. In the second study, a separate sample of 50 depressed outpatients completed the CUDOS and BDI and a measure of scale acceptability.

Results: Almost all patients completed the CUDOS in less than 3 minutes (Mean=102.7 seconds; SD=42.7), and considered the questionnaire very little or a little burdensome (98.0%, n=49). In
the second study comparing the CUDOS and the BDI, significantly more patients indicated that the CUDOS took less time to complete, and was less of a burden to complete. Nearly three times as many patients indicated that they would prefer to complete the CUDOS at every visit in order to monitor the outcome of treatment (40.0% vs. 14.0%, z = 2.31, p < .05).

Conclusions: A consumer-friendly reliable and valid self-administered questionnaire can improve the efficiency of the clinical encounter. The brevity of the CUDOS lends itself to regular administration in clinical practice.

References:


NR320

Monday, May 21, 3:00 PM - 5:00 PM
Metabolic Syndrome in Patients Enrolled in a Clinical Trial of Aripiprazole in the Maintenance Treatment of Bipolar Disorder (Study CN138-010)

David E. Kemp Case Western Reserve University, University Hospitals of Cleveland, 11100 Euclid Avenue, Cleveland, OH, 44106, 9000, Joseph R. Calabrese, Quynh Van-Tran, Andrei Pikalov, James Eudicone, Ross A. Baker

Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate that, over 26 weeks of treatment, the effect of aripiprazole on the prevalence of metabolic syndrome in patients with bipolar disorder is no different to that of placebo. Participants should also be aware that the prevalence of metabolic syndrome in patients with bipolar disorder is high.

Summary:

Objectives: Metabolic syndrome (MetSyn), including obesity, diabetes, dyslipidemia, and hypertension, is higher in patients with bipolar disorder than the general population. Given that aripiprazole has less risk of inducing weight gain and diabetes than other atypical antipsychotics, we compared the effects of 26-week treatment with aripiprazole or placebo on incidence of MetSyn in patients with bipolar disorder.

Methods: Patients with bipolar I disorder were stabilized on aripiprazole for at least 6 weeks prior to double-blind randomization to continued treatment with aripiprazole or placebo for 26 weeks. The incidence of MetSyn in each group was calculated at randomization and at endpoint for evaluable patients using a last observation carried forward approach. MetSyn was defined as meeting at least 3 of the following 5 criteria: waist circumference >102 cm (men) or >88 cm (women); triglycerides ≥150 mg/dL; HDL cholesterol <40 mg/dL (men) or <50 mg/dL (women); systolic BP ≥130 mmHg and diastolic BP ≥85 mmHg; blood glucose ≥110 mg/dL.

Results: At randomization, 27% (18/67) of placebo-treated patients and 24% (14/58) of aripiprazole-treated patients met MetSyn criteria. At study endpoint, 26% (15/54) of placebo-treated and 26% (15/57) of aripiprazole-treated patients met MetSyn criteria. For evaluable patients who did not meet MetSyn criteria at baseline, 8% (3/36) of placebo-treated and 14% (5/35) of aripiprazole-treated patients newly developed MetSyn at endpoint. For evaluable patients with MetSyn at baseline, 31% (4/13) of placebo-treated and 40% (4/10) of aripiprazole-treated patients no longer met MetSyn criteria at endpoint.

Conclusions: In contrast to a 15% age-adjusted prevalence of MetSyn in the general population, the incidence of MetSyn in bipolar patients was approximately 25%. The effect of 26-week treatment with aripiprazole on the incidence of MetSyn was similar to placebo.

References:


NR321

Monday, May 21, 3:00 PM - 5:00 PM
At Risk for Misdiagnosed Bipolar Disorder: Patient Characteristics and Symptomatology

Kevin Nanny, B.S. GlaxoSmithKline, Department of Psychiatry, 5 Moore Drive, RTP, NC, 27709-3398, 9000, Susan Bolge, Ph.D., Eric Bourne, M.S., Thomas R. Thompson, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to identify characteristics of patients currently diagnosed with unipolar depression who may be at risk for misdiagnosed bipolar disorder.

Summary:

Objectives: To identify characteristics of patients currently diagnosed with unipolar depression at risk for misdiagnosed bipolar disorder (MBPD).

Methods: Patients reporting depression diagnosed by a health care provider were identified through the Consumer Health Sciences National Health and Wellness Survey. Information about manic symptoms, comorbid conditions, psychiatric symptomatology, use of health care resources, and patient demographics was collected through Internet-based questionnaires. A self-report adapted version of the DSM-IV criteria identified symptoms suggestive of a manic episode. Psychological well-being was measured by the Psychological General Well-Being Index.

Results: Of the 1602 respondents who met inclusion criteria, 219 (14%) were considered at risk for MBPD. These respondents were younger, had lower socioeconomic status, and more likely to be nonwhite than those not a risk for MBPD in the survey. Those at risk for MBPD rated their depression as more severe and experienced greater impairment of psychological well-being. Comorbid mental disorders, especially anxiety-related conditions, were common in MBPD respondents. Those at risk for MBPD versus those not at risk were also more likely to utilize health care services and take antidepressants. More than 70% of respondents at risk for MBPD reported speaking with a health care provider about their manic symptoms.

Conclusions: Approximately 1 of every 7 respondents diagnosed with unipolar depression reported manic symptoms that put them at risk for MBPD. These reported findings underscore the importance of evaluating unipolar patients for bipolar disorder. Funding provided by GlaxoSmithKline.

References:


2. Dupuy HJ. The Psychological General Well-Being (PGWB) Index. In: Wenger NK, Mattson ME, Furberg CD, Elinson J, eds. Assessment of Quality of Life in Clinical Trials of Cardio-

NR322

Monday, May 21, 3:00 PM - 5:00 PM
Psycho-Education versus Cognitive Behavioural Therapy for Bipolar Disorder: A Multi-site National RCT
Sagar V. Parikh, M.D. University of Toronto, Psychiatry, 399 Bathurst Street (9M-329), Toronto, ON, M5T 2S8, 1220, Ari E. Zaretsky, M.D., Serge Beaulieu, M.D., Pablo Cervantes, Lakshmi N. Yatham, M.D., Irene Patelis-Siotics, M.D., Glenda M. MacQueen, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the challenges to conducting a psychotherapy RCT in bipolar disorder, identify strengths of using the LIFE scale rather than relapse rates as an outcome measure, and identify key benefits of psychoeducation and cognitive behaviour therapy in bipolar disorder.

Summary:

Objective: To evaluate the relative merits and long-term efficacy of two adjunctive psychosocial interventions (Psycho-Education versus Cognitive Behavioural Therapy) for Bipolar Disorder (BD) RCT. Introduction: Pharmacotherapy of BD is necessary but not sufficient to adequately control episodes and prevent relapses. Adjunctive psychosocial interventions have demonstrated considerable promise, particularly psychoeducation and cognitive-behavioural therapy (CBT).

Design: We have just finished conducting a multi-site randomized controlled trial comparing 6 sessions of group psychoeducation with 20 sessions of individual CBT. It is a single blind study with an 18-month study follow-up period and broad inclusion criteria to ensure generalizability. The cost implications of the different interventions are also calculated.

Method: 204 adult subjects with BD I or II were recruited from across Canada. Participants' illness burden and psychosocial functioning was assessed longitudinally for 18 months primarily using a modified version of the Longitudinal Interval Follow-up Evaluation. Medication treatment was monitored under naturalistic treatment conditions. Results & Conclusions: Effects of the two psychosocial treatments on illness burden and psychosocial functioning were assessed longitudinally for 18 months primarily using a modified version of the Longitudinal Interval Follow-up Evaluation. Medication treatment was monitored under naturalistic treatment conditions. Results & Conclusions: Effects of the two psychosocial treatments on illness burden and psychosocial functioning are presented. Due to publication embargos of journals, key findings cannot be disclosed in this abstract; however, the APA conference will be the first venue for disclosure of the study findings.

References:


NR323

Monday, May 21, 3:00 PM - 5:00 PM
Antipsychotic Medications and Hospital Readmission in Adult Bipolar Disorder
Mark Olsson Columbia University, Department of Psychiatry, Department of Psychiatry, Columbia University, 1051 Riverside Drive, New York, NY, 10032, 9000, Myoung S. Kim, Steven C. Marcus, Edward Kim, Gilbert J. L'Italien, Quynh Van-Tran

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the differential risk of early hospital readmission associated with five different second-generation antipsychotic medications (aripiprazole, olanzapine, quetiapine, risperidone, and ziprasidone) for the treatment of adult bipolar disorder.

Summary:

Objective: The purpose of this presentation is to compare the risk of early psychiatric hospital readmission among discharged adult inpatients with bipolar disorder who receive treatment with one of five different second-generation antipsychotic medications: aripiprazole, olanzapine, quetiapine, risperidone, or ziprasidone.

Methods: A secondary analysis will be presented of 2002-2006 Texas Medicaid data focusing on the 180-day period following hospital discharge of adults 18 to 64 years of age who have been treated for bipolar disorder, but not schizophrenia. The analysis will compare the risk of psychiatric hospital readmission among patients receiving antipsychotic monotherapy with aripiprazole, olanzapine, quetiapine, risperidone, or ziprasidone during the first 30 days following hospital discharge.

Results: The study patients were predominantly white (61.8%), female (68.8%), <45 years of age (55.2%), had an index inpatient treatment episode of <30 days (98.5%) and many had received a mood stabilizer during the first 30 days following hospital discharge (59.0%). Approximately half of the patients had been previously treated for a substance use disorder (50.4%). As compared with patients who were treated with quetiapine (28.2%) (n=517), risperidone (29.6%) (n=352), aripiprazole (31.2%) (n=189), or olanzapine (35.2%) (n=284), patients treated with ziprasidone (36.7%) (n=191) were the most likely to be readmitted during the first 180 days following hospital discharge. The pairwise difference in proportions between ziprasidone and quetiapine (p=0.03) was statistically significant. The other p-values for pairwise comparisons with ziprasidone in the proportion of hospital readmissions were as follows: risperidone (p=0.09), aripiprazole (p=0.26) and olanzapine (p=0.75).

Importance: For adults with bipolar disorder, the risk of early psychiatric hospital readmission may differ across the second-generation antipsychotic medications.

References:


Objective: This investigation was undertaken to explore the prevalence and associated features of problem gambling amongst individuals with bipolar I disorder.

Methods: The data for this analysis were procured from the Canadian Community Health Survey: Mental Health and Well-being (CCHS 1.2) conducted by Statistics Canada. Individuals screening positive for a lifetime WMH-CIDI-defined manic episode (i.e. Bipolar I Disorder) or depressive episode (i.e. Major Depressive Disorder) and current (i.e. past 12-month) problem gambling were compared to the general population. Past year problem gambling was operationalized with the Canadian Problem Gambling Index (CPGI).

Results: The sample consisted of 36,984 individuals (>15 years old); the prevalence of problem gambling was significantly higher (11.6%) amongst bipolar respondents as compared to the general population (3.8%, p<0.001) and respondents with major depressive disorder (4.9%, p<0.01). Compared to the general population, the odds ratio for problem gambling was highest amongst individuals with bipolar I disorder (OR=2.3; 95%CI 1.4-3.9) than major depressive disorder (OR=1.3; 95%CI 1.0-1.8). Of the respondents screening positive for bipolar disorder, males were more likely to screen positive for problem gambling (OR=1.7; 95%CI 1.4-2.2), as were respondents without post-secondary education (OR=1.5; 95%CI 1.1-2.0). Bipolar individuals who were married/cohabitating had a decreased risk for problem gambling (OR=0.6; 95%CI 0.5-0.8). Comorbid alcohol dependence (OR=3.0; 95%CI 2.1-4.5) and illicit drug dependence (OR=2.8; 95%CI 1.1-6.9) conferred an increased risk for problem gambling amongst bipolar individuals. Physical activity level (moderate to active lifestyle) was associated with a decreased risk for problem gambling (OR=0.7; 95%CI 0.6-0.9).

Conclusions: Individuals with bipolar I disorder are differentially affected by problem gambling. Opportunistic screening for problem gambling is warranted, particularly in persons with comorbid alcohol or substance dependence.

References:

NR325

NR325

Monday, May 21, 3:00 PM - 5:00 PM

A Pharmacokinetic/Pharmacodynamic Model for Describing the Concentration-Effect Relationship in Acute Mania Following Once-Daily Administration of Extended-Release Divalproex Sodium

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Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the linear relationship between divalproex ER serum levels and efficacy and understand implications for treatment of acute mania.

Summary:
Objective: To evaluate the concentration-efficacy relationship for valproic acid following once-daily administration of extended-release (ER) divalproex in acute mania using a pharmacokinetic (PK)/pharmacodynamic (PD) model.

Methods: A pooled analysis of two double-blind, placebo-controlled, parallel-group, multi-center studies (n=573) of divalproex-ER treatment of acute mania was used to evaluate the relationship between change in Mania Rating Scale (MRS) scores and plasma valproic acid concentrations. Mixed effects models (variations of linear, exponential and Emax) that accounted for the placebo-effect time course (linear and exponential models with and without baseline MRS as a covariate) were evaluated using the NONMEM software.

Results: Valproic acid PK was optimally characterized by a 1-compartment model with 0-order absorption. This PK model was used to estimate plasma exposures during the study since one of the two studies collected near-peak plasma levels (sampling occurred ~12 hours post-dose) and the second study collected trough samples. An exponential time course model optimally described the placebo effect. A statistically significant linear relationship between valproic acid concentrations and MRS change was established after accounting for the placebo effect and differences in baseline MRS across subjects. The model-predicted mean MRS change scores for placebo, 50, 75, 100 and 125 μg/mL valproic acid trough concentrations were -8.3, -10.4, -11.5, -12.5 and -13.6, respectively, after 21 days of once daily divalproex-ER treatment.

Conclusions: The linear relationship between efficacy and plasma valproic acid concentrations observed in this study supports current recommendations for targeting serum valproic acid levels between 85 and 125 μg/mL (within tolerability) for the treatment of acute mania.

References:

NR326

NR326

Monday, May 21, 3:00 PM - 5:00 PM

DSM Criteria for Melancholia Poorly Discriminate Outcome in ECT

Rebecca G. Knapp, Ph.D. Medical University of South Carolina, Biostatistics, Bioinformatics, and Epidemiology, 135 Cannon Street, PO Box 250835, Medical University of SC, Charleston, SC, 29425, 9000, Max Fink, M.D., A. John Rush, M.D., Keith G. Rasmussen, M.D., Martina Mueller, Ph.D., Charles H. Kellner, M.D.

Educational Objectives:
At the conclusion of this presentation, participants will: 1) be acquainted with the relationship between DSM-IV melancholia criteria, as ascertained by SCID-1, and response to ECT; and 2) comprehend limitations for various systems used to subclassify major depressive disorder.

Summary:
Melancholic patients respond rapidly to remission with effective electroconvulsive therapy. The syndrome has been classically defined as a depressive syndrome of sudden onset, with anhedonia, motor and vegetative disturbances, and often, suicidal intent. While clinicians have long recognized the syndrome, in the 1980 DSM classification melancholia was relegated to a features specifier for mood disorders. The presence is ascertained by criteria specified in the SCID 1 examination.

Aim: To determine the relationship between baseline melancholia features and clinical outcome in patients with major depressive disorder referred for ECT.

Method: In the 4-hospital (CORE) collaborative ECT study, a randomized, multicenter, NIMH-funded trial, SCID assessments were obtained at study entry. HAMD24 ratings were obtained thrice weekly during the course of bitemporal ECT, given three
times weekly. DSM-defined melancholic features were ascertained by SCID 1 criteria.

Results: The evaluable sample was severely ill with mean HAMD24 scores of 35.2 (±6.9). Of 489 patients, 311 (63.6%) met DSM criteria for melancholic features. During acute ECT, 62.1% of those with melancholic features remitted, as compared to 78.7% for those without melancholic features (p = 0.002).

Conclusion: In this dataset, ascertaining melancholia features by SCID criteria did not identify depressed patients most likely to respond to ECT, as had been anticipated from the literature. The limitations of the DSM criteria for melancholia as ascertained by SCID are a possible explanation for these findings. In the next iteration of DSM classification, melancholia should be a specific syndrome in mood disorders, defined by criteria such as those developed by Parker and Hadzi-Pavlovic (1996) and Taylor and Fink (2006).

References:

NR327 Monday, May 21, 3:00 PM - 5:00 PM
A Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study of Desvenlafaxine Succinate for Prevention of Depressive Relapse in Adult Outpatients with Major Depressive Disorder
Karl Rickels, M.D., University of Penna Medical Center, Psychiatry, 3535 Market Street, Philadelphia, PA, 19104, 9000, Stuart A. Montgomery, M.D., Julien D. Guelfi, M.D., Karen A. Tourian, M.D., Bruno Pitrosky, Ph.D., S. Krishna Padmanabhan, M.S., Jean-Michel Germain, Ph.D.

Educational Objectives:
1. The safety and efficacy of desvenlafaxine (DVS) in long-term treatment of adults with major depressive disorder (MDD);
2. The importance of relapse prevention through continuous therapy.

Summary:

Objectives: The primary objectives were to compare the efficacy and safety of desvenlafaxine succinate (DVS) versus placebo in reducing the relapse rate of depression in patients with major depressive disorder (MDD).

Methods: This was a phase 3, multicenter, placebo-controlled double-blind (DB) 6-month relapse prevention trial in adult outpatients with MDD who had responded to 12 weeks of open-label treatment with a flexible dose of DVS (200–400 mg/day). The primary efficacy endpoint was time until relapse. Relapse was defined by at least 1 of the following criteria: 1) Hamilton Rating Scale for Depression, 17-item (HAMD$_{17}$) score ≥16 at any visit; 2) Clinical Global Impression Improvement (CGI-I) score ≥6 at any visit; and 3) discontinuation due to unsatisfactory response. Secondary efficacy variables included HAMD$_{17}$ total score, CGI-I, and remission (HAMD$_{17}$ score <7).

Results: There was a significant advantage for DVS compared to placebo in preventing relapse of current depressive episode. Significantly fewer relapses occurred in the DVS group (24%) than the placebo group (42%; log-rank: p = 0.0001). When excluding the first 2 weeks of DB (potential confounding between discontinuation symptoms and relapse), results were still in favor of DVS. For the HAMD$_{17}$ total score, a significant difference in favor of DVS was observed from DB week 3 on (LOCF analysis), and adjusted mean changes at final evaluation were 0.85 and 5.03 for DVS and placebo, respectively. Significantly more patients treated with DVS were in remission from DB week 4 on (LOCF analysis). Most frequent adverse events (AEs) with DVS in DB period included nausea, dizziness, asthenia, abnormal dreams, headache, and sweating, which are consistent with AEs observed in the serotonin-norepinephrine reuptake inhibitor (SNRI) drug class.

Conclusions: DVS was effective in preventing relapse of MDD during the 6-month DB treatment study and was generally safe and well tolerated.

References:

NR328 Monday, May 21, 3:00 PM - 5:00 PM
Quality of Life and Resource Use In Patients with Bipolar Disorder in the United States and Five European Countries
Oscar Leeuwenkamp, Ph.D. NV Organon, Department of Global Health Economics & Strategic Pricing, Molenaarstraat 110, Oss, 5342 CC, 2771, Robert Morlock, Ph.D., Garry Milligan, B.S., Richard Perry, B.S.

Educational Objectives:
1. Understand the relationship between quality of life and resource use in patients with bipolar disorder.
2. Understand the relationship between quality of life and resource use in patients with bipolar disorder.

Summary:

Background: Bipolar disorder is costly to patients and society. The objective of this research was to provide information on patient-reported quality of life and resource utilization for bipolar disorder patients in 5 European countries and the USA.

Methods: US and European physicians completed a questionnaire concerning their patients’ clinical status and therapy. Patients completed a questionnaire that included the EuroQol EQ-5D, which assesses quality of life in 5 key areas: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Patient responses on the EQ-5D items were used to generate EQ-5D utility scores. Patients were also asked to rate their current health on the EQ-5D visual analog scale (VAS) and report their level of resource use during the preceding 12 months. Results are reported as mean ± standard deviation.

Results: In 2006, data on self-reported quality of life were collected from 1762 patients from the US (n=506), France (n=270), Germany (n=329), Italy (n=259), Spain (n=177), and the United Kingdom (n=221). For the entire sample, 58% were female, 47% were aged 25 to 44 years, and 91% were outpatients. The three most common reasons for the physician visit were maintenance (50%) and depressed (20%) or mixed (10%) health states. Mean EQ-5D utility score (76.8±24.8) was higher than EQ-5D VAS score (64.0±20.6) across all countries (all P<0.001). Mean EQ-5D utility score was lowest (64.6±28.7) for patients reporting depressed health state. Mean number of drugs taken was significantly higher for patients with EQ-5D scores in the lowest quartile versus the highest quartile (2.5±1.1 vs 1.8±0.9, P<0.001).
Conclusions: In this large, multinational, cross-sectional survey of physicians and their patients with bipolar disorder, patient-reported quality of life varied substantially by current phase of illness, with the lowest quality of life associated with the depressive phase.

References:

NR329  Monday, May 21, 3:00 PM - 5:00 PM
Antiviral Completion Rates and Sustained Viral In Hepatitis C Patients With Versus Without Pre-existing Major Depressive Disorder

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Educational Objectives:
At the end of this presentation the audience should be able:
1. to recognize that major depressive disorder (MDD) is common among patients infected with hepatitis c
2. to recognize that patients infected with hepatitis c and who have co-morbid MDD have similar antiviral therapy completion and response rates and no greater likelihood of interferon-induced side effects.

Summary:
Objective: To determine and compare antiviral completion and sustained virologic response (SVR) rates between hepatitis C (HCV) patients with- versus those without pre-existing major depressive disorder (MDD). As HCV patients with MDD are often excluded from antiviral therapy because of the presumed risk of worsening depressive symptoms our objective was to examine the validity of this assumption.

Methods: We conducted a retrospective chart review of all patients treated for HCV at the Portland VAMC who signed informed consent. We collected data on genotype, pre-treatment psychiatric diagnosis and antidepressant use, antiviral therapy, side effects, emergency room (ER) visits and in-patient hospitalizations during treatment, as well as completion and SVR. Patients were divided into two groups- MDD (patients who had a pre- antiviral treatment diagnosis and antidepressant treatment of MDD), and controls (no MDD and no antidepressant).

Results: The control and MDD groups had a similar percent of patients with genotype 1. There was no significant difference between groups in the percent of patients with ER visits (MDD- 9/30 or 30% versus controls- 4/25 or 16%) or in-patient hospitalization (MDD- 2/30 or 7% versus controls- 2/25 or 8%). One MDD patient had an ER visit for psychiatric reasons. Side effects of antiviral treatment were not different between groups. Also there was no difference between groups in antiviral treatment completion rates (MDD- 18/30 or 60% versus controls - 17/25 or 68%) or SVR (MDD- 15/30 or 50% versus controls - 13/25 or 52%).

Conclusions: The results of our retrospective review suggest that patients with pre-antiviral treatment MDD on antidepressants are no more likely than patients without MDD to have side effects or adverse events during antiviral treatment. Furthermore, patients with MDD have similar completion and SVR rates. Our results suggest that patients with MDD can be safely and effectively treated with antiviral therapy.

References:

NR330  Monday, May 21, 3:00 PM - 5:00 PM
Bipolar Affective Disorders, Mood States, and the Acoustic Startle Paradigm

Serge Beaulieu, M.D., Ph.D. Douglas Hospital Research Center, Bipolar Disorders Program, 6875 LaSalle Blvd, Mood Disorder Program, Verdun, PQ, H4H 1R3, 1220, Trino J. Baptista, M.D., Ph.D., Mario Roy, M.D., Loic Belingard, M.S., Fernando Corbalan, M.D., Rebecca Sablè, Sybille Saury

Educational Objectives:
At the end of the presentation the participant should have a better understanding of the information processing in the bipolar patients and in the stress sensitization.

Summary:
The aim of our study is to determine if the patients with bipolar affective disorders have different stress responses than normal volunteers and if we can observe a correlation between their actual mood (depressed or euthymic), and the intensity of their acoustic startle response. We have measured the startle responses in two bipolar disorder (BD) groups (BD type I n = 18, BD type II n = 9) compared with normal volunteers (n = 24). In the bipolar groups 8 patients were “depressed” (MADRS > 8, 6 patients diagnosed with a BD type I and 2 with a BD type II). We have measured the electromyographic responses to 106 dB pulses (baseline startle). Some of these pulses were preceded by a 80 dB (PP80) or a 90 dB (PP90) prepulse 60 ms before the pulse. Our results demonstrate that all groups have a significantly lower startle response in the PP80 and PP90 conditions than in the baseline condition, and that the Pre Pulse Inhibition effect (percentage variation between baseline and pre pulse startle conditions) is more important in the PP90 than in the PP80 condition for each group. We observe a significant difference in the amplitude of the startle response between groups when the pulse is preceded by a prepulse. Post hoc analysis shows that Type I bipolar patients, but not type II, have a significantly higher response than normal control participants in the PP80 and PP90 conditions but the pre pulse inhibition effects are not different between the groups. In depth analysis revealed that the level of depression, measured with the MADRS and HAMD scales, is not linked with the amplitude of the startle response. These results are interpreted in relation with those observed in an animal model of depression.

References:
ADHD Features Measured by Wender Questionnaire in Bipolar Disorder Families: Factors and Heritability
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Educational Objectives:
Participants will recognize two findings. First, modified Wender questionnaires is composed with three correlated factors. Second, ADHD features measured by Wender questionnaire in bipolar families did not show strong heritability. However, this sample size was small for estimating heritability, and studies of larger sample may be necessary.

Summary:
Introduction: Higher rates of bipolar disorder amongst the first degree relatives of probands with ADHD, and increased rates of ADHD in the relatives of bipolar probands have been reported in many studies. This suggests some commonality in the genetic basis for both disorders, especially between childhood onset bipolar disorder and ADHD. It also suggests that ADHD features in bipolar disorder may derive from a distinct subset of genes and be a useful subphenotype for mapping studies.

Methods: In order to investigate ADHD features among bipolar families, we applied a modified form of Wender Questionnaires. Firstly, we performed a factor analysis to analyze the questions of Wender scale. A total of 467 subjects composed of mostly bipolar family members, sporadic cases with bipolar disorder, and normal controls were included. Secondly, we examined heritability for the total score of the Wender scale as well as for individual factor scores in 34 bipolar pedigrees. SOLAR was used to calculate heritabilities and age was included as a covariate.

Results: The principal component analysis with direct oblimin rotation found three related factors: affective instability and dysphoric mood, impulsivity, inattention and low performance. This factor structure is similar to previous reports by other researchers in different samples. We found that age itself is significantly correlated to total Wender score and the impulsivity factor score. Heritability measures of total Wender and factor scores were not significant (0.13 < H^2 < 0.17) in our bipolar families.

Conclusion: Factor analysis revealed three correlated factors in Wender scale, but neither the total score nor any specific factor showed strong heritability. The strong correlation with age at questionnaire completion suggests a possible memory or cohort effect. The estimate of heritability is also limited by a small sample size, and our results argue that studies of a larger sample may be necessary.

References:

NR331 Monday, May 21, 3:00 PM - 5:00 PM
TMS in the Acute Treatment of Major Depression: Improvements in Functional Status and Quality of Life
H. Brent Sovason, M.D. Stanford University School of Medicine, Psychiatry and Behavioral Sciences, 401 Quarry Road, Room 94305, Stanford, CA, 94305, 9000, Mustafa M. Husain, M.D., Paul B. Fitzgerald, M.D., Peter Becham Rosenquist, M.D., W. Vaughn McCall, M.D., James Kimball, M.D., William Scott Gilmer, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should understand the evidence for acute efficacy of TMS in the treatment of major depression, and also the magnitude of benefit observed with standard measures of functional status and quality of life.

Summary:
Objective: Clinical outcomes from antidepressant treatment on measures of functional status and quality of life are increasingly recognized as critically important since they inform whether any symptom change is associated with meaningful change in function and life satisfaction. Transcranial magnetic stimulation (TMS) is effective in the treatment of major depression. We describe the functional status and quality of life outcomes from acute treatment with TMS.

Methods: 301 medication-free patients were randomized 1:1 to treatment with active or sham TMS in a 6 week, parallel group, double-blind, multisite, controlled trial, with the Neurometrics Model 2100 System. Treatment parameters were optimized in a fixed, maximum feasible dose design. TMS was administered 5 x/week at 10 pulses/second, 4 seconds on/26 seconds off, 120% of motor threshold, for a total of 3000 pulses/session. Symptom efficacy was evaluated with the MADRS, HAMD24 and HAMD17, and has been previously described. Functional status was assessed using the Medical Outcomes Study-36 Item Short Form (v1) at baseline, 4 and 6 weeks of acute treatment. Quality of life was assessed using the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) at the same time points.

Results: After 4 weeks of treatment, patients assigned to active TMS showed a statistically superior outcome compared to sham on both the General Health (P = 0.049) and Mental Health (P = 0.006) subscales of the SF-36. After 6 weeks, active TMS treatment continued to show statistically significant benefit on the same subscales, and additionally on the Role-Emotional (P = 0.044) subscales, with a trend on the Vitality (P = 0.081) subscale. The Q-LES-Q showed statistically significant superiority in active TMS at 6 weeks of treatment (P = 0.035).

Conclusions: Acute treatment with TMS improves functional status and quality of life outcomes in patients with major depression.

References:

NR333 Monday, May 21, 3:00 PM - 5:00 PM
Asenapine in Acute Mania: A Randomized, Double-blind, Placebo- and Olanzapine-Controlled Trial (ARES 7501005)
Robert M.A. Hirschfeld, M.D. University of Texas Medical Branch, Department of Psychiatry & Behavioral Science, 301 University Boulevard 1.302RSH, Galveston, TX, 77555-0188, 9000, John Paragides, Ph.D., Larry Alphs, M.D., Miriam Cohen, Ph.D., Scott Lancaster, M.S., Tom Macek

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
1. Describe the effects of asenapine on acute mania symptoms in patients with bipolar I disorder.

2. Compare the effects of asenapine and placebo in acute mania.

Summary:

Background: Asenapine is a novel psychopharmacologic agent in development for the treatment of schizophrenia and bipolar disorder. We assessed the efficacy of asenapine versus placebo in acute mania.

Methods: This multinational study was conducted at 55 centers, including 29 sites in the United States. Adults with a current manic or mixed episode of bipolar I disorder and a Young Mania Rating Scale (YMRS) score ≥20 participated in this double-blind, flexible-dose trial. After a 7-day, single-blind, placebo washout period, patients were randomly assigned to 3 weeks of treatment with asenapine 5 to 10 mg twice daily, olanzapine 5 to 20 mg once daily, or placebo. The primary efficacy endpoint was the change from baseline in the YMRS total score on day 21. Data were analyzed using fixed-effects analysis of covariance, with last observations carried forward for patients not completing the trial.

Results: Of 654 patients screened, 488 took ≥1 dose of study medication (asenapine, n=194; olanzapine, n=190; placebo, n=104). Each treatment group was relatively balanced with respect to sex, race, age, and diagnosis. Mean age in the total sample was 39.4 years; 57% were men, 69% were experiencing a manic episode, and 31% had a mixed episode. Mean daily dosages were 18.2 mg/day for asenapine and 15.8 mg/day for olanzapine. At day 21, both asenapine and olanzapine produced significantly greater improvement than placebo in YMRS total score (-10.8 and -12.6, respectively, vs -5.5; both P<0.0001). The superiority of asenapine and olanzapine over placebo was seen from day 2 (-3.0 and -3.4, respectively, vs -1.5; P<0.008 for asenapine, P<0.001 for olanzapine) and was maintained throughout the study. Asenapine was demonstrated to be safe and well tolerated.

Conclusions: Asenapine is effective and safe in the treatment of acute mania associated with bipolar I disorder.

References:

NR334 Monday, May 21, 3:00 PM - 5:00 PM
Acute, Subacute, and Chronic Brain Metabolic Change with Vagus Nerve Stimulation in Depression
Charles R. Conway, M.D. Saint Louis University, Psychiatry, 1221 South Grand Boulevard, Saint Louis, MO, 63104, 9000, Yvette L. Shelene, M.D., John T. Chibnall, Ph.D., Mark S. George, M.D., Arshad A. Bhatt, M.D., James W. Fletcher, M.D., Mark A. Mintun, M.D.

Educational Objectives:
1. To better understand the acute, subacute, and chronic metabolic brain changes occurring as a result of sustained vagus nerve stimulation in individuals with treatment resistant depression.
2. To begin to understand the chronology of these "evolving" brain metabolic changes and the correlation that these changes have with antidepressant treatment outcomes.
3. To begin to understand the potential mechanism of action of vagus nerve stimulation in the treatment of major depressive disorder.

Summary:

Objective: To determine the metabolic effects of sustained vagus nerve stimulation (VNS) in treatment resistant depression (TRD).

Methods: TRD subjects underwent Fluorodeoxyglucose (FDG) PET scans at baseline and after 3/6-months (n = 8), 12 months (n = 6), and 24 months (n = 4) of VNS. PET images in 3-dimensional mode acquisition were reconstructed using a calculation attenuation factor. Images were summed and mean differences from baseline (t-score > 3.5) determined.

Results: Areas of metabolic change after 3 months of VNS included: right thalamus (activation); bilateral inferior temporal gyrus and fusiform gyrus, bilateral medial orbital gyrus, and left gyrus rectus (deactivation). There were no activations at 6 months; however, there was continued deactivation in the temporal regions (left inferior and medial temporal gyrus) and bilateral fusiform gyri.

At 12 months, deactivation of temporal regions was no longer significant; however, activation of the left posterior orbital region was found. At 24 months, activations were observed for left temporal gyrus, left anterior insula, right anterior insula, left cingulate gyrus, and right medial orbital gyrus. Deactivations were noted in the right parietal lobule, right medial frontal gyrus, left medial frontal gyrus, left inferior frontal gyrus, and left medial orbital gyrus.

An "evolving" pattern of change with added duration of VNS was observed, such that metabolic changes after 3 months of VNS were markedly different in region and degree of change than those noted at subsequent intervals.

Conclusions: VNS was associated with "evolving" changes in brain metabolism. Change occurred in regions along the pathway of the vagus nerve and in regions involved in mood disorder treatment responses for other modalities like ECT and pharmacotherapy. The "middle course" of VNS (3-6 months) appears to involve deactivation of temporal regions, whereas the latter course (12-24 months) appears to involve deactivation of prefrontal regions.

References:

NR335 Monday, May 21, 3:00 PM - 5:00 PM
Seasonality of Psychosis, Aggression and Suicidality in Manic Inpatients
Almir Tavares, Jr., M.D. Universidade Federal de Minas Gerais, Psychiatry, rua dos Otoni, 909/1001, Belo Horizonte, 30150-270, 3510, Fernando M. Volpe, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand that some clinical features of mania present with seasonal distribution. Among inpatients, two aspects of mania, aggression and suicidality, are unevenly distributed along the year, in Belo Horizonte, Brazil. Aggression and suicidality were significantly more frequent in the summer, the former correlating with higher temperatures.

Summary:

Which specific dimensions of mania are susceptible to climatic influences is unresolved. Seasonality of three severe features of manic inpatients (psychosis, aggression and suicidality) were studied and correlated with local climatic variables. Psychosis:
delusions, hallucinations, or loosening of associations (but not flight of ideas). **Suicidality:** desire of dying, suicidal ideas, gestures or attempts. **Aggression:** verbal or physical violence towards objects or others.

We included charts of all consecutive admissions for manic or mixed episodes to a psychiatric hospital in Belo Horizonte (Brazil; 2.3 million inhabitants; latitude 19°35' S and longitude 46°53' O; subtropical mesotropical climate; two seasons: a dry and colder, corresponding to autumn and winter; and a warm and rainy, October to March). A total of 425 manic admissions were grouped into 60 monthly clusters.

Cosinor analysis was utilized: the observed values were adjusted to one or more harmonic sinusoidal curves. If harmonic seasonal distribution was not present, peak months were compared with the rest of the year for each mania feature (chi-square tests).

Seasonal cosinor regressions were not significant: harmonic curves do not adequately fit the data. Significant peaks on January were evidenced from graphic inspection of data and confirmed by chi-square analyses for aggression and suicidality, but not for psychosis.

Grouping peak months for each clinical feature, rates of aggression were significantly higher in January - March (62 and 50%; p=0.007), and suicidality was significantly more frequent in December - January (20 and 10%; p=0.019).

Suicidality significantly correlated to rapidly increasing temperatures. Psychosis correlated positively with number of hours of sunshine of index month and with increasing hours of sunshine, and negatively with relative humidity of index month and with difference from previous to index month. The climatic variables did not correlate with aggression.

**References:**


**Unique Mechanism of Action for the Antidepressant Properties of the Atypical Antipsychotic Quetiapine**

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**Educational Objectives:**

At the conclusion of this presentation, the participants should be able to understand the mechanism of action of quetiapine with regard to its clinical antidepressant effect in bipolar disorder and depressive symptoms associated with schizophrenia and related illnesses.

**Summary:**

**Introduction:** Recent clinical findings have shown that quetiapine has a relatively wide therapeutic index and is highly efficacious in treating depression associated with bipolar disorder without destabilizing mood. It is currently the only atypical antipsychotic approved in the US for the treatment of the symptoms of both bipolar mania and depression. A potential explanation for the unique clinical profile of quetiapine is a combination of direct and indirect pharmacological actions mediated by quetiapine and its principal active human plasma metabolite Nor-quetiapine.

**Methods:** An in vitro pharmacological investigation of the receptor targets for quetiapine and Nor-quetiapine.

**Results:** Quetiapine and Nor-quetiapine interact with multiple neurotransmitter systems but of particular relevance to the antidepressant effects, on norepinephrine and serotonin, where Nor-quetiapine has high affinity and is a potent inhibitor of the noradrenergic transporter (K<sub>i</sub> = 35 nM), and has partial agonist activity at the serotonin 5HT1A receptor. These latter findings are unlike other atypical antipsychotics and suggest the ability of quetiapine, either directly or indirectly, to interact with the three principal neurotransmitter systems affecting mood and psychosis: norepinephrine, serotonin, and dopamine. In addition, the binding kinetics of quetiapine at the dopamine D<sub>2</sub> receptor (rapid on, rapid off) may minimize motor and hormonal side effects often seen with other dopamine blockers.

**Conclusions:** The multiple pharmacological mechanisms of action of quetiapine extend beyond those of other atypical antipsychotics, and reveal several important points of commonality with unimodal antidepressants. This may explain the ability of quetiapine to treat the depressive symptoms associated with bipolar disorder as well as the affective symptoms associated with schizophrenia. An additional benefit of quetiapine over unimodal antidepressants is its concomitant dopamine D<sub>2</sub> antagonism which may act to stabilize mood.

**References:**


patients for index antipsychotic, <1% for multiple antipsychotics, 64% for index antipsychotic plus other psychotropics, and 31% for multiple antipsychotics plus other psychotropics. The Cox PH model revealed that the hazard of discontinuing the index antipsychotic was 71% higher among patients on index antipsychotic plus other psychotropics than in patients on the index antipsychotic only. Differences between other polypharmacy categories were not significant. Hazard ratios for discontinuing index antipsychotic use decreased significantly as dose quartile increased; hazards were 88%, 85%, and 59% that of the lowest quartile for the second, third, and fourth dose quartile, respectively.

Conclusions: Combination of index antipsychotic with other psychotropic medications was common among patients with bipolar disorder but associated with a higher discontinuation hazard compared to monotherapy. Lower antipsychotic dosing was also associated with higher hazards of treatment discontinuation.

Supported by funding from AstraZeneca Pharmaceuticals LP.

References:

NR338 Monday, May 21, 3:00 PM - 5:00 PM
The Efficacy and Safety of L-Methionine, Betaine and Folate in the Treatment of Typical and Atypical Unipolar Depression
Robert T. Dunn, M.D. Cambridge Health Alliance, Psychiatry, 1493 Cambridge Street, Cambridge, MA, 02139, 9000, Vanessa Stan, A.B., Lyvia Chiriki, B.A.

Educational Objectives:
Participants should understand the short-term effects of L-methionine, betaine and folate in the treatment of acute unipolar depression in both typical and atypical patients.

Summary:
Objective: Prior studies suggest that S-adenosylmethionine (SAMe) is effective in the treatment of unipolar depression (1), and that methionine and betaine can increase SAMe in the brain (2). This first prospective study examined the efficacy and safety of the combination of L-methionine, betaine and folate in unipolar depression in both typical and atypical depressed patients.

Method: An open label, prospective, non-randomized, 6-week study of fixed doses of methionine, betaine and folate, was conducted in depressed unipolar outpatients. No other psychotropic medications were allowed. Hamilton Depression Rating Scale (HAM-D) and Beck Depression Inventory (BDI) were administered to evaluate depressive symptoms. Clinical Global Impression Scale (CGI) and Brief Psychiatric Rating Scale (BPRS) were administered to evaluate overall psychiatric symptom severity. Patients were classified with either typical or atypical depression based upon a retrospective review of sleep and appetite symptoms (poor appetite/reduced sleep = typical, increased appetite/hyper-somnia = atypical) at baseline. Preliminary analysis of 13 patients was conducted; full data will be presented.

Results: Psychiatric assessments were obtained for 5 men and 8 women (7 typical, 6 atypical). By ANOVA, scores significantly improved with both 10g and 5g doses of L-methionine on the HAMD (F=0.0003 and F=0.0001) and CGI (F=0.0038 and F<0.0001). BDI scores improved significantly for lower dose patients by ANOVA (F=0.0347) and from baseline to endpoint (t=4.2280, p=0.0242) for the higher dose. Mean termination hCg levels were 22.27umol/L for the 10g group and 13.2umol/L for the 5g group, where the upper reference limit is 15umol/L. Partial or nonresponse to selective serotonin reuptake inhibitors or venlafaxine. J Clin Psychopharmacol 2004; Dec;24:661-4.

Conclusions: The combination of L-methionine, betaine and folate has potential to improve acute unipolar depression in both atypical and typical depression patients. Full data will be presented.

Funding Source: NARSAD

References:
1. Alpert JE, et al: S-adenosyl-L-methionine (SAMe) as an adjunct for resistant major depressive disorder: an open trial following

NR339 Monday, May 21, 3:00 PM - 5:00 PM
The Efficacy and Safety of a Combination Treatment of L-Methionine, Betaine and Folate in the Treatment of Unipolar Depression With Two Different Doses of L-Methionine
Robert T. Dunn, M.D. Cambridge Health Alliance, Psychiatry, 1493 Cambridge Street, Cambridge, MA, 02139, 9000, Vanessa Stan, A.B., Lyvia Chiriki, B.A.

Educational Objectives:
Participants should understand
• the short-term effects of L-methionine, betaine and folate in the treatment of acute unipolar depression
• the efficacy of the combination treatment with two different doses of l-methionine

Summary:
Objective: Prior studies suggest that S-adenosylmethionine (SAMe) is effective in the treatment of unipolar depression (1), and that methionine and betaine can increase SAMe in the brain (2). This prospective study examined the efficacy and safety of the combination of L-methionine, betaine and folate in unipolar depression at two different doses.

Method: An open label, prospective, non-randomized, 6-week study of fixed doses of 5g or 10g methionine, 10g betaine and 5mg folate, was conducted in depressed unipolar outpatients. No other psychotropic medications were allowed. Hamilton Depression Rating Scale (HAM-D) and Beck Depression Inventory (BDI) were administered to evaluate depressive symptoms. Clinical Global Impression Scale (CGI) and Brief Psychiatric Rating Scale (BPRS) evaluated overall psychiatric symptom severity. Homocysteine (hCg) levels were drawn at baseline and endpoint. Following the completion of 5 patients, elevated hCg levels at termination led to a decrease in l-methionine doses from 10g daily to 5g daily. Preliminary analysis of 13 patients was conducted; full data will be presented.

Results: Psychiatric assessments were obtained for 5 men and 8 women (5 at 10g l-methionine, 8 at 5g l-methionine). By ANOVA, scores significantly improved with both 10g and 5g doses of l-methionine on the HAMD (F=0.0003 and F=0.0001) and CGI (F=0.0038 and F<0.0001). BDI scores improved significantly for lower dose patients by ANOVA (F=0.0347) and from baseline to endpoint (t=4.2280, p=0.0242) for the higher dose. Mean termination hCg levels were 22.27umol/L for the 10g group and 13.2umol/L for the 5g group, where the upper reference limit is 15umol/L. Partial or nonresponse to selective serotonin reuptake inhibitors or venlafaxine. J Clin Psychopharmacol 2004; Dec;24:661-4.

Conclusion: The lower dose of L-methionine in the combination treatment of L-methionine, betaine and folate maintained efficacy in the treatment of acute unipolar depression. Additionally, safety of the treatment was improved, with hCg levels within normal range with the lower dose. Full data will be presented.

Funding Source: NARSAD

References:
1. Alpert JE, et al: S-adenosyl-L-methionine (SAMe) as an adjunct for resistant major depressive disorder: an open trial following
partial or nonresponse to selective serotonin reuptake inhibitors or venlafaxine. J Clin Psychopharmacol 2004; Dec;24:661.


NR340 Monday, May 21, 3:00 PM - 5:00 PM
Euthymic But Not Depressed Bipolar II Disorder Patients Have Enhanced Creativity Compared to Healthy Controls

Shelley J. Hill
Stanford University, Psychiatry, 401 Quarry Rd, Rm 2130, Stanford, CA, 94305, 9000, Jennifer Y. Nam, Jenifer Culver, Kristine Keller, Po Wang, Terence A. Ketter

Educational Objectives:
Recognize that among patients with BPII, the presence of syndromal depression may reverse the creativity advantage seen during euthymia.

Summary:
Objective: To explore relationships between acute syndromal depression and creativity in patients with bipolar II disorder (BPII).
Method: Depressed BPII, euthymic BPII, and healthy controls (HC) were assessed with the Barron-Welsh Art Scale (BWAS) and the Beck Depression Inventory (BDI). BWAS total scores and BDI were compared across groups and to one another.
Results: Twenty-five depressed BPII (56% female, mean±SD age 36.4±9.3 years, 28% medicated), 11 euthymic BPII (73% female, mean age 32.4±12.3) did not differ statistically with respect to age and gender, but fewer depressed than euthymic BPII had increased BWAS (31.8±12.0) compared to depressed BPII (20.8±11.6, p < 0.02) and HC (19.7±10.5, p < 0.0001). Euthymic BPII had increased BWAS (31.8±12.0) compared to depressed BPII (20.8±11.6, p < 0.02) and HC (19.7±10.5, p < 0.0005). BWAS tended to correlate inversely with BDI among the 36 BPII (r = -0.273, p < 0.11), but not among the 29 HC (r = 0.155, p = 0.43). Medicated and unmedicated patients had similar BWAS among euthymic BPII (31.1±13.0 vs. 35.0±8.5, p = 0.70) and depressed BPII (22.0±16.0 vs. 20.3±10.0, p = 0.76).
Conclusion: Among patients with BPII, the presence of syndromal depression appeared to reverse the creativity advantage seen during euthymia. These preliminary data need to be considered with caution due to the small sample size and varying medication status of patients.

References:

NR341 Monday, May 21, 3:00 PM - 5:00 PM
Antidepressant Effect on Long-Term Mood Morbidity in Bipolar Disorder

S. Nassir Ghaemi
Emory University, Psychiatry, 1365 Clifton Road, NE, Building B, Suite 6100, Atlanta, GA, 30322, 9000, Rif S. El-Mallakh, Claudia F. Baldassano, Michael J. Ostacher, Megan M. Filkowski, B.A., Vanessa A. Stan, Ross J. Baldessarini
G. S. Sachs

Educational Objectives:
To report interim results of the first long-term randomized clinical trial of antidepressant use in bipolar disorder.

Summary:
Objective: Previous studies suggest that TCAs may worsen the course of bipolar disorder, 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, and this will be the final presentation of the data of a 5 year study.
Method: 69 subjects first recovered from a depressive episode on mood stabilizer plus antidepressant were openly randomized to continue (LT; n=31) or discontinue (ST; n=38) antidepressants (up to 1-year follow-up presented). Primary outcome was total affective morbidity at one year (sum of subscale ratings for mania + depression at follow-up visits) on the Clinical Monitoring Form (CMF; scores: 0 euthymia; 1-6 subsyndromal; >6 syndromal depression or mania; 1 point = 1 DSM-IV mood episode criteria). A questionnaire (rated -2 to +2 each) measuring patient opinion on antidepressant use was administered prior to randomization. Subjects were followed up to 3 years.
Results: LT treatment had no benefit for mood symptoms (CMF difference=0.06 points, 95% CI: -0.15, 0.25). This finding was not altered by statistical adjustment for other variables. Rapid cycling predicted more overall morbidity. Neither depressive nor manic morbidity increased with continued treatment (CMF difference=-0.12 points, 95% CI: -0.48, 0.24, & CMF difference=0.22 points, 95% CI: -0.54, 0.98 respectively, again with no meaningful changes in regression models). There was evidence of more statistically non-significant adjusted depressive morbidity in the RC subgroup with LT antidepressant treatment (CMF=2.18 points, 95% CI: -1.04, 5.40, n=15).
Conclusions: Findings are consistent with non-inferiority of AD discontinuation. After acute recovery with antidepressants for bipolar depression, these randomized data demonstrate no long-term benefit with maintenance antidepressant treatment. Final data will be updated prior to presentation.

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

References:

NR342 Monday, May 21, 3:00 PM - 5:00 PM
Lamotrigine Treatment of Neurotic Excoriatio: An Open-Label Study

Jon E. Grant, M.D. University of Minnesota Medical School, Psychiatry, Department of Psychiatry, 2450 Riverside Avenue, Minneapolis, MN, 55454, 9000, Brian L. Odlaug, B.A., Suck Won Kim, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the clinical characteristics of neurotic excoria and be able to understand the biological basis and treatment response seen using lamotrigine for this disorder.
Summary:

Background: Although a relative common behavioral disorder, treatment data for neurotic excoriation is limited. Because of lamotrigine’s possible effects on glutamate, we hypothesized that lamotrigine would reduce the symptoms of neurotic excoriation.

Method: 24 subjects (19 females [79.2%]; mean age 34.1 ± 12.2 years) with neurotic excoriation were treated in a 12-week open-label trial of lamotrigine, as monotherapy. Lamotrigine dosing ranged from 12.5mg/day to 300mg/day. The primary outcome measure was time per day spent picking. Subjects were also assessed with measures examining the symptoms of neurotic excoriation and psychosocial functioning.

Results: Mean time per day spent picking decreased from 118.1 ± 130.0 to 59.9 ± 115.2 minutes (p<.001). Sixteen subjects (66.7%) were considered “very much improved” or “much improved” in terms of skin picking symptoms. Seven (29.2%) subjects reported no picking at study endpoint. Significant improvement was seen on scales assessing the symptoms of neurotic excoriation and social functioning. Greatest response was achieved after 6 weeks when subjects reached the target dose of 200mg/day.

Conclusions: Lamotrigine was associated with improvements in two-thirds of subjects with neurotic excoriation. Placebo-controlled, double-blind studies are needed to evaluate further the safety and tolerability of lamotrigine in the treatment of this disorder.

References:

NR344  Monday, May 21, 3:00 PM - 5:00 PM
A 12-Month Open-Label Evaluation of Long-Term Safety and Efficacy of Desvenlafaxine Succinate in Outpatients With Major Depressive Disorder
James M. Ferguson, M.D.  University of Utah School of Medicine, Psychiatry, 1611 Federal Heights Drive, Salt Lake City, UT, 84103, 9000, Karen A. Tourian, M.D., Gregory R. Rosas, Ph.D., S. Krishna Padmanaban, M.S., Richard Entsueh, Ph.D.

Educational Objectives:
At the conclusion of this session, participants should understand:
1. The safety and efficacy of desvenlafaxine succinate (DVS) in long-term treatment of adults with major depressive disorder (MDD);
2. The benefits of long-term treatment with DVS in adults with MDD in achieving sustained improvement in depression symptoms and the correlation with enhanced health-related quality-of-life improvements.

Summary:
Objectives: To evaluate the long-term safety (primary) and efficacy (secondary) of DVS.
Methods: This phase 3, multicenter, open-label, flexible-dose study in adult outpatients with MDD, aged 18 to 75 years had comparable demographic and baseline characteristics between safety (N=104) and intent-to-treat (ITT)(n=99) populations. Long-term safety was determined by monitoring adverse events (AEs); patient discontinuation due to AEs; 12-lead ECGs; physical examination; vital signs (body weight, pulse, blood pressure); and laboratory determinations (hematology, blood chemistry, urinalysis). The primary long-term efficacy endpoint was mean HAM-D17 total score.
Results: Most patients took 400 mg/day DVS throughout the study: mean >300 mg from day 15 to 360. The treatment emergent adverse events (TEAEs) were consistent with other SNRI drugs; the most frequent were nausea (n=54, 52%) and headache (n=45, 43%), of mild or moderate severity. Nausea was usually transient,
occuring in the beginning of treatment and resolving within a week. Nine (9%) patients had hypertension during the trial, 1 who discontinued participation. Six subjects reported a serious adverse event (SAE), none of which was considered related to DVS. Mean HAM-D total scores steadily decreased from the baseline mean score of 21.15 by -2.35, -5.27, -8.21, -9.77, and -10.2, at visit 1/day 7 through visit 5/day 60, respectively; thus indicating continuous, sustained improvement in depression. There were no increases in HAM-D total score, and mean change total score from baseline was -9.92 at the final observation (LOCF). Similar trends toward improvement were seen in all secondary efficacy variables, which were clinically significant. Post-hoc analyses of variables of particular interest will be presented.

**Conclusion:** Desvenlafaxine succinate is safe, well tolerated, and effective in relieving depression with long-term use in adults with MDD. Improvements in depression symptoms with long-term use of DVS appear to be sustained and correlate with improvements in health-related quality-of-life measures.

**References:**


**NR345**

**Monday, May 21, 3:00 PM - 5:00 PM**

**Rasagiline Is Safe and Well Tolerated In Parkinson’s Disease (PD) Patients With Levodopa-Related Motor Fluctuations Receiving Serotonin Reuptake Inhibitors (SSRIs)**

Jack J. Chen, Pharm.D. Loma Linda University, Neurology, 11262 Campus Street, West Hall, Loma Linda, CA, 92350, 9000

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to describe the safety of combining rasagiline with a selective serotonin reuptake inhibitor in patients with Parkinson disease

**Summary:**

**Objective:** Interactions between non-selective MAO inhibitors and selective serotonin reuptake inhibitors (SSRIs) can provoke a hyperserotonergic state with mild to serious sequelae, including death. Rasagiline mesylate is a novel, selective, potent, and irreversible MAO-B inhibitor with demonstrated efficacy in PD patients with levodopa-related motor fluctuations (PRESTO and LARGO studies). This evaluation assessed the safety and tolerability of rasagiline treatment in a subset of PRESTO patients who were also receiving an SSRI.

**Method:** PRESTO was a randomized, placebo-controlled, double-blind, multicenter study of once-daily rasagiline 0.5 mg/day, 1 mg/day, or placebo in 472 patients with moderate to advanced PD who were “optimally” treated with levodopa, with or without additional dopaminergic therapy. Patients receiving stable doses of an SSRI (citalopram, sertraline, or paroxetine) before entry could participate. Safety was assessed by adverse event (AE) frequencies and vital signs, and tolerability was assessed by early discontinuation rates.

**Results:** Patients taking SSRIs (SSRI+; n=77) were more likely to be female and were more impaired at baseline as measured by UPDRS score than the remainder of the study cohort (SSRI-; n=395). With the exception of vomiting (5% vs 1%, respectively, p=0.02), there were no significant differences between SSRI+ and SSRI- patients in incidence of AEs, nor were there consistent differences in vital signs between groups. Within the SSRI+ cohort, there were no differences in AE incidences or vital sign changes in patients receiving rasagiline compared with those receiving placebo. Proportions of patients discontinuing the study for any reason or due to an AE did not significantly differ among treatment groups (p=0.85).

**Conclusion:** This study showed no deleterious effects of concomitant SSRI (citalopram, sertraline, or paroxetine) use with rasagiline in patients with advanced PD taking levodopa and other dopaminergic therapies.

**References:**


**NR346**

**Monday, May 21, 3:00 PM - 5:00 PM**

**Impact of CYP2D6 Metabolizer Phenotype on the Safety Profile of Paliperidone-ER**

Fiona Dunbar Janssen-Ortho Inc, Clinical, 19 Greenbelt Drive, Toronto, ON, M3C 1L9, 1220, Pierre Chue, Dong Jing Fu, Qiqing Huang, Monique-andre Franc, Nadine Cohen

**Educational Objectives:**

Genetic variation in metabolic enzymes can affect the pharmacokinetic and adverse event profiles of drugs. Risperidone is metabolized to paliperidone mainly by the CYP2D6 enzyme. CYP2D6 poor metabolizer phenotype has been reported to be associated with a higher rate of risperidone adverse drug reactions (ADRs) and discontinuation due to ADRs. At the conclusion of this presentation participants should recognize that genetic variation might influence response to pharmacological therapy and give consideration to the route of metabolism, genotypic variation and potential impact on ADRs. CYP2D6 poor metabolizer phenotype was determined not to be associated with paliperidone-ER adverse events in this analysis.

**Summary:**

**Objective:** Genetic variation in metabolic enzymes may affect the adverse event (AE) profiles of drugs metabolized by the liver. Pre-clinical studies demonstrate that paliperidone does not undergo significant hepatic metabolism typical of risperidone and many other antipsychotic agents. This study assesses if the CYP2D6 poor metabolizer phenotype is associated with an altered paliperidone extended release (ER) AE profile compared to other metabolizer phenotypes.

**Method:** Data were pooled from three double-blind, randomized, fixed-dose, 6-week, placebo- and active-controlled trials evaluating paliperidone-ER in the treatment of subjects experiencing an acute episode of schizophrenia. The CYP2D6 gene was genotyped for a broad panel of alleles and the metabolizer phenotype was predicted based on the allele combinations observed in each subject. Subjects carrying only non-functional CYP2D6 alleles were characterized as poor metabolizers. The frequency of AEs, serious AEs, discontinuation due to AEs, and extrapyramidal symptoms were compared between the “poor metabolizer” and “other metabolizer” groups in subjects randomized to paliperidone-ER treatment. Two-way cross tabulations were performed for each adverse event category and odds ratios were estimated. Chi-square tests and Fisher’s exact test were carried out to test the presence of a difference in the safety profile between “poor” and “other” CYP2D6 metabolizers.
Results: Of the 619 subjects treated with paliperidone-ER in this dataset, 31 (5%) were CYP2D6 poor metabolizers. The CYP2D6 poor metabolizer phenotype did not increase the odds of having AEs in the 4 adverse event categories examined: total AEs, OR=1.1 (95%CI=0.5 to 2.6, p=0.84); serious AEs, OR=2.1 (95%CI=0.5 to 9.3, p=0.28); discontinuation due to AEs, OR=0.9 (95% CI=0.1 to 6.9, p=1.0); extrapyramidal symptoms, OR=0.6 (95% CI=0.2 to 1.9, p=0.49).

Conclusion: In this study with limited patient numbers, the risk of developing adverse events during paliperidone-ER treatment was similar in CYP2D6 poor metabolizers as compared to all other metabolizer phenotypes.

References:

NR347 Monday, May 21, 3:00 PM - 5:00 PM Reducing Inappropriate Anticholinergic Medication Use
Rathi Mahendran, M.Med. Institute of Mental Health/ Woodbridge Hospital, General Psychiatry, IMH/Woodbridge Hospital, 10, Buangkok View, Singapore, 539747, 5590, Emily LIEW, B.Pharm.

Educational Objectives:
Anticholinergic doses can be safely reduced in schizophrenic patients on long-term antipsychotic medications without recurrence of extrapyramidal side-effects. This also reduces anticholinergic side-effect risks and costs.

Summary:
Anticholinergics (most commonly benzhexol) are often routinely prescribed to counteract side-effects and improve patient compliance. In a review of patients with chronic schizophrenia in a psychiatric hospital in Singapore, 643 out of 1096 (59%) long-stay patients were on maintenance benzhexol treatment and 156 patients (14%) were on doses of 6 mg per day or more. Anticholinergic use is associated with autonomic side-effects and long-term use may predispose patients to tardive dyskinesia or exacerbate tardive dyskinesia in affected patients. Current guidelines (WHO) do not recommend prophylactic anticholinergic use in long-term psychiatric patients. Studies have shown that long-term use is unnecessary and most patients do not experience a recurrence of extrapyramidal side-effects (EPSE) when anticholinergic drug therapy is discontinued after 3 months of administration. 162 patients who consented to participate were examined using the Abnormal Involuntary Movement Scale (AIMS), Barnes Akathisia Scale (BAS), and Simpson-Angus Scale (SAS). Benzhexol was tapered by 1 mg fortnightly. Patients were reassessed weekly for development or recurrence of EPSE.

In all, the total dose administered was reduced from 572 mg to 264 mg (53.9%) over a 6 month period. Benzhexol was successfully discontinued in 13.4% of patients. The largest reductions, a 60% decrease in patient numbers was amongst those patients on doses of 8 mg and above. There was also a 38.5% reduction in those on 6 mg of benzhexol. All reductions were unassociated with development or exacerbation of EPSE.

A subjective assessment of autonomic side-effects revealed that these patients no longer experienced any such side-effects. There was a 100% reduction in Urinary Tract Infection episodes.

Conclusion: Anticholinergic doses can be safely reduced in schizophrenia patients on long-term antipsychotic medications. This reduces anticholinergic side-effect risks and costs.

References:

NR348 Monday, May 21, 3:00 PM - 5:00 PM The Prevalence Rate of Impaired Fasting Glucose and the Usefulness of Fasting Glucose as Screening Test in the Psychiatric Patients Taking Antipsychotics
Jin Hwan Choi, M.D. Yang-San Neuropsychiatric Hospital, Psychiatry, Yang-San neuropsychiatric hospital, Yang-san city, Gyoung Nam province, South Korea, Yang-san, 626-644, 5800

Educational Objectives:
We examined the level of fasting glucose and 2-hour glucose after oral glucose loading of the patients who had been taking typical or atypical antipsychotics, and analyzed the correlation of fasting glucose with 2-hour glucose which is a good predictor of death from cardiovascular disease. At the conclusion of the presentation, the participants should be able to recognize the prevalence of impaired fasting glucose associated with the use of antipsychotics and inappropriateness of the fasting glucose as a screening test of antipsychotic-induced hyperglycemia.

Summary:
Instruction: A lot of studies have suggested an association between antipsychotic medications and diabetes or hyperglycemia. The aim of this study is to examine the prevalence of impaired fasting glucose in patients who are taking typical or atypical antipsychotics, and to analyze the correlation of fasting glucose with 2-hour glucose which is a good predictor of death from cardiovascular disease. Then, we can use glucose level as a screening test of antipsychotic-induced hyperglycemia.

Results: Of the 96 subjects, 86 (90%) were taking antipsychotics, and analyzed the correlation of fasting glucose with 2-hour glucose which is a good predictor of death from cardiovascular disease. We divided the subjects into 2 groups, impaired fasting glucose and normal fasting glucose group, based on fasting blood glucose whose criteria is 50 mg/dl. The basic information of the subjects was obtained through direct interview and from medical records. The subjects with preexisting diabetes mellitus were excluded.

References:
Conclusion: Fasting glucose in patients who are taking antipsychotics could not reflect the cardiovascular risk well. Thus it would not be appropriate to use this as a screening test.

References:


NR349 Monday, May 21, 3:00 PM - 5:00 PM
The Targeted Treatment Depression Inventory (TTDI): Results of a One Year National Pilot Study
Richard J. Metzner, M.D. UCLA, Psychiatry & Biobehavioral Sciences, 916 North Foothill Road, Beverly Hills, CA 90210, 9000, Andrew P. Ho, M.D.

Educational Objectives:

At the conclusion of this presentation participants should be able to: (1) discuss the reliability and validity of the TTDI (2) characterize the usage patterns of professionals who employed the TTDI in its first year of availability and (3) determine appropriate uses of the TTDI in their own work

Summary:

The TTDI is the first depression rating scale designed to guide antidepressant selection. It utilizes an M score to quantify the need for modulation with serotonergic agents, an A score to measure the need for activation with catecholaminergic medications and a D score to represent the level of total depression comparable to the scores of other depression tests. In September, 2005 the TTDI was made available to health professionals online at no cost. Scoring was done using a web-based program that permitted creation of a centralized research database. As of December, 2006 the instrument had been used in 50 practice locations across the United States with 361 patients for a total of 471 administrations. The Zung Self-rating Depression Scale was also offered for scoring online and was concurrently administered with the TTDI on 94 occasions. The first 315 TTDI test administrations were evaluated using the Statistical Package for the Social Sciences (SPSS). The results indicated that both the M and A scales had reliabilities of .777 (standardized Cronbach alpha). Analysis using a three component plot rotated in space revealed the M and A scales to cluster separately as two distinct factors. Interestingly, items related to appetite and sleep did not sort as consistently as other indicators of demodulation and deactivation. Correlation between the Zung scores and all three TTDI measures: M (r=.57), A (r=.48), and D (r=.64) were significant at the P<.01 level. We conclude that the TTDI scales are internally reliable measures of two discrete symptom clusters which separately and together demonstrate convergent validity. Preliminary indications that TTDI scores may also evidence predictive validity for optimizing antidepressant treatment are being further investigated.

References:


NR350 Monday, May 21, 3:00 PM - 5:00 PM
Discontinuation of Risperidone, Olanzapine, and Haloperidol in First Episode Psychosis
Park Se Hyeon, M.D. College of Medicine, Inje University, Psychiatry Dept. Busan Paik Hospital, 633-165 Gaegeum-dong, Busanjin-gu, Busan, 614-735, 5800, Shim Joo Cheol, M.D., Kong Bo Geum, M.D., Choe Byeong Moo, M.D., Deanna L. Kelly, M.D., Robert R. Conley, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that haloperidol treatment was associated with a significantly lower rate of discontinuation than risperidone and olanzapine in first episode patients with schizophrenia. And the participant should be able to note that haloperidol at the doses employed was not associated with higher discontinuation rates as one may expect. The cultural and ethnic factors may directly and indirectly influence this finding.

Summary:

Purpose: We evaluated the discontinuation of risperidone, olanzapine, and haloperidol treatment in first episode psychosis.

Methods: This retrospective chart review study was performed at six sites, located in Busan, Korea. First episode psychosis was defined as having a DSM-IV diagnosis of schizophrenia or schizoaffective disorder, and less than one month of previous antipsychotic drug exposure. After screening records of all patients treated with risperidone, olanzapine, and haloperidol between January 1, 2002 and June 30, 2004, 486 patients were included into this study. Discontinuation of initiated antipsychotic medication was evaluated at 3 month intervals for up to one year.

Results: Among these included 486 patients, 310 patients were initiated on risperidone, 146 patients on olanzapine, and 39 patients on haloperidol. No differences were noted among groups with regard to the composition of age and sex. The mean doses of antipsychotics at the time of discontinuation were 3.2±1.8 mg/day for risperidone, 11.6±5.7 mg/day for olanzapine, 6.5±3.4 mg/day for haloperidol. During treatment with antipsychotics the percent of patients who discontinued at 3, 6, 9 and 12 months were 41.6%, 56.6%, 63.2% and 67.7% respectively. A significant different in the rate of discontinuation was found among drugs, suggesting a lower discontinuation with haloperidol (Log-Rank Chi-Square=6.9, df=2, p=0.049), while pairwise comparisons at each point between drugs did not show significant difference. Overall 21.3% (70/329) of patients discontinued their antipsychotic by one year similar to other studies. Haloperidol was associated with a significantly lower in the rate of discontinuation than risperidone and olanzapine in first episode patients with schizophrenia.

References:


NR351  Monday, May 21, 3:00 PM - 5:00 PM

Antidepressant Treatment Patterns and Related Costs Among U.S. Employees

Howard Birnbaum, Ph.D. Analysis Group, Inc., Analysis Group, Inc., 111 Huntington Avenue 10th floor, Boston, MA, 02199, 9000, Paul E. Greenberg, M.A., Jackson Tang, B.S., Matthew Hsieh, B.A., Eric Wu, Ph.D., Camille Reygrobellet, Pharm.D., Rym Ben-Hamadi, M.S.

Educational Objectives:

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

- Understand the impact of non-stability of treatment patterns on both direct and indirect cost savings
- Evaluate the extent to which patients with major depressive disorder on a stable treatment regimen have a better medical profile (i.e., fewer comorbidities, substance abuse, injuries/accidents, lower urgent care usage) than those on a non-stable treatment regimen

Summary:

Objective: Classify patients treated for depression into treatment stability groups and compare their medical profiles and costs.

Methods: We examined 1999-2004 data from US employers' claims database of 2.9 million beneficiaries. Analysis was restricted to employees, ages 18-64, with >1 diagnosis of major depressive disorder (ICD-9: 296.2x, 296.3x) and >1 prescription filled for selective serotonin reuptake inhibitor, serotonin/norepinephrine reuptake inhibitor, or buproprion, following a 6-month washout period of no prescription of any antidepressant. Patients were classified into stable, intermediate, or non-stable treatment groups based on the number and time of occurrence (first or subsequent 3 months) of the changes in antidepressant treatment pattern over 6 months. Outcomes analyzed included medical profiles (physical/mental comorbidities; substance abuse; injuries/accidents; urgent care use), direct and indirect costs, and depression-related and non-depression related costs. Outcomes were calculated for 6-month pre- and 12-month post-index periods and compared descriptively across treatment groups using Chi-Square tests (for rates) and ANOVA (for costs). For sensitivity analysis, multivariate regressions were performed to further control for baseline characteristics and medical profiles.

Results: Of the 5,225 patients meeting inclusion criteria, 60.8% were in stable, 24.5% in intermediate, and 14.7% in non-stable treatment groups. No statistically significant differences existed in medical profiles and depression-related and non-depression-related costs between the three groups in the 6-month pre-index period. In the 12-month post-index period, patients in the stable group had a less severe medical profile and lower costs compared to intermediate and non-stable groups. Stable group patients generated cost savings of $1,842 compared to intermediate group and $5,231 compared to non-stable group. Patients in the intermediate group yielded savings of $3,389 compared to the non-stable group. Multivariate analysis confirmed these findings.

Conclusion: Non-stability of treatment yields statistically significant increase in both direct and indirect costs.

References:


NR352  Monday, May 21, 3:00 PM - 5:00 PM

Lamotrigine and Valproate: Management of a Safe Combination.

Christine U. Greiner Clinic and Policlinic for Psychiatry of the University of Regensburg, Clinical Pharmacology, Franz-Josef-Strauss Allee 11, Regensburg, 93053, 4280, Markus Wittmann, M.D., Ekkehard Haen

Educational Objectives:

At the conclusion of this poster presentation, the participants should have the information of how to combine two drugs, which are potentially contraindicated, in a way to earn the highest therapeutic benefit and to prevent from severe adverse side effects early rather than to confirm them lately.

Summary:

Introduction: By now 35 psychiatric hospitals cooperate in the working group pharmacotherapy in psychiatric diseases (AGATE) to document serious adverse drug effects of psychoactive substances. Lamotrigine is known as a drug used in the treatment of depression, and bipolar disorders. Concentrations are monitored on a routine base in our hospital. Our laboratory adds a clinical pharmacological comment to the value. This comment relates the concentration not only to effectiveness but also to the dose given to the individual patient. Clinical pharmacological comments thus define nine categories on the basis of three options for the therapeutic (A, B, C) and three for the dose-related reference range (1, 2, 3).

Method: We thus try to identify a patient's risk to develop an adverse drug effect rather than to proof an adverse drug effect (ADE) after it occurred. 457 blood specimens sent to our laboratory for quantitative lamotrigine analysis.

Results: Lamotrigine coadministered with valproate illustrates concentrations often too high in relation to the dose given. Valproate was concomitantly given in 63 (13.8%) of the 457 lamotrigine specimens. In 53 (84.1%) of these samples lamotrigine concentrations were detected too high in relation to the lamotrigine dose administered. Only 8 (12.7%) patients, who received both, lamotrigine and valproate, showed concentrations matching the dose, whereas 2 (3.2%) serum samples revealed concentrations too low in relation to the given dose.

Conclusion: Dose-related reference ranges have to be established for each substance, deriving from pharmacokinetic data. We therefore suggest, that one can predict a patients' risk for developing ADE from the nine-field table: specimens in category A3 and B3 are supposed to show disproportional rise in serum concentration, while increase of the dose is moderate. Therefore severe side effects associated with serum concentrations above the therapeutic reference range of the drug can be avoided early.

References:

2. Faught, E; Morris, G; Jacobson, M; French, J; Harden, C; Montours, G; Rosenfeld, W. Adding lamotrigine to valproate: incidence of rash and other adverse effects. Epilepsia 1999; 40(8), 1135-1140.

NR353  Monday, May 21, 3:00 PM - 5:00 PM

The Efficacy of Topiramate for Weight Loss and Psychiatric Symptom Severity in Overweight or Obese Patients Maintained on Atypical Antipsychotics

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Ewha Womans University Dong Dae Mun Hospital, 70, Chongro-e-ka, Chongro-ku, SEOUL, 110-783, 5800, Yu Mi Sung, M.D., Kyoung Won Paik, M.D., Kyu Wol Yun, M.D., Young Chul Kim, M.D., Weonjeong Lim, M.D.

**Educational Objectives:**

We intended to evaluate the efficacy of topiramate for weight loss and psychiatric symptom severity in overweight or obese patients maintained on psychotropic medications. We also aimed to evaluate that the higher dosage of topiramate is more effective for weight reduction and symptom improvement.

**Summary:**

**Purpose:** Psychiatric patients usually have medicated atypical antipsychotic agents. Weight gain is common while on that agents. It is well recognized that weight gain secondary to antipsychotics will be accompanied by increase in related disorder such as diabetes, hypertension and coronary heart disease. Topiramate is a new antiepileptic drug and is associated with weight loss induced by psychotropic medications. The purpose of this study was to evaluate the efficacy of topiramate for weight loss and psychiatric symptom severity in overweight or obese patients maintained on atypical antipsychotics. The study also aimed to evaluate that the higher dosage of topiramate is more effective.

**Methods:** Fifty three overweight or obese individuals who had started atypical antipsychotics in the previous 6 months were recruited in the Department of Psychiatry at Ewha Womans University Dongdaemun Hospital from September, 2005 to February, 2006. Subjects were randomized to receive either 50mg (n=21), 100mg (n=13), 150mg (n=9) or 200mg (n=10) of topiramate daily for 8 weeks. They were diagnosed with schizophrenia, schizoaffective disorder or organic psychotic disorder according to the DSM-IV. Weight, body mass index (BMI), total cholesterol, triglyceride, glucose level and the Clinical Global Impression Severity (CGI-S) Scale score were collected at baseline and endpoint (at 8 week). The weight-loss effect and the psychiatric symptom improvement effect of topiramate at different dosage were analyzed using one-way ANOVA (SPSS 11.0).

**Results:** By 8 weeks, all groups experienced significant weight loss and decrease in psychiatric symptom severity score. Weight loss and symptom improvement were not significantly different according to the topiramate dosage.

**Conclusion:** We conclude that the weight of psychiatric patients whose weight gain is due to atypical antipsychotics was controlled by topiramate with improvement of psychiatric symptom. Because the lower dose was clinically effective in producing weight loss and symptom improvement, it would seem that the lower dose warrants further clinical evaluation.

**References:**


**NR354 Monday, May 21, 3:00 PM - 5:00 PM**

**Effects of Ziprasidone on the Immobilization Stress-Induced BDNF mRNA Expression in Rat Brain**

Young Hoon Kim, M.D. School of Medicine and Paik Institute for Clinical Research, Inje University, Psychiatry, Gaegeum-Dong 633-165 Bunji, Busanjin - Gu., Busan, 614-735, 5800, Jung Goo Lee, M.D., Chan Hong Lee, M.S., Sung Woo Park, Ph.D.

**Educational Objectives:**

Antipsychotic drugs can alter the brain levels of neurotrophins may also indicate the neurotrophins play a role in pathogenesis of schizophrenia. This study aimed to investigate the effects of chronic ziprasidone administration on the BDNF mRNA expression in rat hippocampus. At the conclusion of this presentation, the participant should able to demonstrate that ziprasidone has neuroprotective effect and this effect may be related to its antipsychotic effect in patients with schizophrenia.

**Summary:**

Neurotrophins are known to play an important role in the survival, differentiation, and maintenance of developing and in the formation of synaptic circuitry in the brain. Antipsychotic drugs can alter the brain levels of neurotrophins and may also indicate the neurotrophins play a role in pathogenesis of schizophrenia. Long-term treatment with atypical antipsychotics is known to be correlated with an improvement of cognition in the schizophrenia patients. Ziprasidone is a recently introduced atypical antipsychotic drug that exhibits functional antagonism at dopamine and serotonin receptors. This study aimed to investigate the effects of chronic ziprasidone administration on the BDNF mRNA expression in hippocampus. We used in situ hybridization to examine in rats the effects of chronic administration of ziprasidone on chronic immobilization stress-induced changes in gene transcription. Repeated immobilization stress (2 hr daily for 3 weeks) (p<0.05) and chronic haloperidol (1.0mg) (p<0.01) treatment alone decreased mRNA level of brain-derived neurotrophic factor (BDNF) in rat hippocampus. Chronic ziprasidone (2.5mg) treatment (daily for 3 weeks) alone not significantly increased BDNF mRNA expression in the hippocampus when compared to controls. But chronic administration of ziprasidone markedly increased the stress-induced decrease in BDNF mRNA (p<0.01). These results suggest that ziprasidone has neuroprotective effect in schizophrenia and this effect may be related to its antipsychotic effect in patients with schizophrenia.

**References:**


**NR355 Monday, May 21, 3:00 PM - 5:00 PM**

**Fluoxetine Reduces the Expression of Heat Shock Protein 70 in Rat C6 Glioma Cells**

Jun-Seok Lee, M.D. Kwandong University Myongji Hospital, Department of Psychiatry, 697-24 Hwajung-Dong Dukyang-Gu, Goyang, 412-270, 5800, Byung-Hwan Yang, M.D.

**Educational Objectives:**

70kDa heat shock protein (HSP70) is up-regulated by adrenergic-corticotropic hormone and different stress conditions in the brain. Thus, the expression of HSP70 is known to be a sensitive indicator of the damage to the neural cell. This study investigated the influence of fluoxetine on HSP70 expression and the modulatory effect of fluoxetine on dexamethasone-induced HSP70 expression in C6 glioma cells. At the conclusion of this study, prolonged treatment with fluoxetine reduces HSP70 expression in C6 glioma cells. This result might suggest that fluoxetine improves stress tolerance and acclimatization in a stressful condition induced by dexamethasone.
Objective: 70kDa heat shock protein (HSP70) is up-regulated by adrenocorticotrophic hormone and different stress conditions in the brain, such as hypoxia, ischemia, and exposure to toxic compounds. Thus, the expression of HSP70 is known to be a sensitive indicator of the damage to the neural cell. This study investigated the influence of fluoxetine on HSP70 expression and the modulatory effect of fluoxetine on dexamethasone-induced HSP70 expression in C6 glioma cells.

Methods: The expression of HSP70 was investigated in rat C6 glioma cells. There were 4 different subject groups; 1) those treated with dexamethasone (10 μM) only, 2) those treated fluoxetine (10 μM) only, 3) those treated simultaneously with fluoxetine and dexamethasone, and 4) those treated with dexamethasone after fluoxetine pretreatment. Each group was treated and monitored at 1, 6, 24, and 72 hours. Crude extracts from control, dexamethasone, and fluoxetine-treated C6 glioma cells were separated on a 10% SDS-PAGE and probed with anti-HSP70 mAb.

Results: 1) The expression of HSP70 in the “dexamethasone only” treated group did not change.

2) The expression of HSP70 in the “fluoxetine only” treated group decreased with time and reached the lowest point in 72 hours (p = 0.01).

3) The expression of HSP70 in the group “treated simultaneously with fluoxetine and dexamethasone” decreased with time and reached the lowest point in 72 hours. (p = 0.03).

4) For the groups treated with “dexamethasone after a fluoxetine pretreatment” showed a significant decrease of the expression of HSP70 compared to the control group at 24 hours (p = 0.01) and 72 hours (p = 0.02).

Conclusion: Prolonged treatment with fluoxetine reduces HSP70 expression in C6 glioma cells. This result might suggest that fluoxetine improves stress tolerance and acculturization in a stressful condition induced by dexamethasone.

References:


Summary:

Objective: Significant decrease in recurrent distressing dreams item, B, C, D symptom score and total CAPS score at baseline, 4-week, and 8-week treatment compared to baseline(recurrent distressing dreams item: 2.70±1.88 and 1.25±1.49; B, C, D symptom score: 2.30±2.49, 1.20±1.05, 3.10±1.68, and 4.00±3.59, 1.55±1.50, 6.50±1.50, 3.23; overall CAPS score: 8.20±6.26 and 5.40±5.89). There were significant correlation between dosage of terazocin and improvement of PTSD symptoms. Adverse effects such as fatigue and orthostatic hypotension were showed, which were mild and self-limited.

Conclusion: These results suggest that terazocin improve severe trauma-related nightmares and overall PTSD symptoms. Randomized controlled study with more subjects would be necessary in the near future.

References:

10.7±5.1, p=0.8), on the proportion of subjects maintaining baseline improvement (CGI-I≤2, 58% vs. 63%, p=0.8), or the proportion maintaining baseline tolerability (no impairing adverse effects, 58% vs. 41%, p=0.3). However, the IR-MPH group missed more doses (7.3±6.8 vs. 3.3±4.2, p=0.02) and was less likely to be fully compliant (17% vs. 46%, p=0.07) than the OROS-MPH group.

Conclusion: These data extend the small head-to-head literature of different MPH formulations suggesting similar efficacy, but is the first to demonstrate better compliance with OROS-MPH than IR-MPH treatment. Considering the increased risk of abuse potential or diversion of immediate release MPH relative to the OROS formulation, these findings may have important public health and safety implications.

References:

NR358 Monday, May 21, 3:00 PM - 5:00 PM
Randomized Double-Blind Study of Methylphenidate in ADHD Adults with and without Comorbid Depression or Anxiety Disorders
Joseph Biederman, M.D. Massachusetts General Hospital, Pediatric Psychopharmacology, 55 Fruit Street, Warren Building 705, Boston, MA, 02114, 9000, Eric Mick, Thomas J. Spencer

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand more about impact of psychiatric comorbidity and concomitant use of serotonergic uptake inhibitors (SRI) on the efficacy of an extended release formulation of methylphenidate in adults with ADHD.

Summary:
Objective: The main aim of this study was to examine the impact of psychiatric comorbidity and concomitant use of serotonergic uptake inhibitors (SRI) on the efficacy of an extended release formulation of methylphenidate in adults with ADHD.
Methods: Subjects were outpatient adults satisfying full diagnostic criteria for DSM-IV ADHD randomized (1:1) to 6 weeks of treatment with OROS®-MPH or placebo. Subjects with a lifetime history of psychiatric comorbidity (no active symptoms) or subjects treated for anxiety disorders and depression on a stable medication regimen for at least three months were allowed in the study. Subjects were assessed with the Adult ADHD Investigator System Report Scale (AISRS), and the Hamilton ratings of anxiety (HAM-A) and depression (HAM-D). All procedures were approved by the Human Research Committee.
Results: One hundred-eighty-two ADHD adults (36.1±9.0 years, 55% Male, AISRS Score 28.5±5.8) were randomized to either OROS-MPH (N=89, 81.2±31.0 mg) or placebo (N=93, 97.9±27.4mg). At endpoint, OROS-MPH treated subjects had significantly greater reduction in AISRS score than placebo treated subjects (-14.5±10.8 vs. -9.2±9.6, p=0.0006). Twelve percent (N=21) of the sample was being treated with an SRI at baseline and an additional 43% (N=78) had a lifetime history of comorbid depression or anxiety. Due to inclusion criteria, however, neither of these groups was elevated on the HAM-A (4.2±3.7 and 3.9±2.5) or HAM-D (5.1±4.6 and 4.8±3.8). Stratification of the sample by comorbidity and SRI use indicated no statistically significant difference in the magnitude of ADHD response (p=0.8) or tolerability (p=0.8).
Conclusion: These data demonstrate the efficacy of MPH in treating ADHD symptoms in adults and suggest that this efficacy is not accounted for or moderated by a history of comorbid depression or anxiety. Furthermore, these results suggest that concurrent SRI therapy does not interfere with the efficacy of MPH in the treatment of adults with ADHD.

References:
NR360 Monday, May 21, 3:00 PM - 5:00 PM
Assessing Tachyphylaxis During the Prevention of Recurrent Episodes of Depression with Venlafaxine XR for Two Years (PREVENT) Study
Anthony J. Rothschild, M.D. University of Massachusetts Medical School and UMass Memorial Healthcare, Department of Psychiatry, 361 Plantation Street, Worcester, MA, 01605, 9000, Boadie W. Dunlop, M.D., David L. Dunner, M.D., Edward S. Friedman, M.D., Alan J. Gelberg, M.D., Peter Holland, M.D., James H. Kocsis, M.D.

Educational Objectives:
At the conclusion of this session, participants should be better able to:
1. More clearly understand the phenomenon of antidepressant tachyphylaxis.
2. Be able to identify risk factors for tachyphylaxis in patients receiving long-term antidepressant treatment.

Summary:

Objective: Assess the occurrence and predictors of tachyphylaxis in patients receiving maintenance therapy with venlafaxine XR, fluoxetine, or placebo.

Methods: These data were collected from a multi-phased, double-blind, placebo-controlled clinical trial designed to assess the efficacy of venlafaxine XR across 2 years of maintenance treatment in patients with a history of recurrent major depressive disorder (MDD). The primary outcome for this analysis was the cumulative probability of tachyphylaxis in patients receiving venlafaxine XR, fluoxetine, or placebo at the end of each year of maintenance treatment. Tachyphylaxis was defined as a Rothschild Scale for Tachyphylaxis score >7 in patients with a prior satisfactory therapeutic response and not experiencing a recurrence of MDD prior to or concurrent with tachyphylaxis. Kaplan-Meier survival analysis was used to determine time to tachyphylaxis. Baseline characteristic data (e.g., age, gender, ethnic origin, body mass index, weight, duration of current episode) were used to identify predictors of tachyphylaxis.

Results: The year 1 population consisted of 292 patients (venlafaxine XR [n=114], fluoxetine [n=72], and placebo [n=106]); 114 patients (venlafaxine XR [n=43], fluoxetine [n=43], and placebo [n=28]) were treated during year 2 of treatment. The rates of tachyphylaxis across all treatment groups during years 1 and 2 were 48.6% and 40.4%. Kaplan-Meier estimates of the probability of tachyphylaxis did not differ significantly between treatment groups during either year. Of the patient characteristics assessed, age was found to be a significant predictor of tachyphylaxis. The mean age of those patients experiencing tachyphylaxis (year 1: 43.1; year 2: 45.7) was significantly greater (P<0.001) than those who did not (year 1: 38.2; year 2: 38.8).

Conclusions: In this analysis there were no significant treatment differences in the probability of tachyphylaxis among patients receiving venlafaxine XR, fluoxetine, or placebo. Older age was predictive of a higher risk for tachyphylaxis in this patient population.

References:

NR361 Monday, May 21, 3:00 PM - 5:00 PM
Effect of Risperidone Dose on Prolactin Secretion in Psychotic Adolescents: Relationships Between Plasma Risperidone and 9-Hydroxyrisperidone Concentrations
Fabrice Duval Centre Hospitalier, Psychiatry, 27 Rue du 4eme RSM, Rouffach, 68250, 4279, Marie-Sabine Guillou, Marie-Claude Mokrani, Marc-Antoine Crocq, Nessim Chokmani, Jun He, Jean-Paul Macher

Educational Objectives:
At the end of this presentation the participant should be able to understand why antipsychotic-induced hyperprolactinaemia should become a focus of interest in the drug treatment of psychiatric patients, especially in adolescents.

Summary:

Background: Evidence on safety of atypical antipsychotics in adolescents is limited. In contrast to other atypicals, treatment with risperidone can result in a sustained elevated prolactin (PRL) level leading possibly to sexual dysfunction, hypogonadism and osteoporosis. To date, the relationships between plasma concentrations of PRL, risperidone (RIS) and its active 9-hydroxy-metabolite (9-OH-RIS) in psychotic adolescents have been little investigated.

Method: PRL levels were determined at baseline in 16 hospitalized drug-naive adolescents (aged 14 to 18 years; mean age[SEM]: 15.7[0.3] years; 8 female, 10 male) meeting the DSM-IV criteria for schizophreniaform disorder. PRL, RIS, 9-OH-RIS levels were subsequently determined after 4 weeks of oral risperidone treatment (mean dose: 2.9[0.3] mg daily; range: 1 to 6 mg). The design of the study was open and risperidone dosage could be adjusted individually according to clinical response. The side effects were evaluated using the Udvalg for Kliniske Undersøgelser (UKU) scale.

Results: Risperidone induced hyperprolactinemia (day 0: 22[2] ng/ml; day 21: 66[6] ng/ml; p<0.00001). PRL levels were correlated with risperidone doses (r=0.58; p<0.02), RIS (r=0.60; p<0.02) and 9-OH-RIS plasma levels (r=0.54; p<0.03). Risperidone doses were correlated with RIS (r=0.81; p<0.0002) and 9-OH-RIS (r=0.76; p<0.0006) plasma levels. Sexual side effects were mild and no patient required antiparkinsonian medications.

Conclusion: These data suggest that the risperidone's effect on PRL release is dose-dependent. In order to reduce some potentially negative long-term effects in this population of patients, determining the minimum effective dose of risperidone in each individual appears crucial.

References:
NR362  Monday, May 21, 3:00 PM - 5:00 PM
A Placebo-Controlled Trial of the NR2B Specific NMDA Antagonist CP-101,606 Plus Paroxetine for Treatment Resistant Depression (TRD)
Sheldon Preskorn, M.D. Clinical Research Institute, Research, 201 S. Hillside, Wichita, KS, 67211, 9000, Bryan Baker, M.S., Kelli Onno, R.N., Sheela Kolluri, Ph.D., Frank Menniti, Ph.D., Jaren Landen, Ph.D.

Educational Objectives:
- At the conclusion of this presentation, the participant will know about the NR2B specific NMDA antagonist CP-101,606 and understand its potential implications for the treatment of refractory depression.

Summary:
Background and objective: Preclinical and clinical studies using the nonselective NMDA antagonist ketamine suggest that directly targeting the NMDA receptor complex may bring about rapid and relatively sustained antidepressant effects. The objective of the current study was to examine the effects of an NR2B selective NMDA receptor antagonist CP-101,606.

Methodology: The study employed a double-blind, randomized, placebo-controlled parallel group design. Subjects meeting DSM-IV criteria for recurrent major depression were treated with open label paroxetine, 40 mg/day for six weeks. After 3 weeks of paroxetine treatment, subjects were admitted to the research unit and received a single-blind continuous placebo infusion. At week 6, non-responders were continued on paroxetine and re-admitted to receive either a second placebo infusion (n = 15) or a matching infusion of CP-101,606 (n=15). 4/7 initial subjects reported a mild or moderate dissociative state; thus, the infusion dose and duration were reduced for the remaining subjects (first 7 subjects received 0.75 mg/kg/hr for 1.5 hours followed by 0.15 mg/kg/hr for 6.5 hours or matching placebo; final 23 subjects 0.5 mg/kg/hr for 1.5 hours or matching placebo). Paroxetine was continued up to 4 weeks after the second infusion. Depressive Symptom severity was assessed using the MADRS and HAMD.

Results: CP-101-606 infusion produced statistically significant improvement in depressive symptoms on both MADRS and HAMD on days 5 and 8 (difference between CP-101,606- placebo Day 5 MADRS was -8.4 (80% CI: [-12.3, -4.5]) Average reduction in symptom severity was approximately two times greater in active versus the placebo-treated patients. Dissociative symptoms produced by the active infusion were generally modest and resolved within 8 hours.

Conclusion: NR2B selective NMDA glutamate receptor antagonism may produce meaningful, rapid and sustained improvement in patients with TRD.

References:

NR363  Monday, May 21, 3:00 PM - 5:00 PM
Switch From Venlafaxine to Desvenlafaxine Succinate is Well Tolerated in Patients With Major Depressive Disorder
Saeed Ahmed, M.D. Wyeth Research, Global Therapeutic Area Director, 500 Arcola Road, Collegeville, PA, 19426, 9000,

Brook Zitek, D.O., Philip T. Ninan, M.D., Bruno Pitrosky, Ph.D., Gregory Rosas, Ph.D., Qin Jiang, M.S., Raj Tummalra, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to:
  - Understand differences in tolerability between treatment-naive and treatment-experienced patients.
  - Assess the effect of previous treatment on incidence of TEAEs.
  - Discuss the implications of previous antidepressant treatment when prescribing a drug for the treatment of depression.

Summary:
Objective: To examine differences in tolerability in patients with major depressive disorder (MDD) who switched from venlafaxine extended-release (XR) to desvenlafaxine succinate (DVS) compared to patients who switched from placebo to DVS.

Methods: Outpatients with Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition MDD who had completed either of 2 previous double-blind, 8-week acute studies (in which they were randomized to treatment with DVS, venlafaxine XR, or placebo) were given the option to enroll in a 10-month, open-label extension study, receiving DVS treatment starting at 200 mg/d. Tolerability in the first month was assessed after switch to DVS in the open-label extension study for "treatment-naive" patients (those switching from placebo to DVS) and "treatment-experienced" patients (those switching from venlafaxine XR to DVS).

Rates of nausea, treatment-emergent adverse events (TEAEs), and discontinuation were compared between treatment groups using Fisher’s exact test.

Results: Patients previously treated with placebo (n=186, PBO/DVS) and patients previously treated with venlafaxine XR (n=183, VEN/DVS) entered the open-label extension study. Incidence rates of nausea in week 1 were 35% for the PBO/DVS group and 4% for the VEN/DVS group (P<0.001). By week 2, the incidence had decreased to 3% PBO/DVS and 0% VEN/DVS (P=0.03). Rates in the day 15-30 interval did not differ significantly between the groups (2% for both). A similar pattern was observed for overall TEAEs as well as discontinuation rates due to TEAEs. A total of 9% of the PBO/DVS patients discontinued due to TEAEs in the first week vs 1% in the VEN/DVS group.

Conclusion: The more favorable adverse event profile and lower discontinuation rate due to TEAEs in patients who switched from venlafaxine XR to DVS compared to patients who switched from placebo to DVS suggests that switching from venlafaxine XR to DVS can be achieved with minimal tolerability problems.

References:
Educational Objectives:
At the conclusion of this presentation on weight change associated with short- and longer-term treatment with DVS, the participant should be able to:
- Recognize the potential for weight changes with DVS and placebo during short- and longer-term treatment of patients with MDD.
- Understand the incidence of potentially clinically important weight change.
- Assess the significance of potentially clinically important weight gain with DVS.

Summary:
Objective: To characterize weight change with short- and longer-term treatment with desvenlafaxine succinate (DVS) in patients with major depressive disorder (MDD).
Methodology: Data from 7 short-term, double-blind, placebo-controlled studies and 1 longer-term relapse prevention trial were analyzed. Adult outpatients with DSM-IV MDD received DVS or placebo for 8 weeks in the short-term studies. In the longer-term study, responders to 12 weeks of open-label DVS treatment were randomized to double-blind treatment with DVS or placebo for 6 months. Mean weight changes and the incidence of potentially clinically important changes (±7% from baseline) were evaluated.
Results: In the short-term studies, 2014 patients (DVS: n=1211; placebo: n=803) comprised the overall safety population. In the relapse prevention study, 594 patients received open-label treatment with DVS; 375 patients progressed to the double-blind relapse-prevention phase (DVS: n=190; placebo: n=185). Small but statistically significant decreases from baseline in mean body weight occurred during short-term treatment with DVS (-1.0 kg DVS vs +0.1 kg placebo; P<0.001). Less than 1% of DVS-treated patients experienced a potentially clinically important weight gain. There was no clear indication of dose response for this effect. Likewise, during the relapse prevention study, small but statistically significant mean decreases from baseline for weight (-0.8 kg) occurred in the 12-week open-label phase. Throughout the course of the 6-month, double-blind, placebo-controlled relapse prevention phase, small mean increases in weight were observed with both DVS and placebo. The final on-therapy change in weight with DVS across the total exposure period was similar to placebo; the DVS, but not placebo, change was significantly different from baseline. Both groups had <1 kg increases from baseline at the final on-therapy evaluation (no significant difference between DVS and placebo).
Conclusion: Persistent weight gains or losses were not observed in patients administered DVS in short and longer-term treatment.

References:

NR365 Monday, May 21, 3:00 PM - 5:00 PM
Treating the Painful Physical Symptoms of Depression with Desvenlafaxine Succinate Versus Placebo in Depressed Outpatients

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
- Identify DVS as a potentially effective treatment for the painful physical symptoms of depression.
- Understand the patterns of improvement for the individual VAS items in depressed outpatients treated with DVS.

Summary:
Objective: To evaluate the clinical effect of desvenlafaxine succinate (DVS), a novel serotonin-norepinephrine reuptake inhibitor (SNRI), in the treatment of symptoms of anxiety, using the full set

NR366 Monday, May 21, 3:00 PM - 5:00 PM
Improvement of Anxiety Symptoms in Patients With Major Depressive Disorder Treated With Desvenlafaxine Succinate: A Pooled Analysis
Karen A. Tourian, M.D. Wyeth Research, Director, Clinical Research and Development, Neuroscience, 500 Arcola Road, Collegeville, PA, 19426, 9000, Saeed Ahmed, M.D., Albena Patroneva, M.D., Brook Zitek, D.O., Jay Graepel, Ph.D., Bruno Pitrosky, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
- Recognize the potential for weight changes with DVS and placebo on the stomach pain item did not reach statistical significance (P=0.617). Patients with baseline VAS-PI overall pain scores >30 also experienced significantly greater improvements in overall pain compared with placebo (P<0.001) at week 8.

Conclusions: DVS improves the painful physical symptoms associated with MDD.

References:

NR366 Monday, May 21, 3:00 PM - 5:00 PM
Improvement of Anxiety Symptoms in Patients With Major Depressive Disorder Treated With Desvenlafaxine Succinate: A Pooled Analysis
Karen A. Tourian, M.D. Wyeth Research, Director, Clinical Research and Development, Neuroscience, 500 Arcola Road, Collegeville, PA, 19426, 9000, Saeed Ahmed, M.D., Albena Patroneva, M.D., Brook Zitek, D.O., Jay Graepel, Ph.D., Bruno Pitrosky, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
- Identify DVS as a potentially effective treatment for the painful physical symptoms of depression.
- Understand the patterns of improvement for the individual VAS items in depressed outpatients treated with DVS.

Summary:
Objective: To analyze pain symptom data in patients with major depressive disorder (MDD) treated with desvenlafaxine succinate (DVS) or placebo.
Methods: Data from 6 double-blind, placebo-controlled DVS clinical trials were pooled for this analysis. Patients with MDD were assessed using the overall pain and individual pain items of the Visual Analog Scale-Pain Intensity (VAS-PI). A secondary analysis of patients with baseline VAS-PI overall pain scores >30 was also conducted.
Results: Patients treated with DVS 100-400mg/day (N=1048) and placebo (N=718) were included in this analysis. The change from baseline on VAS-PI overall pain for the total population was significantly greater in the DVS group compared with the placebo group (P<0.001) at week 8. DVS-treated patients experienced significant improvements on the back, chest, and arms, legs and joint individual items of the VAS-PI (P<0.001). Significant improvements on the overall pain and individual item scores began at week 2 and continued until study completion. The difference from placebo on the stomach pain item did not reach statistical significance (P=0.617). Patients with baseline VAS-PI overall pain scores >30 also experienced significantly greater improvements in overall pain compared with placebo (P<0.001) at week 8.

Conclusions: DVS improves the painful physical symptoms associated with MDD.
of short-term, randomized, controlled trials conducted in patients with major depressive disorder (MDD).

Methods: The efficacy of DVS in treatment of MDD was evaluated in 7 randomized, double-blind, placebo-controlled, 8-week trials. All studies enrolled adult outpatients with Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition MDD. Patients were excluded if an anxiety disorder was the primary diagnosis. Eligible patients were randomly assigned to DVS (n=1186), at doses ranging from 100 mg/d to 400 mg/d, or placebo (n=797) for 8 weeks. The primary efficacy outcomes measured in this pooled analysis were the 17-item Hamilton Rating Scale for Depression (HAM-D17) item 10 (Anxiety/Psychic) and the Covi Anxiety total score. The Covi Anxiety scale was measured in 6 of the 7 trials. Patients with a Covi Anxiety score >9 or whose Covi score exceeded their Raskin Depression total score were excluded from study enrollment. Changes from baseline were analyzed using a mixed-effects model for repeated measures (MMRM) analysis, which included the fixed, categorical effects of treatment, protocol, visit, and the treatment-by-visit interaction, as well as the continuous, fixed covariate of baseline score. Secondary analyses evaluated changes from baseline to end point using analysis of covariance (ANCOVA) using last-observation-carried-forward (LOCF) and observed cases (OC) analyses.

Results: Improvement from baseline at week 8, the study end point, was significantly greater for the DVS group than for the placebo group on both the HAM-D17 Anxiety/Psychic item and Covi Anxiety total scores in both the MMRM and ANCOVA (LOCF and OC) analyses.

Conclusion: In this pooled analysis, DVS was significantly superior to placebo in the treatment of anxiety symptoms associated with depression.

References:

NR367
Monday, May 21, 3:00 PM - 5:00 PM
Sexual Abuse, Health Status and Treatment Response to Paroxetine Controlled Release (CR) in Fibromyalgia
Ashwin A. Patkar, M.D. Duke University, Psychiatry and Behavioral Sciences, 2218 Elder St, Box DUMC 3419, Durham, NC, 27705, 9000, Kathleen Peindl, Ph.D., Stan Kruliewicz, Paolo Mannelli, M.D., Chi-Un Pae, M.D., Prakash S. Masand, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the clinical implications of history of sexual abuse in patients with fibromyalgia, in particular its relationship with health status and treatment response.

Summary:
Objective: We investigated whether history of sexual abuse was associated with measures of health status and response to treatment in a double blind, randomized, placebo controlled trial of paroxetine controlled release (CR) in fibromyalgia. We hypothesized that sexual abuse will be associated with poor treatment response.
Method: 116 subjects were randomized to receive paroxetine CR (dose 12.5-62.5 mg/day) or placebo for 12 weeks. Subject selection was independent of abuse history. Patients with current depressive or anxiety disorders were excluded. History of Sexual abuse was recorded using the Sexual and Physical Abuse Questionnaire. Health Status was determined using the SF-36 and the Sheehan Disability Scale (SDS). Symptom severity was determined using the Fibromyalgia Impact Questionnaire (FIQ) and the Visual Analogue Scale for Pain (VAQ). Treatment response was defined as ≥ 25% reduction in (FIQ) from randomization to end of treatment.

Results: About 95% of the subjects were women. The rate of reported sexual abuse was 44.3%. Subjects reporting sexual abuse had higher scores on the SF-36 (p=.017), the SDS (p=.017) and the VAS for pain (p=.023), but not on the FIQ (p=.42) compared to those without such history. In logistic regression, the paroxetine CR group was significantly associated with treatment response (O.R.= 2.51, C.I.= 1.12-5.64, p=0.02), however, history of sexual abuse was not related to response (O.R.=1.16, C.I.= 1.18-1.60, p=0.35).

Conclusions: A significant proportion of patients with fibromyalgia report a history of sexual abuse. While history of sexual abuse appears to be related with greater impairment in health status and higher ratings of pain, contrary to our expectations, response to paroxetine CR in fibromyalgia was unrelated to history of sexual abuse.

References:

NR368
Monday, May 21, 3:00 PM - 5:00 PM
Effects on Lipids of Switching from Olanzapine or Quetiapine to Aripiprazole in a VA Population
Erica J. Duncan, M.D. Atlanta VA/Emory University School of Medicine, Psychiatry and Behavioral Sciences, Atlanta VAMC; Mental Health/116A, 1670 Clairmont Road, Decatur, GA, 30033, 9000, Boadie W. Dunlop, M.D., Maya Sternberg, Ph.D., Myung Kim, Ph.D.

Educational Objectives:
At the conclusion of this presentation the participant should have a greater appreciation of the effects that switching to aripiprazole from olanzapine or quetiapine may have on lipids in a clinical population requiring antipsychotic treatment.

Summary:
Background: Accumulating evidence indicates that the atypical antipsychotics can cause lipid elevations at a greater rate than older typical agents. Additional evidence indicates that this risk is not equivalent among the atypicals. Hyperlipidemia is associated with increased morbidity and mortality; thus medication-associated alterations in lipid profiles need to be considered along with other clinical factors when prescribing antipsychotics. A therapeutic strategy that could reduce this risk has important healthcare implications.

Objective: To evaluate whether patients switched to aripiprazole treatment after prior treatment with olanzapine or quetiapine would demonstrate improved lipid profiles.
Methods: We conducted a retrospective nonrandomized case control analysis of 137 VA patients between 7/1/1999 and 8/1/2006 who received a period of at least 60 continuous days of outpatient treatment with either olanzapine (N=76) or quetiapine (N=61), followed by subsequent treatment period of at least 60 continuous days with aripiprazole. All patients had at least one lipid measurement during both treatment periods. Lipid levels dur-
ing the treatment periods were compared using Wilcoxon Signed Rank Test.

Results: Patients switching to aripiprazole after treatment with olanzapine had significant improvements in mean total cholesterol (-14.4 mg/dl, p=0.004), low-density lipoprotein (LDL, -10.8 mg/dl, p=0.011), high-density lipoprotein (HDL, +6.2 mg/dl, p<0.0001), and triglycerides (-59.9 mg/dl, p<0.0001). Maximum lipid concentrations recorded during treatment were also significantly improved for all lipid fractions after switch from olanzapine to aripiprazole treatment. Patients switching to aripiprazole after quetiapine showed significant change only in mean HDL concentration (+4.7 mg/dl, p<0.0001). All other mean and maximum measures of lipid concentrations did not differ significantly when subjects were switched from quetiapine to aripiprazole.

Conclusions: This preliminary analysis from a VA clinical population indicates that switching to aripiprazole may improve lipid profiles of patients prescribed olanzapine or quetiapine.

Funding: Bristol-Myers Squibb

References:

NR369 Monday, May 21, 3:00 PM - 5:00 PM
Treatment Effects of Selegiline Transdermal System on Symptoms of MDD: A Meta-Analysis of Placebo-Controlled Efficacy Trials

Donald S. Robinson, M.D. Worldwide Drug Development, Consulting, 102 East Avenue, Burlington, VT, 05401, 9000, Michelle Gilmor, Ying Yang, Ph.D., George Moonsamy, Ph.D., Albert Azzaro, Ph.D., Dan Oren, M.D., Bryan Campbell, Pharm.D.

Educational Objectives:
At the conclusion of the presentation, the participant should be able to:
1. Describe the results of a meta-analysis investigating the treatment effects of STS for specific symptoms of MDD.
2. Use knowledge of the positive treatment effects of STS on a broad spectrum of individual symptoms rated by the HAM-D28 and MADRS when deciding upon specific pharmacotherapy for MDD.

Summary:
Introduction: Selegiline transdermal system (STS) is efficacious for acute and continuation treatment of major depressive disorder (MDD). When selecting pharmacotherapy for MDD, clinicians often consider presenting symptoms. The differential therapeutic effects of STS on individual symptoms of MDD may be of clinical interest when choosing antidepressant treatment.

Objective: This meta-analysis explores the treatment effects of STS for specific symptoms of MDD, based on a line-item analysis of the 28-item Hamilton Rating Scale for Depression (HAM-D28) and the Montgomery-Asberg Depression Rating Scale (MADRS).

Methods: Change in score from baseline to end of treatment for each item of the HAM-D28 and MADRS was assessed using a multilevel model for the meta-analysis of continuous outcome data from all 5 short-term, randomized, placebo-controlled STS efficacy trials in patients with DSM-IV MDD. Utilizing a random-effects model with trial effects fixed and adjusting for baseline scores, confidence intervals (95%) were computed for treatment differences between STS and placebo.

Results: STS exhibited significant treatment effects on core depression symptoms (HAM-D Bech 6 items: depressed mood, guilt, work and activities, retardation, psychic anxiety, general somatic symptoms), reverse vegetative symptoms (oversleeping, overeating), motoric retardation, suicide, and genital symptoms (libido). STS treatment was associated with significant improvement in all MADRS items except for reduced sleep and appetite, with the most prominent being reported sadness, lassitude, and poor concentration.

Conclusions: STS, an MAOI antidepressant potentiating the activity of 3 monoamine neurotransmitters (serotonin, norepinephrine, and dopamine), appears efficacious for a spectrum of individual depressive symptoms rated by the HAM-D28 and MADRS. Item analyses of specific symptoms can provide useful guidance to clinicians in individualizing drug therapy based on presented symptoms of depression.

References:

NR370 Monday, May 21, 3:00 PM - 5:00 PM
A Fourteen Week Randomized, Single-Blind Trial of Lamotrigine vs. Sodium Valproate for Adjunct Treatment of Acute Mania Followed by Maintenance Monotherapy

Samantha Yard, B.A. Beth Israel Medical Center, Psychiatry, 1st Ave at 16th St., New York City, NY, 10003, S000, N. Simay Gokbayrak, B.A., James Prosser, M.D., Edward Kilbane, M.D., Lisa J. Cohen, Ph.D., Igor I. Galynker, M.D.

Educational Objectives:
At the end of the session, participants will appreciate the efficacy and utility of Lamotrigine as a therapeutic agent in the treatment of mania in Bipolar Disorder

Summary:
Objective: Lamotrigine is a mood stabilizer that has been approved for maintenance treatment of Bipolar Mood Disorder I (BPD I). This study compared the efficacy and tolerability of lamotrigine and sodium valproate as adjunctive therapy in the treatment of acute mania and the transition to maintenance monotherapy in these patients.

Methods: Twenty three psychiatric inpatients diagnosed with BPD I and recently hospitalized with an acute manic episode were randomly assigned to receive either lamotrigine or sodium valproate in addition to a combination of a neuroleptic and a benzodiazepine. Upon discharge, subjects were transitioned to mood stabilizer monotherapy. Symptom severity was assessed using the Global Assessment Scale (GAS), the Young Mania Rating Scale (YMRS), and the Hamilton Rating Scale for Depression (HRSRD).

Results: There was a statistically significant increase over time in the GAS score, and a significant decrease in YMRS scores for all subjects regardless of treatment group. The over-time change in HDRS was not statistically significant. Drop-out rates were significantly higher (p<0.05) for the sodium valproate group than for the lamotrigine group.

Conclusion: Lamotrigine and Sodium Valproate appear equally effective as adjunct treatment agents for acute mania. Lamotrigine may be superior to sodium valproate in transition to maintenance treatment for BPD I.
References:

NR371 Monday, May 21, 3:00 PM - 5:00 PM
Risk of Lipid Elevation with Risperidone, Olanzapine, Quetiapine and Haloperidol in a VA Population
Erica J. Duncan, M.D. Emory University School of Medicine, Psychiatry and Behavioral Sciences, Atlanta VA; Mental Health/ 116A, 1670 Clairmont Road, Decatur, GA, 30033, 9000, Boadie W. Dunlop, M.D., Robert M. Harner, Ph.D., Sandra Woolson, M.P.H.

Educational Objectives:
At the conclusion of this presentation the participant should have a greater appreciation of the relative effects risperidone, olanzapine, quetiapine, and haloperidol on lipids in a clinical population requiring antipsychotic treatment.

Summary:
Background: Accumulating evidence indicates that atypical antipsychotics can cause lipid elevations at a greater rate than older typical antipsychotics. Additional evidence indicates that this risk is not equivalent amongst the atypicals. Hyperlipidemia is associated with increased morbidity and mortality, so it is important that our field incorporate the relative risks of antipsychotics for inducing alterations in lipid profiles along with other clinical factors when prescribing drugs of this class. Based on findings from previous studies, we hypothesized that patients receiving risperidone or haloperidol would have a more favorable lipid profile than patients receiving olanzapine or quetiapine.

Methods: We conducted a computerized retrospective nonrandomized case control analysis of 4009 VA patients receiving outpatient prescriptions for an antipsychotic between 7/1/1999 and 8/1/2006. For each patient, the first prescription for one of four antipsychotics for at least 60 continuous days [risperidone (n=1492), olanzapine (n=1572), quetiapine (n=545) or haloperidol (n=396)] was analyzed for levels of total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides during the prescription period.

Results: One-way ANOVA on total cholesterol was significant for the medication effect (F(3,3998)=9.16, p<0.0001). Means for the four medications were ordered from lower to higher as follows: haloperidol<risperidone<olanzapine<quetiapine. Tukey’s studentized range test indicated haloperidol<olanzapine (p=0.0004) and <quetiapine (p=0.002) but not risperidone (p=0.2). For triglycerides, the order of means from lower to higher was in the same order. Tukey’s test indicated haloperidol<olanzapine (p=0.0009) and <quetiapine (p=0.002) but not risperidone (p=0.6). The medications differed more modestly in HDL (F(3,3408)=4.46, p=0.05) with means in order: haloperidol<risperidone<quetiapine<olanzapine. LDL did not separate amongst medication groups.

Conclusions: In this preliminary analysis from a VA clinical population, treatment with risperidone and haloperidol were associated with a more favorable lipid profile than olanzapine and quetiapine.

Funding: Janssen Pharmaceutica

References:

NR372 Monday, May 21, 3:00 PM - 5:00 PM
Time-Dependent Changes of Plasma Homovanillic Acid in the Process of Recovery From Depression
Ryosuke Den, M.D. Keio University, Neuropsychiatry, 35 Shinanomachi, Shinjuku-ku, Tokyo, 160-8582, 5880, Koichiro Watanabe, Ph.D., Toshiaki Kikuchi, M.D., Hirokazu Shida, M.D., Haruo Kashima, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the time-dependent change of monoamines in the recovery phase of depression. And there is a clinical implication of focusing the process of recovery from mental illness.

Summary:
Purpose: To elucidate changes of dopamine in the process of recovery from depression by investigating the time-dependent changes in plasma homovanillic acid (HVA), with reference to the hypothesis that dopamine facilitates recovery rather than as the etiology of depression.

Methods: This study investigated six outpatients. They were eligible if diagnosed as having major depressive disorders according to DSM-IV, and were drug naive at baseline. After full description of the purpose of this study, written informed consent was obtained from all participants. The subjects were randomly assigned to the sulpiride group (150 to 300 mg) or the paroxetine group (10 to 40 mg).

Blood samples were taken weekly before breakfast and were analyzed the pHVA by HPLC. The clinical statuses of patients were evaluated weekly with the MADRS (Mongomery-Asberg Depression Rating Scale) and the Zung Self-rating Depression Scale. Patients with an at least 50% decrease in the total MADRS scores from the baseline value were defined as responders. This study was approved by the institutional review board at our hospital.

Results: Four patients were classified as responders. Among them, there were no significant changes in pHVA levels irrespective of antidepressants. However, the levels of pHVA tended to increase linearly in a time-dependent manner. The pHVA levels in two non-responders tended to increase further with time, with an exception of transient decrease at week 1. Difference between two antidepressants was not observed.

Conclusions: As far as we know, few studies have mentioned the potential roles of dopamine in the recovery phase of depression. There was no significant difference between responders and non-responders with respect to the time-dependent changes of pHVA. Further studies using larger number of subjects should be carried out to investigate the involvement of dopamine in recovery phase of depression.

References:

NR373 Monday, May 21, 3:00 PM - 5:00 PM
Ross J. Baldessarini, M.D. McLean Hospital, Mailman Research Center, 115 Mill Street, MRC 316, Belmont, MA, 02478-1048, 9000, Henry Henk, Ph.D., Jane Chang, M.P.H., Leslie Leahy, Ph.D.
Educational Objectives:

By this presentation, participants should improve their therapeutic practice by learning that [1] high rates of antidepressant use early in treatment of bipolar I and II disorder patients, and long thereafter, contrasts to a lack of evidence of their efficacy/safety, and of specific FDA-approval for use in bipolar disorders, and [2] that psychotropic drug polytherapy emerges early as the dominant treatment for bipolar disorder patients, despite lack of testing for additional effectiveness/safety of most drug combinations in current common, empirical clinical use.

Summary:

Background: Treatment of bipolar disorders (BPD) has evolved rapidly in recent years, with FDA-approval of several mood-stabilizing and animantic agents, and expanded off-label and combination treatments. Accordingly, we analyzed treatment patterns in a national sample of newly treated BPD patients.

Methods: We used HIPAA-compliant, national health-plan claims data (2000-2004) to identify ICD-9 BPD patients (type I [55%], II [15%], or NOS [30%]) with continuous benefits, without psychotropic-drug prescription-fills for >6 months, comparing psychotropic prescriptions dispensed initially vs. at 12-month follow-up.

Results: Among 7,567 BPD patients (57% men) aged 35.5±12.4 years, initial prescription-fills included 1 (86.3%) or >2 mood-altering drugs (13.7% of patients). Initial monotherapies ranked: antidepressants (56.1%) > anticonvulsants (13.9%) ≥ antipsychotics (10.6%) > lithium (5.7%); anticonvulant-use ranked: valproate (10.2%) > lamotrigine (2.9%) > carbamazepine (0.8%). Initial (overlapping) combinations included antidepressants (9.9%) > antipsychotics (8.9%) > anticonvulsants (7.3%) > lithium (2.3%), with the same rank-order at one year, when only 36.1% of patients received monotherapy, 25.7% received ≥2 psychotropics, and 38.2% received none. Psychotropics/person (initial vs. one-year) ranked: none (0.0% vs. 38.2%), one (86.3% vs. 36.1%), two (12.5% vs. 20.0%), three (1.1% vs. 5.6%), >4 drugs (0.0% vs. 0.5%), averaging 1.15/person initially vs. 1.52 among those treated at 12 months.

Discussion: Utilization-rates for antidepressants were very high despite lack of compelling evidence of their efficacy or safety in BP-depression, and polytherapy came to dominate treatment by one year. Prevalent psychotropic nontreatment at 12 months (38%) encourages development of better-tolerated mood-stabilizing treatments. Supported by grants from Novartis Corp, SJ Anderson Foundation & McLean Psychopharmacology Research Fund (to RJB).

References:


NR374 Monday, May 21, 3:00 PM - 5:00 PM
Clinician Weight as a Factor in Prescribing Atypical Antipsychotics

Seth Alexander Cohen, M.D. Puget Sound Psychopharmacology Service, Psychiatry, 130 Nickerson Street, Suite 204, Seattle, WA, 98109, 9000, Nick Redding, M.S., Alyson Petras, Arif Khan, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the role that clinician weight plays in considering the weight and metabolic effects associated with the atypical antipsychotics, as well as the role clinician weight plays in choosing a weight neutral versus non-weight neutral antipsychotic.

Summary:

Objective: To determine the relationship between the weight of the prescribing clinician and their degree of concern about weight and metabolic disturbances associated with the atypical antipsychotics, as well as their choice of medications.

Method: A nationwide survey was completed by 234 practicing clinicians. This questionnaire covered areas including clinician choice of medication, dosing strategies, perceived outcomes (effectiveness, tolerability, predictability), concerns about weight, metabolic disturbances, QTc increases, costs as well as clinician height and weight or BMI. For purposes of analysis prescribers were divided into non-obese (BMI<30) and obese (BMI>30) groups. The antipsychotics were divided into weight and metabolically neutral (ziprasidone and aripiprazole) and weight and metabolically non-neutral (risperidone, olanzapine and quetiapine) groups. We conducted chi-square analyses to determine if obese or non-obese prescribers were more likely to indicate a moderate or extreme concern regarding the weight and metabolic effects of the non-neutral medications. Additionally, we compared these two groups to determine whether obese or non-obese prescribers were more likely to prescribe a moderate amount or a lot of the neutral medications.

Results: 87.3% of non-obese prescribers were moderately or extremely concerned about the weight increases and metabolic disturbances associated with the non-neutral agents while 95.9% of obese prescribers reported such concern (x²=10.92, df=1, p=0.001). 63.6% of non-obese clinicians and 75.0% of obese clinicians prescribed a moderate amount or a lot of the neutral medications (x²=2.75, df=1, p=0.09).

Conclusions: Obese clinicians report greater concern about the weight and metabolic effects of risperidone, olanzapine and quetiapine than non-obese clinicians. Obese clinicians may be more likely than non-obese clinicians to prescribe ziprasidone and aripiprazole.

References:


effects of ethanol on the expression of NPY in the hippocampus of the rat brain.

Summary:

Objectives: Neuropeptide Y (NPY) consists of 36 amino acid and is one of the most abundant peptides found in the mammalian brain. The distribution of binding sites for NPY in CNS is consistent with the possibility that NPY can modulate cognitive processes. Mounting evidence suggests that ethanol exerts effects on learning and memory by altering cellular activity in the hippocampus and related structures. The present study was designed to investigate the effects of ethanol on the expression of NPY in the hippocampus of the rat brain.

Method: Adults male Spraque-Dawley rat were used. They were assigned to ethanol exposure group (N=8) and normal control without ethanol exposure (N=8). After 8 weeks of ethanol exposure, immunohistochemical analysis was performed. We compared the NPY expression in the hippocampus between two groups.

Results: 1) In the ethanol exposure group, the number of NPY-positive cells was significantly decreased in the dentate gyrus and CA1 region of hippocampus compared with normal control. 2) There was no difference in the number of NPY-positive cells in CA3 regions between two groups.

Conclusion: This study demonstrates that the presence of significant neuronal damage in the hippocampus after long-term ethanol exposure. Furthermore, these findings suggest that dentate gyrus and CA1 region may be more susceptible than CA3 region to ethanol-induced neuronal damage. Our results support possible mechanisms involved in the role of NPY in ethanol induced memory deficit.

References:

NR376  Monday, May 21, 3:00 PM - 5:00 PM
Assessment of Amphetamine-like Properties of Bupropion After Repeated Administration in Healthy Volunteers (NCT00285155)

Hugues Chevassus INSERM/CHU de Montpellier, Centre d'Investigation Clinique CIC0001, Hôpital Saint-Eloi, 80, avenue Augustin Fliche, Montpellier, 34295 cedex 5, 4279, Florence Galtier, Anne Farret, Clarisse Roux, Claire-Anne Poncon, Jean-Pierre Gagnol, Pierre Petit

Educational Objectives:

At the conclusion of this presentation, the participant should be able to know that bupropion displays some amphetamine-like properties that may be relevant for clinical practice.

Summary:

Introduction: Bupropion is largely used as an antidepressive and smoking cessation therapy. Its chemical structure and biological mechanisms are closely related to those of amphetamine-like drugs. We thus evaluated the pharmacological similarities between bupropion and the amphetamine-like compound methylphenidate, after repeated administration in man.

Methods: Twelve young male volunteers completed this double-blind, placebo controlled, cross-over study, after informed consent. Bupropion and methylphenidate were orally administered for a first half-dose-6-day period (150 and 10 mg respectively) followed by a full-dose-8-day period (300 and 20 mg respectively).

Outcomes were assessed after one night partial sleep-deprivation, before and after treatment, and comprised subjective feelings (self-rating questionnaires), cognitive functions (neuropsychological test battery), vital signs, appetite (visual analogue scales after a standardized breakfast), food consumption (ad libitum test meal). Data are means ± SEM. Comparisons were performed by ANOVA.

Results: Bupropion, similarly as methylphenidate, decreased the score of asthenia (44.2 ± 3.1 and 41.9 ± 3.7 respectively vs. 53.0 ± 4.1 for placebo; P<0.05), despite an impairment of sleep onset (-4.3 ± 3.3 and -1.9 ± 3.8 respectively vs. +7.5 ± 3.7; P<0.05). Both bupropion and methylphenidate increased resting diastolic blood pressure (67.9 ± 1.2 and 65.7 ± 1.0 respectively vs. 62.5 ± 1.4 mmHg; P<0.05), body temperature (36.5 ± 0.1 and 36.5 ± 0.1 vs. 36.3 ± 0.1°C; P<0.05) and decreased body weight (-0.7 ± 0.2 and -0.6 ± 0.2 respectively vs. +0.2 ± 0.3 kg; P<0.05). No significant change could be observed with either bupropion or methylphenidate on heart rate, cognitive functions, appetite and energy consumption.

Conclusion: Our results suggest that bupropion has amphetamine-like properties, which can be revealed after 2 weeks of treatment, and are comparable to those of methylphenidate.

Sponsor: CHU Montpellier; Funding: French Ministry of Health

References:

NR377  Monday, May 21, 3:00 PM - 5:00 PM
SSRI Prescription Patterns of Psychiatrists and Primary Care Physicians in Treating Depression

Douglas A. Kalunian, M.D., Quintiles, Medical and Scientific Services, 10201 Wateridge Circle, San Diego, CA, 92121, 9000, Elisa Cascade, Amir H. Kalali, M.D., Penny K. Randall, M.D., Karl M. Jacobs, M.D.

Educational Objectives:

1. At the conclusion of this presentation, the participant should be aware of which discipline (primary care physicians or psychiatrists) more commonly treats depressed patients with SSRI monotherapy versus combination therapy.
2. At the conclusion of this presentation, the participant should be aware of which discipline (primary care physicians or psychiatrists) tends to treat patients with newly diagnosed depression versus ongoing/continuing depressive disorders.

Summary:

Introduction: Primary Care Physicians (PCPs) have offered the first line of treatment for depressed patients for the last few decades. With increasing demands on practices, we sought to explore the current trends in Selective Serotonin Reuptake Inhibitor (SSRI) treatment of patients with depression by PCPs and psychiatrists, to assess how the burden of care for these patients is being handled.

Methods: We analyzed retail pharmacy prescription volume from Verispan to determine the proportion of new patient starts on SSRIs by psychiatrists versus PCPs. Next, to investigate whether there are differences in psychiatrist use of SSRIs relative to PCPs, we analyzed data from Verispan's Prescription Drug and Diagnosis Audit (PDDA) database from October 2005 to September 2006.
NR378

Monday, May 21, 3:00 PM - 5:00 PM
Predictors of Non-Adherence with Psychotropic Medications in Primary Care Patients

Rajnish Mago, M.D. Thomas Jefferson University, Psychiatry, 833 S Chestnut St East, Suite 210 E, Philadelphia, PA, 19107, 9800, Shahrazad Movandadi, Ph.D., Thomas Ten Have, Ph.D., Cynthia Zubritsky, David Oslin, M.D.

Educational Objectives:

At the end of this presentation, the participant should be able to appreciate the high prevalence of non-adherence with psychotropic medication and understand the subgroups that are at greatest risk for non-adherence.

Summary:

Background: Non-adherence to medication is common in patients with mental disorders. For developing interventions aimed at increasing rates of adherence, a better understanding of the factors associated with non-adherence is essential.

Methods: Data on non-adherence using the Morisky Medication Adherence Scale were obtained in a subset of patients in the Primary Care Research in Substance Abuse and Mental Health for the Elderly (PRISM-E) study, a multicenter study comparing outcomes of patients treated in integrated care and specialty referral settings. Patients in this study were randomly allocated to treatment in the two settings and followed for 12 months.

Results: Morisky scale data on non-adherence was available for 182 patients. 93 of these patients (51.1%) were non-adherent at some point in the follow up.

In univariable analysis, non-adherence at follow-up was significantly more likely in patients with major depressive disorder, non-white patients, those with less than high school diploma, and those not working and/or volunteering.

In multivariable logistic regression, when compared to patients with other depressive disorders or other behavioral health issues, patients with major depressive disorder were more non-adherent at follow-up (OR=3.31, p=0.009). Non-adherence also was more common among patients of non-white race (OR=2.51, p=0.02). Furthermore, there was a trend whereby those with less than a high school education were more likely to be non-adherent (OR=2.05, p=0.10). However, when controlling for all other variables, financial status and working/volunteering were not significantly related to non-adherence.

Conclusions: The results of this study support previous reports of the lack of efficacy of use of combination antipsychotic therapy for psychopathology in clinical practice. Prospective controlled trials are needed to substantiate perceptions that combination antipsychotic therapy is effective for psychopathology in clinical practice.

References:


NR379

Monday, May 21, 3:00 PM - 5:00 PM
Antipsychotic Efficacy of Polypharmacy vs. Monotherapy in Patients with Schizophrenia and Schizoaffective Disorder: A Prospective Study

Jean Pierre Lindemayer, M.D. New York University School of Medicine, Psychopharmacology, 600 East 126th Street, Dunlap 1518, Wards Island, NY, 10035, 9000, Anzalee Khan, M.S., Sashank Kaushik, M.D., Saurabh Kaushik, M.D., Adel Iskander

Educational Objectives:

1. Participants will gain an understanding of the differences between monotherapy and polypharmacy treatments in schizophrenia.

2. Participants will be able to review and evaluate the clinical efficacy of monotherapy and polypharmacy treatments in schizophrenia.

Summary:

Background: Despite extensive research and recommendations regarding the optimal prescription of antipsychotic drugs, polypharmacy and excessive dosing still prevail. The aim of this study is to identify the efficacy between polypharmacy and monotherapy on patients with schizophrenia or schizoaffective disorders.

Method: We examined data of patients who participated in two randomized, double blind clinical trials, 1 open-label clinical trial and 1 randomized parallel group clinical trial of patients with schizophrenia or schizoaffective disorder on two antipsychotics and either remained on two antipsychotics or patients who were switched to one new antipsychotic treatment. Thirty three patients, age 18 - 65 years, diagnosed with DSM-IV criteria of schizophrenia or schizoaffective disorder and currently on two pre-study antipsychotics were enrolled in the study.

Results: Eighteen patients were in the polypharmacy group and fifteen patients were in the monotherapy group. No significant differences between groups were observed in change in psychopathology as measured by the PANSS. Change in Simpson Angus Scale from baseline to endpoint indicate that values of the group effect show that there was a 1.09 point difference in score for the polypharmacy group, and the difference between polypharmacy and monotherapy groups was statistically significant (F (1,29) = 12.646, p = .001).

Conclusions: The results of this study support previous reports of the lack of efficacy of use of combination antipsychotic therapy for psychopathology in clinical practice. Prospective controlled trials are needed to substantiate perceptions that combination antipsychotic therapy is effective for psychopathology in clinical practice.

References:


antipsychotic therapy is clinically beneficial and to provide guidelines on when and for whom antipsychotic polypharmacy should be considered.

References:


NR380 Monday, May 21, 3:00 PM - 5:00 PM
Agomelatine, A Novel Antidepressant, Has a Favorable Safety and Tolerability Profile in the Treatment of Major Depressive Disorder
Ibrahim Gunay, M.D. Novartis Pharmaceuticals Corporation, Clinical Development, One Health Plaza, #403/320, East Hanover, NJ, 07936-1080, 9000, Maurizio Fava, M.D.

Educational Objectives:
At the conclusion of the presentation, the participant should be able to discuss the favorable safety and tolerability of the novel antidepressant agomelatine (a melatoninergic MT1 and MT2 receptor agonist and 5-HT2c receptor antagonist), as seen through meta-analysis of data pooled from a series of well-controlled studies of patients with Major Depressive Disorder. Specifically, participants should be able to cite the similar safety and tolerability profiles of agomelatine and placebo based on analysis of adverse events and rates of discontinuation as well as laboratory parameters.

Summary:
Purpose: Agomelatine is a novel antidepressant with a unique pharmacologic profile (a melatonergic MT1 and MT2 receptor agonist and 5-HT2c receptor antagonist). The efficacy and safety of agomelatine 25-50 mg as a treatment for Major Depressive Disorder (MDD) has been evaluated in a series of well-controlled trials. The current study evaluates the safety and tolerability of agomelatine 25-50 mg using pooled data from these trials.

Methods: Data were pooled from eight studies. Six were prospective, large-scale, multicenter, randomized, double-blind, placebo-controlled studies—one 8-week, dose-finding study; three 6-week, fixed-dose studies of agomelatine 25 mg (one included agomelatine 50 mg); and two 6-week, flexible-dose studies of agomelatine 25-50 mg. Two others were smaller studies evaluating agomelatine in elderly and largely resistant hospitalized patients, respectively. Safety and tolerability were assessed by clinical examination, adverse events (AEs), vital sign measurements, and laboratory tests.

Results: Data were analyzed from 1120 patients treated with agomelatine 25-50 mg and 998 patients treated with placebo. Overall, the agomelatine and placebo treatment groups had similar frequencies of treatment-emergent AEs (52.8% versus 51.8%), serious AEs (2.3% versus 1.7%), and rates of discontinuations due to AEs (5.7% versus 5.9%), with psychiatric disorders the most common AEs leading to discontinuation in both groups (2.2% versus 2.5%). The most common treatment-emergent AE was headache (13.7% and 14.0% of agomelatine- and placebo-treated patients, respectively). Frequencies of other common AEs were similar between agomelatine and placebo, with the exception of dizziness (5.4% versus 3.1%) and upper abdominal pain (2.3% versus 1.3%). The majority of AEs were mild-to-moderate and did not require intervention. Cardiovascular AEs were lower on agomelatine than on placebo. No clinically relevant changes or differences between groups were detected in laboratory parameters.

Conclusions: These findings demonstrate that agomelatine 25-50 mg has favorable safety and tolerability as seen in the treatment of patients with MDD.

References:


NR381 Monday, May 21, 3:00 PM - 5:00 PM
Lamotrigine as an Antidepressant Augmentation Agent in Treatment Refractory Unipolar Depression
James G. Barbee IV, M.D. Louisiana State University Health Sciences Center, Psychiatry, 1401 Foucher St., Gumbel Bldg. Rm 312, New Orleans, LA, 70112-2825, 9000, Nowal J. Jamhour, M.A., Jonathon W. Stewart, M.D., Richard C. Shelton, M.D., Frederick W. Reimherr, M.D., Peter M. Thompson, M.D., Thomas R. Thompson, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to discuss the evidence from this multicenter double-blind placebo-controlled clinical trial regarding the efficacy of lamotrigine when added to paroxetine or paroxetine CR in a group of patients with treatment-resistant nonpsychotic unipolar depression.

Summary:
Background: Treatment resistant depression remains a significant public health problem. Reports have suggested that lamotrigine may improve the response to antidepressant therapy, either when given upon starting the antidepressant (as an "accelerator") or after antidepressant monotherapy has failed to result in an adequate response (as an "augmentation" agent). The current study is the first double-blind, placebo-controlled study on the efficacy of lamotrigine as an augmentation agent in treatment refractory unipolar depression.

Method: 195 patients with Major Depressive Disorder were entered into the study and received open-label treatment with paroxetine or CR (in dosages up to 50 or 62.5mg respectively). Of these patients, 98 patients failing to respond adequately to paroxetine monotherapy (Ham-D score of ≥15 at week 8) were randomized into the double-blind portion of the study and received, in addition to paroxetine, either placebo or up to 400 mg lamotrigine for a 10-week period. Montgomery-Asberg Depression Rating Scale (MADRS), Hamilton Rating Scale for Depression (Ham-D), and Clinical Global Impressions (CGI) scales were used as primary and secondary outcome variables. Other outcome measures, including percentage of improvement and achievement of remission status were added, based on MADRS and Ham-D scores.

Results: Both lamotrigine and placebo groups improved significantly from randomization in the double-blind portion of the study. Treatment group differences were statistically significant on the Ham-D and near-significant on the MADRS. Baseline analysis revealed a significant treatment-by-sex interaction on both MADRS and Ham-D for men only; lamotrigine group scores were significantly lower than placebo group scores. Within the lamotrigine group, there were significant and near-significant associations between outcome and open-label response, sex, body mass index, and Thase-Rush classification. Within the placebo group,
there was a significant effect of atypical/melancholic classification on outcome.

**Conclusion:** These results provide partial support for the efficacy of lamotrigine augmentation in treatment resistant depression.

**References:**

**NR382 Monday, May 21, 3:00 PM - 5:00 PM**

**Agomelatine, a Novel Antidepressant, Is Effective in Major Depressive Disorder Across Gender and Severity of Depression**

Alan F. Schatzberg, M.D. Stanford University, Psychiatry and Behavioral Sciences, Stanford University School of Medicine, 401 Quarry Road, Stanford, CA, 94305-5717, 9000, Rocco Zaninelli, M.D.

**Educational Objectives:**
At the conclusion of the presentation, participants should be able to discuss the efficacy of agomelatine, a novel antidepressant, with a unique combination of pharmacologic properties (a MT1 and MT2 receptor agonist and 5-HT2c receptor antagonist) in the treatment of patients with Major Depressive Disorder (MDD). In particular, the participant should be able to recognize that the efficacy of agomelatine is consistent across subpopulations of patients based on gender and severity of depression, as seen through meta-analysis of data pooled from pivotal trials that demonstrated agomelatine's efficacy in overall study populations of patients with MDD.

**Summary:**
**Purpose:** Agomelatine is a MT1 and MT2 receptor agonist and 5-HT2c receptor antagonist that has demonstrated efficacy versus placebo at a dose of 25-50 mg in three pivotal trials of patients with Major Depressive Disorder. The current study evaluates the impact of gender and baseline depression severity on the effect of treatment with agomelatine 25-50 mg through meta-analysis of data from these trials.

**Methods:** Data were pooled from three large-scale, multicenter, randomized, double-blind, positive placebo-controlled studies: one 8-week (a fixed daily dose study) and two 6-week, flexible-dose studies of agomelatine 25-50 mg. Pooled data were analyzed by gender and depression severity, with subgroups stratified by the median baseline Hamilton Depression Rating Scale (HAM-D) total score ($\geq 27 = $ less severe; $> 27 = $ more severe) of the combined population. The primary efficacy criterion was HAM-D total score.

**Results:** Data were evaluated from 721 patients: 358 patients (122 males, 236 females) randomized to agomelatine 25-50 mg and 363 patients (114 males, 249 females) randomized to placebo. Overall, pooled analysis of HAM-D total score showed a significant difference in favor of agomelatine versus placebo (difference = 2.86 ± 0.56; $P < 0.001$). In males, change from baseline in mean HAM-D total score was -13.7 with agomelatine and -9.9 with placebo (difference = 3.83 ± 1.01; $P < 0.001$). Similarly, in females, the change was -13.5 with agomelatine and -11.2 with placebo (difference = 2.46 ± 0.70; $P < 0.001$). Among the “more severe” patient subgroup (n = 153; agomelatine; n = 142; placebo), changes from baseline in mean HAM-D total score (-14.8 with agomelatine and -11.4 for placebo) demonstrated an increased treatment effect with agomelatine (difference = 3.40 ± 0.93; $P < 0.001$). In the “less severe” population (n = 205; agomelatine; n = 221; placebo), changes were -12.6 with agomelatine and -10.4 with placebo (difference = 2.39 ± 0.72; $P < 0.001$).

**Conclusions:** This meta-analysis demonstrates the antidepressant efficacy of agomelatine 25-50 mg is consistent across gender and severity of illness.

**References:**

NR384  Monday, May 21, 3:00 PM - 5:00 PM
5-HT2A Receptor Antagonists Given in the Acute Withdrawal from Daily Ethanol Injections Cannot Reverse Established Sensitization in Mice.
Roseli B. Lacerda, Sr., Ph.D. Universidade Federal do Parana, Farmacologia, Rua Barão dos Campos Gerais 524 ap 42, Curitiba, 80030-400, 3510, Ivete C. Ferraz, Sr., M.D., Guilherme E. Nasser, Jr., Juliana Simioni, Jr., Bernardino A L Paggi, Jr., Mariana S C Fernandes, Jr.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to demonstrate that, contrary to what was observed for cocaine, ethanol-induced sensitization is not reversed by 5HT2A antagonist treatment.

Summary:
In the search for medications to treat drug abuse, there have been many studies examining drugs that would either inhibit the induction or expression of stimulant sensitization. The prevailing hypothesis is that by blocking sensitization development and expression that one can inhibit the augmented stimulant acquisition behaviors noted in self-administration of stimulants. But, when presenting for treatment, patients would have already established a sensitized response previously. There have been only a few studies demonstrating that certain drugs when given to animals for several days in the withdrawal period following a sensitization regimen can reverse sensitization to cocaine, but no evidence is reported for ethanol. The present study aimed to evaluate the effect of mianserin (an antagonist of 5HT2A receptor) for reversing previously established ethanol induced sensitization. Male Swiss mice received daily i.p. saline (S) or ethanol 2g/kg (E) for 21 days, being evaluated 20 minutes after the injection in the Activity Cages (AC) for 15 minutes in the 1st, 7th and 21st days. After the 21st day test, treatment was withdrawn for 3 days and then, they were randomly challenged with saline, ethanol 2g/kg or mianserin 10 or 20mg/kg. During the next 7 days mice received daily the same treatment, forming the following groups: SS, SE, SM1, SM2, EE, EM1, EM2, (n=11 to 20/group). In the 8th day all mice were challenged with ethanol 2g/kg and exposed to AC. Data were analyzed through ANOVA and Newmann Keuls test. As previously demonstrated, ethanol chronic administration induced behavioral sensitization. The two doses of mianserin were not able to reverse established sensitization. These data suggested that in contradiction to what was reported for cocaine, the 5HT2A antagonism was not able to reverse ethanol induced sensitization. It is discussed that cocaine- and ethanol-induced sensitization involved different mechanisms.

References:

NR385  Monday, May 21, 3:00 PM - 5:00 PM
Differential Effects of Atypical Antipsychotic-induced Insulin Resistance on Neurocognition in Schizophrenia
Simon S. Chiu, M.D. University of Western Ontario, Psychiatry, Regional Mental Health Care St Joseph Health, 467 Sunset Drive, St. Thomas, ON, NSP 3V9, 1220, Jason Carr, Ph.D., Zack Cernovsky, Ph.D., Jin Hyatsu, Jr., B.S.C., Robbie Campbell, Jr., M.D., Mariwan Husni, M.D.

Educational Objectives:
- At the end of the session, the participant should be able to:
  1. understand the link between insulin resistance, obesity and cognition in schizophrenia and the brain-metabolic cross-talks of insulin signaling;
  2. relate the effects of atypical antipsychotics to changes in insulin resistance and neurocognition;
  3. evaluate the specific domains of neurocognition sensitive to insulin resistance in schizophrenia

Summary:
Introduction: In schizophrenia, neurocognitive impairment is less responsive to atypical antipsychotic treatment, raising the issue whether insulin resistance is related to neurocognition deficits in schizophrenia.

Objective: To examine whether neurocognition measures are differentially correlated with Insulin Resistance Index (IR) assessed with HOMA (Homeostasis Model Assessment) in non-diabetic schizophrenic patients.

Method: The study was cross-sectional. The subjects were required to complete SCID diagnostic interview for schizophrenia and computerized Neuro-Cognitive Screening Test (NCS) [R. C. Gur PhD University of Penn, USA]. Body composition, fasting blood samples were ordered for lipid profile glucose and insulin levels. HOMA-IR = [fasting glucose level (mmol/L) ] x [fasting insulin level (µunit/ml)] / 22.5.

Results: We recruited 37 chronic schizophrenics (mean age: 43; male/female: 27/10) 35/37 on clozapine (mean dosage: 310 mg) 2/37 on olanzapine (mean dosage 15 mg). The mean BMI (Body Mass Index) was in the obese range: 32.4, mean fasting glucose :4.9 mmol/l; and mean insulin level :12.6 µU/ml Mean HOMA-IR: 2.70 correlated significantly (p < 0.05) with BMI, triglyceride and insulin levels. We followed the two-step process to define the relationships of log HOMA-IR with each neurocognitive variable. As no distinct curvilinear relationships emerged from bivariate scatterplots, we next used the Pearson correlation coefficient. Log transformed HOMA-IR correlated significantly ( p < 0.05, 1-tailed) with neurocognitive measures of facial expression identification (r = -.31), delayed semantic memory (r = -.31), delayed visual memory (r = -.31) and verbal analogies test (r = +.23). More severe IR led to poorer neurocognition.

Conclusion: Our finding of significant correlation between insulin resistance and the decline of neuro-cognitive functioning provides evidence for generalized cognitive "processing deficits" mediated by insulin signaling in schizophrenia. Pharmacological targeting insulin resistance with insulin sensitizers may improve neurocognitive deficits in schizophrenia.

References:
**NR386** Monday, May 21, 3:00 PM - 5:00 PM

Acceptance of a Recommendation of a Long-Acting Antipsychotic Route in First-Episode Schizophrenia: Initial Findings of a Prospective Randomized Study

Peter J. Weiden SUNY Downstate Medical Center, Psychiatry, 450 Clarkson Avenue, Box 1203, Brooklyn, NY, 11203, 9000, Stephen M. Goldfinger, Amjad Hindi, Ayako Sunakawa, Nina R. Schoeller

**Educational Objectives:**

At the end of the presentation, the participant will learn about the potential benefits and barriers to initiating an atypical antipsychotic by long-acting route in patients who have recently been treated for a first episode of schizophrenia.

**Summary:**

**Overview:** A long-acting atypical antipsychotic has theoretical advantages for first-episode schizophrenia patients, given the very high rates of nonadherence, and have the most to lose from an otherwise preventable relapse. One important question is the acceptability of a recommendation for long-acting antipsychotic, compared to remaining on an oral route, for patients who have had a first-episode of schizophrenia.

**Methods:** First-episode patients were invited into a maintenance study comparing long-acting and oral atypical antipsychotic treatment after an acute first-episode is treated.

Consenting patients meeting criteria for maintenance antipsychotic were randomized to receive either a recommendation of long-acting atypical (risperidone) or a recommendation of oral atypical antipsychotic in a 2:1 ratio. Of the randomized patients to date (N=32), nine (28%) were randomized to continuing on their oral antipsychotic and 23 to the long-acting route (72%).

**Results:** Most patients randomized to a long-acting route were initially reluctant (41%) or opposed (44%) to trying a long-acting medication route when it was initially presented to them. Despite these obstacles, 21 of the 23 (92%) randomized to the long-acting route accepted at least one long-acting injection. Since the possibility of a long-acting injection may have been a reason for refusing Phase II, adding these nine patients to the patient base sets a lower boundary acceptance rate of 21 out of 42 (50%).

**Conclusion:** Our preliminary results show that the majority of first-episode schizophrenia patients who agree to maintenance antipsychotic therapy are likely to accept a long-acting injection version of the medication when presented in an integrated treatment fashion. When indicated, a long-acting route can usually be initiated in first-episode patients that transition to an outpatient service already standardized on oral atypical antipsychotic regimen.

**References:**


**NR387** Monday, May 21, 3:00 PM - 5:00 PM

Decreased Prefrontal Choline as Determined by Magnetic Spectroscopy Associated with Improved Negative Symptoms in Individuals with Asperger’s Syndrome Treated with Risperidone

Donna Lynn Londino, M.D. Medical College of Georgia, Psychiatry and Health Behavior, 1515 Pope Avenue, Augusta, GA, 30912, 9000, Elizabeth L. Siroti, M.D., Maria E. Johnson, M.D., Hessenenthaler Mark, M.D., Julian Hutcheson, Jeffrey L. Rausch, M.D.

**Educational Objectives:**

1. At the conclusion of this presentation, the participant will appreciate that certain clinical features diagnostic to Asperger’s may be considered negative symptoms of the disorder.

2. At the end of this session, the participant will understand current magnetic resonance spectroscopy in Asperger’s syndrome.

3. By the conclusion, the participant will appreciate the potential association between excess choline in the right prefrontal cortex of individuals with Asperger’s and negative symptoms.

4. At the end of the session, the participant will consider that risperidone may be beneficial for symptoms of Asperger syndrome by decreasing choline concentrations in the prefrontal cortex.

**Summary:**

We have published prior data suggesting improvement in the behavioral deficits, identified as “negative symptoms” in Asperger’s syndrome with the use of risperidone. Utilizing these pilot data and considering the relationship demonstrated by Muphy et al (2002) between increased prefrontal concentration of choline (by magnetic resonance imaging) and social function, we hypothesized that risperidone treatment might be associated with decreased concentrations of choline in the prefrontal cortex. Subjects underwent magnetic resonance spectroscopy (MRS) before participating in a 12-week course of risperidone. Measures of the concentrations and ratios of N-acetylaspartate (NAA), creatine, and choline were obtained in both the left and right hemispheres. The primary outcome measures were the Scale for the Assessment of Negative Symptoms (SANS). Secondary outcome measures included a modified Asperger Syndrome Diagnostic Scale (ASDS). After completion of 12 weeks of treatment, a post-risperidone MRS was obtained and measures of prefrontal metabolites were compared with changes in the primary and secondary rating instruments.

In 18 study completers, significant (P=0.025) improvements were observed with risperidone on SANS scores and in social functioning, measured by the ASDS replicating previous findings. In addition, before treatment we observed higher choline ratios in right prefrontal cortex compared with left, whereas after treatment, choline concentrations were nearly identical on the right and left prefrontal cortices. Post-treatment choline concentrations on the right were significantly correlated with post-treatment SANS ratings (P<0.05) such that lower right choline concentrations were associated with lower negative symptom scores. These data are consistent with the hypothesis that higher right brain choline concentration may be associated with greater negative symptoms and decreases in prefrontal choline after risperidone treatment associated with negative symptom improvement.

**References:**


**NR388** Monday, May 21, 3:00 PM - 5:00 PM

Switching Strategies to Aripiprazole From Other Antipsychotics in Stabilized Schizophrenia: A Randomized, 12 Week, Open Label, Parallel Group Study

Chi-Un Pae, M.D. Duke University, Psychiatry and Behavioral Sciences, 2218 Elder St., Suite 201, Durham, NC, 27705,
NR389 Monday, May 21, 3:00 PM - 5:00 PM

Metformin Plus Sibutramine in the Treatment of Weight Gain and Metabolic Dysfunction During Olanzapine Administration: A Double-Blind, Placebo Controlled Pilot Study

Euderruh Uzcategui Los Andes University, Department of Psychiatry, Mérida, Venezuela, Mérida, 99999, 3070, Yamily ElFakh, Nairy Rangel, Tatiana Galeazzi, Trino Baptista

Summary:
Introduction: Excessive weight gain, hyperglycemia and dyslipidemia are often observed during olanzapine administration. The antidiabetic metformin induces a small weight loss in olanzapine-treated subjects (1), which could be amplified with the addition of sibutramine (2).

Methods: In a double blind protocol, 30 patients with schizophrenia or bipolar disorder receiving olanzapine (10-20 mg/day) for more than 4 consecutive months, were randomly assigned to metformin plus sibutramine (n = 15, 850-2550 and 10-20 mg/day respectively) or placebo (n = 15) for 12 weeks. Body weight, body mass index, blood lipids, the insulin resistance index (HOMA-IR), serum leptin levels and the Brief Psychiatric Rating Scale were assessed at baseline and after treatments.

Results: Drug treatment was well tolerated at the maximal dose. A small, marginally significant decrease in body weight (kg) was observed in the experimental group, whereas it remained stable during placebo: [-1.6 ± 0.9 vs. + 0.01 ± 0.7, t (28) = 1.4, p = 0.12]. Triglyceride levels (mg/dL) remained stable during drug treatment and significantly increased during placebo: [+ 5.0 ± 11 vs. + 0.0 ± 10, t (28) = 2.7, p = 0.01]. No significant change in psychopathology level was observed with any treatment.

Discussion: Combined treatment with metformin and sibutramine may assist olanzapine-treated patients in body weight and lipid profile control.

Studies with larger samples must replicate and extend this finding.

References:
2. Nikolic-Balkoski G, Laskovic N, Barisic-Rojnic J, Leposavic Lj: Change in quality of life among healthy population during the period of last ten years in FR Yugoslavia. In Environmental...
NR391        Monday, May 21, 3:00 PM - 5:00 PM
Creating a Suicide Risk Assessment Tool for Use in the Emergency Department
Brian P. Miller, M.D. Sharp HealthCare, Behavioral Health, 7850 Vista Hill Ave, San Diego, CA, 92123, 9000, Roseann Giordano, R.N.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to identify risk factors for suicide in patients who present to the emergency department. Identify objective tools and rating scales available for assessment of suicide risk. Become familiar with a standardized training program for emergency room nurses and other non-mental health professionals.

Summary:
Assessment of suicide risk factors and determination of the most appropriate treatment setting are commonplace tasks for the mental health care provider. The Joint Commission on Accreditation of Healthcare Organizations (JCAHO) has set as one of the National Patient Safety Goals for 2007 that a documented suicide risk assessment for patients being treated in psychiatric hospitals and patients being treated for emotional or behavioral disorders in general hospitals be completed. Use of standardized risk assessment tools makes this task more consistent across providers, and provides objective data to guide treatment decisions. We present a project undertaken to establish a standard assessment tool to be used for that purpose. The project takes place at Sharp Grossmont Hospital, which has 491 acute care beds, and over 100,000 emergency department visits per year. The initial phase of the project focuses on assessing patients in the emergency department (ED), but we plan to introduce this method throughout the hospital. A review of the literature was performed and a proposed instrument identified. The instrument can be completed by a nurse, social worker, or other healthcare provider. The project includes development of education and training materials to be delivered to non-mental health professionals providing patient care in the ED. Pre- and post-test scores are compared to assess the level of competence of mental health professionals in performing suicide risk assessment.

References:

NR392        Monday, May 21, 3:00 PM - 5:00 PM
Initial Symptom Severity Level And Relapse during a 3-Year Follow up of Patients With Schizophrenia
Bryan Johnstone, M.D. Eli Lilly and Company, US Outcomes Research, Lilly Corporate Center, DC 5024, Indianapolis, IN, 46285, 9000, Baojin Zhu, Ph.D., Haya Ascher-Svanum, Ph.D., Bruce J. Kinon, M.D.

Educational Objectives:
At the conclusion of this session the participant should be able to recognize that initial level of symptom severity is associated with differential rates of relapse in the treatment of schizophrenia patients in usual setting. Patient with more severe symptoms appear to be significantly more likely to relapse in the following 3-years, as evident by higher rates of psychiatric hospitalizations, and suicide attempts.

Summary:
Objectives: To assess whether initial symptom severity is associated with differential rates of relapse and its parameters during a 3-year prospective follow up of patients with schizophrenia treated in usual care settings.
Methods: We used data from a large, multi-site 3-year prospective non-interventional study of patients with schizophrenia treated in usual care settings in the U.S. A total of 1603 patients who had not relapsed in the 6 months prior to enrollment were divided into two groups based on PANSS total scores at enrollment: patients with mild symptomatology (PANSS < 70) and patients with more severe symptomatology (PANSS >= 70). A validated patient self-report questionnaire provided information about relapse and its three parameters: use of hospitalization for psychiatric purposes, emergency psychiatric services, and suicide attempts. Relapse was defined as the occurrence of any of the three parameters. Group comparisons on 3-year cumulative rates of relapse and the three parameters of relapse were made using Mantel-Haenszel Chi-square method.

Results: In patients with mild symptoms, 32.5% of the patients relapsed. Among the three parameters, 20.1% were hospitalized, 15.8% had psychiatric emergency services, and 4.4% attempted suicide. Compared to patients with mild symptomatology, patients with more severe levels of symptomatology were significantly more likely to relapse (37.1% vs. 29.1%, p<0.01) and experience one of the three parameters, hospitalized for psychiatric purposes (22.9% vs. 17.8%, p<0.05), use of psychiatric emergency services (18.5% vs. 14.0%, p<0.05), and attempt suicide (6.2% vs. 3.1%, p<0.01).

Conclusions: Patients with more severe symptoms at enrollment appear more likely to relapse than those with mild symptom levels, and experience significantly higher rates of hospitalizations, ER visits and suicide attempts.

References:
ipant should be able to recognize that means restriction could lower method-specific suicide rate.

Summary:

Background: Restricting the availability of lethal method would lower the method-specific suicide rate. However, it is an unresolved question to what extent of the effect of means restriction is on the method-specific suicide rates. The aim of the study was to estimate the effects of restricting availability of pesticides on pesticide suicide rates (a method of differential access before and after intervention) in comparison with the hanging suicide rates (a method of equal access over time).

Methods: Age-adjusted hanging and solids/liquids (mainly pesticides) suicide rates in Taiwan in 1983-2004 were compared. We modeled the changes in age-adjusted suicide rates as a linear function of the times, method, and the interaction of time and method and calculated the regression coefficients to examine the effects on method-specific suicide rates stratified by sex and age.

Results: There were significant downward slopes in the sex-specific suicide rates by pesticide and hanging during the period of 1983-1993 in Taiwan. In males, the slope for pesticide suicide rates was -0.98 (95%CI=−1.12, -0.80); for hanging suicide rates, the slope was -0.20 (95%CI=−0.36, -0.04). In females, the slope for pesticide suicide rates was -0.82 (95%CI=−0.96, -0.67); for hanging suicide rates, the slope was -0.12 (95%CI=−0.21, -0.04). The regression coefficients were -0.78 (males) and -0.69 (female) for the solids/liquids suicide rates in relation to hanging suicide rates in 1983-1993, indicating the death rate was falling faster in solids/liquids suicide than in hanging suicide.

Conclusion: We conclude that the solids/liquids suicide rates (a differential access method) would decrease greater and faster than hanging suicide rates (an equal access method) after restriction of their availability. It is implicated that restricting the availability of pesticides may be an effective measure for suicide prevention.

References:


NR394 Monday, May 21, 3:00 PM - 5:00 PM Suicide, Attempted Suicides, and Mortality Among the Elderly in the United States

Robert Kohn, M.D. Brown University, Psychiatry and Human Behavior, 345 Blackstone Boulevard, Providence, RI, 02906, Harry Friedmann, M.S.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that anger appears to be a contributing factor to enhance risk for suicidal attempts in patients with MDD and comorbid alcoholism.

Summary:

Objective: It has been widely acknowledged that suicide in the elderly has been understudied. Less is known about suicide attempts and its consequent mortality among the elderly despite their higher risk for suicide than other age groups.

Methods: The Centers for Disease Control initiated a surveillance to collect injury data sampled from USA hospital emergency departments. The data for the years 2000-2003 provided an opportunity to systematically examine suicide attempts, which were previously only examined in small regional studies. During this period there were 123,072 suicides resulting from 1,446,031 attempts, both nonfatal plus completed. Suicide fatal injury data were obtained from the WISQARS fatal database. The data on the elderly were examined by two age groups, the old (age 60-74), and old-old (age over 75). Those 25-59 years old (adults) were included as a contrast.

Results: Men across all three age groups had markedly higher rates than women per 100,000 (men: 22.45 adults; 22.32 old; 40.33 old-old; women: 6.15 adults; 4.35 old; 3.94 old-old). The rate of suicide among women decreased form the adult to old to old-old age group, while it increased dramatically among men. Self-harm decreased with age (men: 126.78 adults; 19.87 old; 18.52 old-old; women: 149.49 adults; 22.18 old; 13.14 old-old). Mortality from a suicide attempt was markedly higher among the old and old-old.

Conclusions: Although the self-harm data may be under-reported this report shows that the elderly who have the highest rate of suicide make less non-fatal attempts resulting in higher rates of mortality.

References:


NR395 Monday, May 21, 3:00 PM - 5:00 PM The Relationship of Impulsiveness and Anger to Attempted Suicide in Patients With Major Depressive Disorder and Comorbid Alcohol Use Disorder

Yoon-Young Nam, M.D. Seoul National Hospital, Planning and Public Relations Team, National Seoul Hospital, Seoul, 143711, 5800, Chan-Hyung Kim, M.D., Sun-Hee Park, M.D., Seung-Eob Kim, M.D., Yoo Kyung Eoh, M.A., Hong Shick Lee, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that anger appears to be a contributing factor to enhance risk for suicidal attempts in patients with MDD and comorbid alcoholism.

Summary:

Objective: The present study was aimed to examine whether comorbid alcohol use disorder would predict the suicidal risk in patients with major depressive disorder (MDD) and its association with impulsiveness and anger.

Methods: The present study included 161 patients (48 male, 113 female) with current major depressive disorder. Subjects with comorbid alcohol use disorder were 45. The demographic and clinical characteristics of subjects with and without alcohol use disorder were compared. Multiple logistic regression analysis was used to examine the relationship between lifetime history of attempted suicide and comorbid alcoholism after adjustment for clinical factors known to be associated with suicidal behavior.

Results: Subjects with a lifetime history of attempted suicide were 35% of all subjects with MDD. Patients with a lifetime history of comorbid alcoholism were significantly more likely to have a lifetime history of attempted suicide. The comorbid alcoholism group had higher suicidal ideation scores, but did not differ with respect to suicidal intent or maximum lethality of attempts from group without alcoholism. The alcoholism group had higher depression, impulsiveness and anger behavior scores. Comorbid alcoholism and anger behavior was the independent variables related to lifetime suicide attempts in a multiple regression model. However, after adjusting interaction between alcoholism and

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anger behavior, anger behavior was the only predictor of lifetime suicide attempts.

Conclusions: Alcoholism is known to be a risk factor of attempting suicide. Anger is frequently associated with alcohol related behavioral problems and comorbid alcoholism in MDD. Anger appears to be a contributing factor to enhance risk for suicidal attempts in patients with MDD and comorbid alcoholism.

Key Words: Major depressive disorder
- Suicidal risk
- Suicide attempt
- Alcohol use disorder
- Anger
- Impulsiveness.

References:

NR396 Monday, May 21, 3:00 PM - 5:00 PM
Suicidality Incidence in Paroxetine Clinical Trials In Adults
John E. Kraus, M.D. GlaxoSmithKline, Neurosciences MDC, PO Box 13398, Five Moore Drive, Research Triangle Park, NC, 27709-3398, 9000, David J. Carpenter, Pharm.D., John T. Davies, M.S.C., Regan Fong, Ph.D., Pamela S. Barrett, Pharm.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to understand the incidence of suicidality in paroxetine clinical trials in adults.

Summary:
Objective: Paroxetine was associated with increased suicidality (ideation behavior) in adolescents in placebo-controlled clinical trials. This analysis examines to what extent this finding extends to paroxetine-treated adults in clinical trials.

Methods: The dataset comprised 14,911 patients from 57 placebo-controlled trials of paroxetine in depressive and non-depressive disorders (MDD [N=19], Intermittent Brief Depression [N=2], Dysthymia [N=1], Bipolar Depression [N=1], Panic Disorder [N=9], OCD [N=5], SAD [N=5], GAD [N=4], PTSD [N=3], PMDD [N=6], Fibromyalgia [N=1] and alcoholic patients [N=1]). Definitive suicidal behavior (DSB: preparatory act, suicide attempt, or completed suicide) and definitive suicidal behavior or ideation (DSBI; the primary endpoint) incidences were compared between treatments. An independent expert panel blindly reviewed and categorized potential cases as suicidal or non-suicidal. Results are presented as odds ratios (OR) with 95% confidence intervals (CIs).

Results: For all indications combined, there were no significant differences between paroxetine and placebo for DSB (83/8958 [0.93%] vs. 65/5953 [1.09%]; OR = 0.9 [CI 0.7, 1.3]; p=0.649) or DSB (50/8958 [0.56%] vs. 40/5953 [0.67%]; OR = 1.2 [CI 0.8, 1.9]; p=0.483). This was true in the subset of all depression studies and in the subset of all non-depression studies. In MDD patients, however, the incidence of DSB was greater for paroxetine (11/3455 [0.32%] vs. 1/1978 [0.05%]; OR = 6.7 [CI 1.1, 149.4]; p=0.058). All 11 paroxetine cases of suicidal behavior in MDD patients involved a suicide attempt (none were completed), and 8 of these 11 were ≤ 30 yrs old.

Conclusion: Suicidality incidence was similar between paroxetine and placebo overall, but a higher frequency of suicidal behavior was found for paroxetine relative to placebo in adults with MDD, particularly young adults. In light of findings from prior analyses of adolescent datasets, the current data highlight the need for careful monitoring of all patients during paroxetine therapy, regardless of age or diagnosis.

References:

NR397 Monday, May 21, 3:00 PM - 5:00 PM
Course and Predictors of Suicide Ideation Following Inpatient Psychiatric Admission
John C. Cheif, M.D. Laureate Psychiatric Clinic and Hospital, Laureate Psychiatric Clinic and Hospital, 6655 S Yale Avenue 1st Floor, Tulsa, OK, 74136, 9000, Brian C. Lund, Pharm.D., William R. Yates, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to: (a) describe the course of suicide ideation following inpatient psychiatric admission, (b) recognize potential risk factors for resistance to improvement in suicide ideation during the first two days of inpatient psychiatric admission, (c) discuss the implications of these findings on the design of future intervention studies involving patients hospitalized for suicide ideation.

Summary:
Introduction: The impact of antidepressants on suicide risk has received increasing focus. To assist with the design of future intervention studies, this study was designed to characterize the natural course of suicide ideation during the high risk period following inpatient psychiatric admission; further, to identify potential predictor variables.

Methods: A total of 112 depressed patients admitted to an adult crisis stabilization unit for suicide ideation were followed naturalistically for two months. Suicide ideation was measured with the Beck Scale for Suicide Ideation (BSI), including daily assessment during the first week, with decreasing frequency thereafter. Multiple linear regression was used to identify independent predictors of suicide ideation change during two time periods, from admission to day two, and discharge to two months.

Results: BSI scores dropped precipitously post-admission, from 20.2 (95% CI 18.9-21.5) at admission to 10.3 (95% CI 8.9-11.7) at day two. Subsequent changes were modest, dropping to 7.0 (95% CI 5.7-8.5) at two months. Discharge typically occurred between days three and five. Significant independent predictors for less improvement in suicide ideation by day two of hospitalization were higher education levels, increased depressive symptomatology, comorbid anxiety disorder and atypical antipsychotic exposure during hospitalization. Significant independent predictors for less improvement in suicide ideation after discharge included a history of recurrent depression, more prior psychiatric hospitalizations and fewer psychiatrist visits.

Discussion: The most pronounced improvement in suicide ideation occurred within the first two days of hospitalization. Intervention studies must be sensitive to this time period and initiate recruitment as soon as possible upon admission. The most notable course predictor was atypical antipsychotic exposure, which blunted suicide ideation improvement during the first two days of hospitalization, even after adjustment for depression severity and...
diagnosis. Since atypical antipsychotics are common augmenting agents, this relationship warrants further investigation.

References:

NR398 Monday, May 21, 3:00 PM - 5:00 PM
Possibly Suicide-Related Adverse Events in Adult Placebo-Controlled Studies of Sertraline

Douglas Vanderburg, M.D. Pfizer Inc, Neuroscience, 235 East 42nd Street, 325/10/11, New York, NY, NY 10017-5755, 9000, Evan Batzar, M.S., Charlotte M. E. Kremer, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will understand the relative incidence of possibly suicide-related adverse events during short- and long-term treatment with sertraline vs. placebo across multiple indications.

Summary:
Objective: Suicide is an inherent risk in many psychiatric disorders. Previously at the request of FDA, an analysis of possibly suicide-related adverse events (PSRAEs) in adult short-term placebo-controlled trials of sertraline was conducted. A new analysis has now been performed on an expanded study sample encompassing adult placebo controlled studies regardless of duration.

Materials and Methods: Pfizer-sponsored, Phase 2-4 short- and long-term, completed, placebo controlled, adult Major Depressive Disorder (MDD) and non-MDD studies of sertraline were included. In addition to the FDA defined search strategy, all serious adverse event and death listings were searched for PSRAEs during the double-blind phase of the study through 30 days of stopping double blind treatment. All identified PSRAEs were blinded, evaluated and classified independently by two psychiatrists, using the classification system provided by the FDA. Because of the long-term nature of a number of the studies, an exposure-adjusted analysis was also performed.

Results: A total of 126 studies (22,057 patients; sertraline, n=10,923; placebo, n=9,006; active comparator, n=2,128) was included. The incidence rates of PSRAEs were as follows: suicide, 0.04% (95% CI 0.01, 0.09) with sertraline vs. 0.03% (95% CI 0.01, 0.10) with placebo; suicide attempt, 0.22% (95% CI 0.14, 0.33) vs. 0.12% (95% CI 0.06, 0.22), respectively; preparatory acts toward imminent suicidal behaviour, 0.02% (95% CI 0.00, 0.07) vs. 0.02% (95% CI 0.00, 0.08) respectively; and suicidal ideation, 0.26% (95% CI 0.17, 0.37) vs. 0.32% (95% CI 0.22, 0.46), respectively. Similar results are observed in analyzing PSRAEs per years of treatment.

Conclusions: These data from adult short and long-term placebo-controlled trials, analyzed in accordance with an FDA-defined search strategy, show no statistically significant difference in the incidence of possibly suicide related adverse events between sertraline and placebo.

References:
effect of 12 hours and DBDS-MPH designed to replace two doses of IR-MPH with an expected duration of effect of 8 hours.

2) The mechanism of action of methylphenidate. Methylphenidate blocks the dopamine transporter thereby increasing intrasynaptic dopamine.

3) The duration of action in the blood and brain of the new longer acting formulations of MPH by comparing plasma and PET scan findings 10 hours after administration of OROS-MPH and DBDS-MPH.

Summary:

Introduction: A new generation of long acting methylphenidate (MPH) compounds has greatly improved the management of patients with ADHD. Osmotic controlled-release MPH (OROS-MPH) was designed to replace three doses of immediate release (IR)-MPH given four hours apart with an expected duration of effect of 12 hours; Diffucaps Bead-Delivery System (DBDS)-MPH was designed to replace two doses of IR-MPH with an expected duration of effect of 8 hours. The main aim of this study was to investigate the duration of action of OROS-MPH and DBDS-MPH in the brain using PET scanning with a dopamine transporter (DAT) ligand (C-11 Altrpane).

Methods: Twenty-one subjects between 18 and 55 years old with no DSM-IV axis I disorders were enrolled. After baseline scans, subjects were scanned 10 hours after receiving 40 mg of DBDS-MPH or 36 mg OROS-MPH on different days.

Results: Plasma d-MPH levels were lower for DBDS-MPH than OROS-MPH at hour 9 (4.1±1.3 vs. 5.4±2.0, t=4.3, p <0.001), hour 10 (3.8±1.2 vs. 5.2±2.0, t=5.2, p <0.0001), and hour 11 (3.2±0.9 vs. 4.3±1.8, t=4.3, p <0.001). At 10 hours, DAT occupancy of OROS-MPH was significantly greater than DBDS-MPH in all sub-territories of the striatum including the right caudate (44.3±11.8 vs. 34.8±12.9, t=5.1, p=0.001) and left caudate (42.7±10.9 vs. 30.9±13.8, t=5.1, p=0.001). DAT occupancy was significantly correlated with plasma concentration of d-MPH (correlation coefficient 0.78) and not significantly different between formulations.

Conclusions: This study compared the relationship between peripheral and central pharmacokinetic properties of two long-acting oral delivery system formulations of MPH. Despite similar dosing, OROS-MPH had greater plasma concentrations and greater brain effects (DAT occupancy) at 10 hours compared with DBDS-MPH. These results identify important differences in the pharmacokinetic and pharmacodynamic effects of long-acting formulations.

References:


NR402 Tuesday, May 22, 12:00 PM - 2:00 PM

Computation of induced electric currents in three dimensional head model due to transcranial magnetic stimulation

nahla nagy, M.D. Ain Shams Faculty of Medicine, Neuropsychiatry department, 21 Ismail Ramzy st, Heliopolis, Cairo, 00202, 7290, Dina Samy, Noha Hassan, Emad Rasmy

Educational Objectives:

At the conclusion of this presentation the participants should be able to recognize the wide diffusion of induced electric currents resulting from transcranial magnetic stimulation with differential distribution in superficial and deep brain areas on both sides.

Summary:

To date, most effort focused on stimulating localized areas in the brain and limiting hazards posed by transcranial magnetic stimulation (TMS). However, the actual measurement of resulting induced electric currents (J) and their distribution is still a complicated task. The purpose of this study is to compute the magnitude and distribution of J following TMS.

NR401 Tuesday, May 22, 12:00 PM - 2:00 PM

Regional Gray Matter Density Changes in Bipolar Depression

John O. Brooks III, M.D. PAVAHCS & Stanford University, Psychiatry & Behavioral Sciences, 3801 Miranda Avenue, 118J, Palo Alto, CA, 94304, 9000, Julie C. Bonner, M.D., Allyson C. Rosen, Ph.D., Po W. Wang, Terence A. Ketter, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to discuss the changes in gray matter density that are associated with bipolar depression.

References:


Methods: A software head model was created from 120 MRI transverse slices obtained from normal control. The slices were manually segmented and stacked above each other to give 3D reconstruction (Able software Corp, Lexington, MA, USA). The above model was imported to Maxwell 3D, where materials were assigned their electrical conductivities and permittivities using eddy current solver (Ansoft Corporation, France). Modelled coils as figure of eight was placed over the right dorsolateral prefrontal cortex producing magnetic field of 2 tesla at frequency of 8HZ. Results showed the maximum distribution of J as hot spots under the junctional center of the coil and minimum on both sides. The mean currents in different brain structures were computed as high as 56.24a/m² in CSF, compared to values of 4.85a/m² in grey matter and 1.46a/m² in white matter.

References:

NR404 Tuesday, May 22, 12:00 PM - 2:00 PM Hippocampus, Glucocorticoids and Neurocognitive Functions in Patients With First Episode Major Depressive Disorder
Semra Ulusoy Kaymak, M.D., Hacettepe University, Faculty of Medicine, Psychiatry, semraulesoyt@yahoo.com, Turkey
Ankara, 06100, 4890, Ilkan Tatar, M.D., Mustafa Aldur, M.D., M.P.H.

Educational Objectives:
Hippocampal volume was smaller in the drug free patients with first episode major depression. This finding supports that the decrease in hippocampal volume exists in the beginning of the disease. Some cognitive problems seem to be associated with the hippocampal shrinkage. New treatment strategies of cognitive problems may have the hippocampus as a target region. However, peripheral glucocorticoids revealed no correlation with decrease in hippocampal volume. The glucocorticoids, which are thought to be responsible for hippocampal damage, should be investigated with direct methods rather than peripheral glucocorticoid measurements.

Summary:
Introduction: A number of studies using magnetic resonance imaging (MRI) have reported decreased hippocampal volume in major depressive disorder (MDD) but results have been inconsistent. However the hippocampal volume in MDD and the relationship between cognitive functions, excess of glucocorticoids and hippocampal volume in MDD is still subject for discussion.1,2

Methods: The hippocampal volume (3T MRI) was examined in 20 female drug free patients with first episode MDD (mean age: 31.95±8.52) and in 15 age matched healthy females. Hippocampal volumes were normalized to whole brain volumes to account for differences in brain size. Dexamethasone Suppression Test (DST) was used to evaluate the levels and feedback mechanism of glucocorticoids. Digit Span, Logical Memory and Visual Reproduction subtests of Wechsler Memory Scale Revised, Wisconsin Card Sorting Test, Trail Making Test and Verbal Fluency Test were included in the neuro-cognitive assessment battery.

Results: Volumes of right (t6.7, df=33, P<0.001) and left (t6.01, df=33, P<0.001) hippocampus of the patients were found significantly lower than those of the controls. Patients, compared to healthy subjects, were found to have significantly lower scores on measures of attention, working memory, psychomotor speed, executive functions, visual and verbal memory. The performance of the patients particularly in attention, short term verbal memory, word production and executive function domains were positively correlated with hippocampal volumes. However, hippocampal volume reduction was not correlated with DST positivity.

The findings of the study support the reduction of hippocampal volume even in the first episode of MDD and also emphasize the role of hippocampus in cognitive dysfunction. In contrast, the results do not support the idea that glucocorticoids appears to be associated with hippocampal damage.

References:

NR403 Tuesday, May 22, 12:00 PM - 2:00 PM Abnormal Neural Activities during Judging the Appropriateness of Facial Affect in Patients With Schizophrenia
Ji-Woong Kim College of Medicine, Konyang Univ, Dept. of Psychiatry, Dept of Psychiatry, Konyang University Hospital, 685, Gasowon-dong, Seo-Gu, Daejeon, South Korea, Daejeon, 302-718, 5800, Sang Hyuk Lee, Jae-Jin Kim, M.D., Bum Seok Jeong, Jin-Kyun Park, Sung-Eun Kim

Educational Objectives:
We investigated the brain activities during affective ToM (theory of mind) processing, in healthy controls and schizophrenic patients. We identified activation of neural network that is made up of several interactive units that are known to be involved in ToM processing in the control group. But, we cannot observe this activation in patients with schizophrenia. At the conclusion of this presentation, the participant should be able to understand that hypofunction of this network in patients with schizophrenia may be associate with one of the mechanisms of the social inappropriateness and decreased social function in patients with schizophrenia.

Summary:
It has been suggested that impaired social functioning in patients with schizophrenia may be related to impairment of emotional perception and theory of mind. We think that the neuroimaging study investigating the issue of the interaction between emotion processing and theory of mind (ToM) processing may contribute the understanding the mechanism of social cognitive deficit observed in patients with schizophrenia. Fourteen patients with schizophrenia and fifteen healthy control subjects participated in this study. We used functional magnetic resonance imaging to examine brain activation during the judgmental task for the appropriateness of facial affects (affective ToM task) as opposed to gender matching tasks (control task).

Patients with schizophrenia showed hypofunction of neural network that is made up of several interactive units such as medial frontal cortex, left temporal pole, that are known to be involved in ToM and emotional processing. This study suggests that hypofunction of this network may be associated with one of the mechanisms of the social inappropriateness and decreased social function in patients with schizophrenia.

References:

References:

NR405  Tuesday, May 22, 12:00 PM - 2:00 PM  
Treatment Effect Detected by Proton Magnetic Resonance Spectroscopy in Patients With First Episode Depression

Semra Ulusoy Kaymak, M.D. Ankara Hacettepe Hospital, Psychiatry, semraulusoyt@yahoo.com, Turkey/Ankara, 06100, 4890, Demir, Karl #305; O&287;uz, & #351;entürk, Ulu& #287;

Educational Objectives:

The effects of antidepressant treatment in left dorsolateral prefrontal cortex in depression can be evaluated with proton magnetic resonance spectroscopy. While Choline (Cho) is considered to be a marker of membrane turnover, Myoinositol (ml) is seen as a marker of glial cells. We detected a significant increase in ml/creatin (Cr) ratios and a decrease in Cho/Cr ratios after treatment in patients with first episode major depression; however, no changes were determined in NAA values, which is a marker of the neurons. All these findings connote the role of non-neuronal cells, particularly glial cells, in pathophysiology of depression.

Summary:

Recent neuroimaging studies support metabolic, structural alterations in dorsolateral prefrontal cortex (DLPFC), particularly left, in patients with major depressive disorder (MDD). However, there was no clear result on the biochemical changes in DLPFC in patients with first episode MDD. The first aim of this study was to examine the biochemical characteristics of DLPFC as measured by proton (1H) magnetic resonance spectroscopy (MRS) in patients with drug naive first episode MDD and healthy comparison. And the second was to determine the effect of the antidepressant treatment on the metabolites of DLPFC in patients with first episode MDD.

Methods: Seventeen female drug free moderate-severe MDD patients and 13 matched control subjects were studied. Single voxel (1.5 cm³) proton magnetic spectra (TR/TE: 3000/135 and 3000/30 ms) were obtained from left DLPFC for all groups and repeated after antidepressant treatment (8 weeks) for patients.

Results: There were no significant differences in any of the metabolite ratios (N-acetyl aspartate (NAA)/Creatine (Cr), myoinositol (ml)/Cr, and Choline (Cho)/Cr) between patients and comparison subjects. After treatment, Cho/Cr ratios (TR/TE: 3000/135) of patients decreased (P=0.034) and ml/Cr ratios (TR/TE: 3000/30) increased (P=0.032) significantly compared to pretreatment values, although there was no difference in NAA/Cr ratios.

Conclusion: Decreases in the Cho/Cr ratios after treatment might be considered as sign of decrease in membrane turnover. Increases in the ml/Cr ratios might also reveal the effect of the antidepressant treatment on the probable damage in the glial cells. In this study an increase of ml/Cr ratios and a decrease of Cho/Cr ratios after treatment, in the absence of changes in NAA values which is a marker of the neurons, connote the role of non-neuronal cells, particularly glial cells, in pathophysiology of MDD.

References:


NR406  Tuesday, May 22, 12:00 PM - 2:00 PM  
Gender-Related Differences of Brain Function in Major Depression - A Functional Magnetic Resonance Imaging (fMRI) Study Performed By a Perceptual Organization Paradigm

Thomas Sobanski, M.D. Thueringen-Kliniken Saalfeld-Rudolstadt, Psychiatry and Psychotherapy, Rainweg 68, Saalfeld, 07318, 4280, Gerd Wagner, Ph.D., Georgios Sofianos, M.D., Natascha Bischoff, Ph.D., Eckart R. Straube, Ph.D., Heinrich Sauer, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that gender-related clinical differences in major depression may in part be due to distinct gender-related alterations of brain function. As an interesting result of our functional magnetic imaging (fMRI) study we found that the gender bias of fMRI activations was most pronounced within brain structures supposed to be involved in the pathophysiology of the disease.

Summary:

Abstract: Introduction: Gender-related differences of distinct clinical features in major depression are well-established. For instance incidence and prevalence rates in both sexes diverge significantly and the course of the disease varies to a large extent. Nevertheless, up to now little is known on the neurobiological processes underlying these dissimilarities. Hormonal fluctuations have been hypothesized to contribute to the gender bias. Some authors report gender-related differences of 5-HT and noradrenergic neurotransmission.

Methods: The aim of the present pilot study was to assess gender-related differences of regional brain function in major depression. Functional magnetic resonance imaging (fMRI) scans were performed in a group of 10 inpatients with major depression and a control group matched for age and gender. The regions of interest were: frontal lobe; anterior and posterior cingulate gyrus; hippocampus; parahippocampal gyrus; temporal and parietal lobes. fMRI scans were assessed by block design during neurocognitive stimulation with a perceptual organization paradigm. Data were analyzed by the SPM software. Statistical analysis was based on the random effect model.

Results: Depressive patients showed significant gender-related neurophysiological differences that were most pronounced in the frontal lobes (DLPFC, VLPFC, frontopolar gyrus) and the anterior cingulate gyrus. Male depressives had stronger fMRI activations in these areas. Female depressives had stronger activations of the posterior cingulate gyrus and the hippocampus. In healthy controls there was no gender bias of hippocampus activations.

Discussion: Our results add further evidence to the point of view, that distinct alterations of brain function underlie gender-related clinical differences in major depression. The gender bias of fMRI activations was most pronounced within brain structures supposed to be involved in the pathophysiology of the disease.

References:


NR407  Tuesday, May 22, 12:00 PM - 2:00 PM  
Association of Delirium Symptoms with Medication in Terminal Cancer

Pierre Gagnon, M.D. Laval University, Pharmacy, 11 côte du Palais local 4561, Quebec, PQ, G1R2J6, 1220, Pierre Allard,
M.D., Bruno Gagnon, M.D., Chantal Merette, Ph.D., Francois Tardif, M.S.C., Claudia Emond, M.S.C., Valerie Jomphe, M.S.C.

Educational Objectives:

Educational objectives: at the conclusion of this session, the participant should be able to:

- Describe pharmacoanalogical delirium risk factor in terminal cancer patients
- Use psychotropics properly in psychosomatic and palliative medicine

Summary:

Background: Delirium is a severe and frequent complication in terminal cancer reported to be associated with opioids, benzodiazepines, corticosteroids and co-analgesics. However, there is a lack of prospective data to confirm this hypothesis.

Objective: To describe the association between the use of medications with delirium symptoms in terminal cancer.

Methods: 1516 patients admitted for terminal cancer in 7 palliative care units in Canada, who survived longer than 48 hours, were followed from admission until death (average survival: 21 days; average age: 68.4 years) between May 2002 and January 2005. All data were prospectively recorded and delirium symptoms, as rated with the Confusion Rating Scale (CRS), were correlated using multivariate analysis with daily equivalent of opioids (morphine SC), benzodiazepines (lorazepam PO), and corticosteroids (dexamethasone PO), as well as with frequency of prescription of co-analgesics.

Results: We compared the medication taken 48h before the apparition of significant delirium symptoms to the overall delirium-free population. The prevalence of significant delirium symptoms on admission (as defined by a CRS ≥2) was 20% (n = 507) and the incidence during stay was 46% (n = 701). Delirium was associated with higher dosage of opioids (>90 mg daily; OR= 1.451; p=0.0045) and more frequent prescription of co-analgesics (OR=1.59, p=0.0022). A non significant relation was obtained with corticosteroids (OR=1.022; p=0.8652). Surprisingly, higher benzodiazepine dosage showed an inverse correlation with delirium symptoms (≥2mg daily; OR=0.679; p=0.0077).

Conclusions: Analysis of risk factors in terminal cancer remains a complex and challenging task. Opioids and co-analgesics were associated with delirium as predicted by previous studies. The inverse correlation with benzodiazepines remains surprising and may be related to confounding variables, such as physician prescription practice in face of higher delirium risk.

References:

NR408 Tuesday, May 22, 12:00 PM - 2:00 PM
Lamotrigine Improved ADAS-Cog Scores in Subjects With Dementia and Concurrent Psychosis
Ovidio A. De Leon, M.D. University of Illinois Hospital, Psychiatry, 912 S Wood Street M/C 913, Chicago, IL, 60612, 9000, Henry Riordan, Ph.D., Christine K. Moore, Ph.D., Paul Greene, Ph.D.

Educational Objectives:

Based on this presentation, the participant should be able to describe the improvement noted in cognitive performance in patients with dementia after treatment with lamotrigine.

Summary:

Introduction: Lamotrigine has been shown to improve cognitive scores in a controlled study of patients with Alzheimer’s disease (AD) and may have antipsychotic effects as demonstrated in studies of other psychiatric disorders. We evaluated the efficacy of lamotrigine (maximum dose 400 mg/day) versus placebo as adjunctive therapy in treating psychoses in subjects with dementia for 10 weeks.

Method: Medically stable subjects at least 50 years old with current psychosis associated with AD, vascular dementia, or mixed dementia were eligible for participation. A Mini-Mental State Examination (MMSE) score of 14 to 26 and a score of 3 or higher on any hallucination and delusion items of the Neuropsychiatric Inventory-Nursing Home edition (NPI/NH) were required. Subjects with a history of any psychiatric disorder with psychotic symptoms were excluded. Stable concomitant psychotropic therapy was permitted.

Results: Twenty-one subjects were randomly assigned to treatment (12 lamotrigine, nine placebo). More than half (62%) of subjects was female; overall mean age was 76.7 (SD=10.6) years. Baseline MMSE scores were comparable between treatment groups (19.2 [4.4] and 18.3 [4.3] for lamotrigine and placebo, respectively). Six patients discontinued treatment early (5 lamotrigine, 1 placebo), two taking lamotrigine due to adverse events. No adverse events led to discontinuation in the placebo group. No significant treatment differences were noted in the change from baseline to endpoint on measures of psychosis. However, there was a significant improvement in the total Alzheimer’s Disease Assessment Scale (ADAS-Cog) score at Week 10 (mean change [SE] = -3.64 [1.9] and 5.01 [2.1] for lamotrigine and placebo, respectively, using a last observation carried forward approach; p=0.007).

Conclusions: Adjunctive lamotrigine was not effective in treating psychosis in elderly demented subjects as measured by traditional psychiatric scales. However, short-term adjunctive treatment with lamotrigine appeared to improve the overall cognitive performance of subjects with dementia who have psychotic symptoms.

References:

NR409 Tuesday, May 22, 12:00 PM - 2:00 PM
Tolerability of Intramuscular Aripiprazole in Patients with Acute Agitation Associated with Alzheimer’s, Vascular or Mixed Dementia (Study CN138-131)
Chinedu Momah State University of New Jersey, Rutgers University, Rutgers University, State University of New Jersey, Brunswick, NJ, NA, 9000, Stephen Rappaport, David T. Crandall, Robert D. McQuade, Andrei Pikalov, Dan A. Oren, Richard Whitehead

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the tolerability of intramuscular aripiprazole at three separate doses in patients with acute agitation associated with Alzheimer’s vascular or mixed dementia, and discuss the exploratory efficacy findings of aripiprazole treatment in these patients.
the differences in costs among treated and untreated AD subjects receiving anti-dementia therapy have lower annualized direct administrative claims-based data was conducted between 1/1/2000_7/31/2005. All subjects were continuously enrolled for at least 6 months pre- and 12 months post-index, and were followed for a maximum of 4 years. Direct medical costs and comorbidities were evaluated at 12-months intervals. They were compared across cohorts using t-test for univariate and repeated measures models for multivariate adjusting for medical comorbidities, complications of dementia and other variables.

Results: Mean age was similar between diagnosis only and treated cohorts (76.46 vs. 76.54, respectively; p=0.679). The untreated (diagnosis only) cohort (N=7,791) had higher rates (p<0.001) of baseline urinary tract infection (11.9 vs. 8.6%), gangrene (5.2 vs. 3.3%), malnutrition (1.25 vs 0.51%), and aspiration pneumonia (1.44 vs. 0.60%) compared to treated patients (n=7,520). In the multivariate model, the treated cohort had lower adjusted mean direct medical costs ($2,900 vs $3,942, p<0.001) compared with the untreated cohort in year one. However, over the entire 4 year period, the cost effect was not observed.

Conclusion: This study demonstrates that anti-dementia therapy lowers the mean direct medical costs of care in an AD population during the first year of treatment. However, the treatment effect on mean direct medical costs dissipates during subsequent years of therapy.

References:

NR410 Tuesday, May 22, 12:00 PM - 2:00 PM
Direct Medical Costs in Alzheimer’s Disease: A Longitudinal Study Evaluating the Impact of Treatment
Howard Fillit, M.D. Alzheimer’s Drug Discovery Foundation, Executive Director, 1414 Avenue of the Americas, Suite 1502, New York, NY, 10019, 9000, Michael Pollack, M.S., Wing Chow, Pharm.D., Mark Cziraky, Pharm.D., FAHA

Educational Objectives:
At the conclusion of the presentation, the participant will better understand the effect of anti-dementia therapy on direct medical costs in Alzheimer’s disease and related dementias.

Summary:
Introduction: Alzheimer’s disease (AD) affects ~10 percent of elderly persons. Previous studies demonstrated that subjects with AD receiving anti-dementia therapy have lower annualized direct medical costs. Using a large managed care database, we studied the differences in costs among treated and untreated AD subjects over a 4 year period.

Methods: Retrospective cohort study using Healthcare administrative claims-based data was conducted between 1/1/2000_7/31/2006. Subjects were classified on index date as either AD diagnosis only, defined as the first AD-specific ICD-9 code, or receiving AD treatment, defined as the first prescription claim of an AD treatment, identified within an intake period of 1/1/2001 - 7/31/2005. All subjects were continuously enrolled for at least 6 months pre- and 12 months post-index, and were followed for a maximum of 4 years. Direct medical costs and comorbidities were evaluated at 12-months intervals. They were compared across cohorts using t-test for univariate and repeated measures models for multivariate adjusting for medical comorbidities, complications of dementia and other variables.

Results: Mean age was similar between diagnosis only and treated cohorts (76.46 vs. 76.54, respectively; p=0.679). The untreated (diagnosis only) cohort (N=7,791) had higher rates (p<0.001) of baseline urinary tract infection (11.9 vs. 8.6%), gangrene (5.2 vs. 3.3%), malnutrition (1.25 vs 0.51%), and aspiration pneumonia (1.44 vs. 0.60%) compared to treated patients (n=7,520). In the multivariate model, the treated cohort had lower adjusted mean direct medical costs ($2,900 vs $3,942, p<0.001) compared with the untreated cohort in year one. However, over the entire 4 year period, the cost effect was not observed.

Conclusion: This study demonstrates that anti-dementia therapy lowers the mean direct medical costs of care in an AD population during the first year of treatment. However, the treatment effect on mean direct medical costs dissipates during subsequent years of therapy.

References:
Conclusions: Clinicians’ greater emphasis on participants’ responses and reoprts of anhedonia has implications for how depression is diagnosed in this population.

References:

NR413 Tuesday, May 22, 12:00 PM - 2:00 PM
Typical or Troubled? Addressing the Unmet Need of School-based Mental Health Education

American Psychiatric Foundation Board of Directors Maria Llorente is corresponding Miami VA, Psychiatry, 1201 NW 16 ST #116A, Miami, FL, 33125, 9000

Educational Objectives:
1. be familiar with the Typical or Troubled Curriculum
2. recognize the feasibility of implementation of this program in a variety of school settings

Summary:
Introduction: While adolescence can be a difficult time for teenagers and their parents, true mental health problems are often unrecognized. 90% of adults with mental health problems experienced symptoms during their adolescence, and approximately 11% of youth aged 9-17 years have psychiatric disorders resulting in significant functional impairment. To address this critical unmet need for early recognition and intervention, the American Psychiatric Foundation developed a model program for school-based mental health education, designed to raise the awareness of mental disorders in teens for school personnel. A primary aim of this program was then to determine the interest level the feasibility of implementing this training program in high schools in the US.

Methods: The curriculum was piloted in Denver, Colorado and then developed a request for proposals from community organizations, high schools and school districts to implement the program in up to five area schools. APF worked in conjunction with three partner organizations: American School Counselors Association, National Mental Health Association, and School Social Work Association of America.

Results: 139 applications were received, with 64 sent forward by the partner organizations. 16 applications from 14 states were accepted for funding, encompassing 56 schools, 50% of whom were in rural areas, 4000 teachers, and, importantly, 77,473 students. Applications came from 3 school districts, 5 individual schools, and 8 community organizations. The funding costs associated with implementation of this program were $14.75 per teacher.

Conclusions: Highly diverse high schools and school districts have demonstrated a tremendous amount of interest in this educational program. Large numbers of school personnel were able to be trained in a highly cost-effective manner. Results from pre and post testing will be presented.

References:
2. Lobo D, Pérez-Echevarría MJ, Artal J: Validity of the escaloed versión of the General Health Questionnaire (GHQ-28) in span-
ish population. Psychological Medicine, 1996; 135-40.

NR415 Tuesday, May 22, 12:00 PM - 2:00 PM
Psychosocial Training for Caregivers of Patients With Alzheimer's Disease May Prevent or Reduce Caregiver Burden: Impact of Psychosocial Intervention Program on Caregivers' Perceived Health

Luis Agüera Ortiz, Sr., M.D. CSM Arganzuela, Unidad de Salud Mental, C/ Ronda de Segovia 52, 2 planta., Madrid, 28005, 4700, Manuel Martín Carrasco, Sr., M.D., Carmelo Pelegrin Valero, Sr., M.D., Pedro Roy Millán, Sr., M.D., Colso Iglesias García, Sr., M.D., M Jesús Martín Organista IV, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to recognize the importance of the society involvement during Alzheimer disease. Educating patient caregivers and teaching them strategies for solving problems is critical to reduce caregivers stress and for optimal patient management.

Summary:
Background: Most patients with Alzheimer's disease (AD) are living with their families for a long time and frequently Alzheimer's family caregivers experience physical and psychical stress associated to the caring of these patients.
Aim: EDUCA study evaluated benefits of Psychosocial Intervention Program (PIP) on caregivers' burden. This communication is focused on the evaluation of the PIP impact on caregivers' perceived health.
Methods: This epidemiological, longitudinal, parallel-group, open-label, multicenter study conducted by psychologists recruited 115 primary caregivers taking care of patients with clinical diagnosis of AD (DSM-IV-TR criteria, MMSE score 10-26) and at least 2 impaired instrumental activities of daily living (IADL score). Caregivers were randomized to receive either PIP (n=60) or usual advising (n=55). PIP comprised of 8 individual classes (every 1-2 weeks during 4 months) of teaching strategies to reduce caregiver burden and to manage patient's behavior disorders. After a 4-month (at PIP finishing) and a 10-month follow-up period the stress and perceived health of the caregiver were measured using validated scales (Zarit, and SF-36 respectively).

Results: Profile of the cared AD patient was 77-year-old woman, with moderate dementia (MMSE=18.74) and high impairment of daily living activities (mean IADL=2.17). The caregiver profile was 60-year-old woman, usually patient's wife, mean length of caregiving = 3 years and care daily time >12 hours, without refund. Changes in caregiver burden (baseline Zarit score - final Zarit score) showed an improvement for PIP group (-8.09 points) and a worsening for withoutPIP group (+2.08 points), with statistically significant differences (p=0.0083).

Conclusions: Psychoeducational training can minimize caregiver distress and help them to develop strategies for solving problems. This is the reason that PIP improves the perceived health of caregivers of patient with AD.

References:


**Educational Objectives:**

At the conclusion of this presentation, the participants should be familiar with the findings from the British national psychiatric morbidity survey on the prevalence of chronic fatigue and its association with physical illness and symptoms of common mental disorders.

**Summary:**

Background: Chronic fatigue is usually defined as “self-reported persistent fatigue lasting six or more consecutive months”, and is recognized to have association with physical illness. Although many psychiatric factors have also been individually investigated in their association with chronic fatigue, the relationship between physical illness and chronic fatigue has not been established after adjusting these psychiatric factors.

Objective: To describe the prevalence of chronic fatigue in the general population, and to investigate the extent to which its association with physical illness is independent of other psychiatric symptoms.

Methods: Data from the second British National Survey of Psychiatric Morbidity (2000) were analyzed. The survey sampled people aged 16-74 years. Chronic fatigue (significant reported fatigue lasting six months or more) was ascertained using the revised Clinical Interview Schedule (CIS-R). Information on reported physical illness and socio-demographic factors was considered. Psychiatric symptoms were also assessed using the CIS-R.

Results: The prevalence of chronic fatigue was 15.0% and this showed a significant association with the number of reported physical illnesses (odds ratio (OR) per reported illness 1.79, 95%CI 1.68 to 1.90). It was higher in mid-life, in women, in participants with less skilled occupations, and in those with lower educational attainment. Chronic fatigue was strongly associated with the presence of depressive symptoms (OR 5.37), anxiety-related symptoms (OR 4.68), and with sleep complaints (OR 4.41). After adjustment for all socio-demographic and psychiatric factors, number of reported physical illnesses was less strongly but still significantly associated with chronic fatigue (OR 1.51, 1.39 to 1.63).

Conclusions: Physical illness is strongly associated with chronic fatigue. Symptoms of common mental disorders are also associated with chronic fatigue, but the association between physical illness and chronic fatigue is evident even after adjusting for psychiatric symptoms. The assessment of physically ill people should include chronic fatigue and psychiatric symptoms.

**References:**


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**Summary:**

The purpose of the study is to find the relationships of heart rate variability (HRV) and the variances of self report depression and anxiety, and to recognize whether the HRV index may be an objective tool for evaluating anxiety and depression in community mental health survey. Total samples of 414 policemen volunteers were recruited (80.7% male; 19.3% female) in community health survey. The mean age is 38.56±9.0 (19-65). Depression and anxiety were measured by well-validated self-report questionnaires with Zung self-rating anxiety scale (SAS) and Zung self-rating depression scale (SDS). The HRV were derived from a 5-minute segment of ECG recording with the sitting position hearing the relax music. The HRV indices included physical stress index (PSI), SDNN, RMSSD, high frequency (HF-HRV), low frequency (LF-HRV), the ratio of LF to HF (LF: HF-HRV) and total power (TP-HRV) components. The results showed the total scores of SAS and SDS are significantly higher in high PSI group. Both the total scores of SAS and SDS are significantly higher in high PSI group. Both the SAS and SDS scores are significantly higher in high PSI group. From the conclusion of this presentation, the participant would be able to recognize the HRV index may be an objective tool for evaluating anxiety and depression in community mental health survey.

**References:**


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**NR418**

**Heart Rate Variability, Anxiety and Depression in Community Mental Health Survey**

Jia-Fu Lee, Ph.D. Armed Forces Beitou Hospital, Psychiatry, No.60, Sinmin Rd, Beitou District, Taipei, 112, 5830, Chia-Chi Chen, M.S., Yao-Chin Huang, M.D., Chia-Ho Peng, M.D.

**Educational Objectives:**

Here, we examined the relationships of cardiac autonomic function as index by heart rate variability (HRV) and the variances of self report depression and anxiety. The results showed significantly higher SAS scores in Low HRV group than the High HRV group (with index of SDNN, RMSSD, HF-HRV). Both the SAS and SDS scores are significantly higher in high PSI group. From the conclusion of this presentation, the participant would be able to recognize the HRV index may be an objective tool for evaluating anxiety and depression in community mental health survey.

**Summary:**

To describe the prevalence of chronic fatigue in the general population, and to investigate the extent to which its association with physical illness is independent of other psychiatric symptoms. The assessment of physically ill people should include chronic fatigue and psychiatric symptoms.
clinical intent as a consequence of the behaviour. However, the difficulty of evaluating the often ambiguous intentions underlying these gestures, has driven many researchers, mostly suicidologists, to homologate them to other self-harming behaviors with a more clear suicidal intent, as for instance self-poisoning.

The aim of this work is to highlight through a review of the literature on self-injurious behaviors, the need for a clear definition of the concept of self-injurious behaviors and to point out the problems caused by the lack thereof, in particular in the management of the patient’s needs.

Method: Using PubMed, Eric and Psyclnfo research engines we carried out a systematic review of the literature dealing with self-injurious behaviors, published from the end of the 1960s up to the present.

Results: Self-injury (or self-harm) and attempted suicide are used interchangeably as if they were one and the same phenomenon. Many recent empirical researches highlight the importance for professionals to be able to consistently appreciate and name self-injury, as distinct from suicidality, to improve their own therapeutic effectiveness.

The need for this emerges from the World Health Organisation recommendation to label these behaviors as “non fatal suicidal behaviors”.

Conclusion: Since most recent researches show that, although sharing comorbidity factors, suicidal and nonsuicidal behaviors are conceptually different and postulate different therapeutic approaches, there is a strong need for a widely accepted agreement on the use of a standardized terminology to differentiate suicidal from non-suicidal self-injury.

References:

NR420 Tuesday, May 22, 12:00 PM - 2:00 PM Psychopathology in Patients With Suicide Attempts By Self Poisoning as Seen In An Intensive Care Unit
Ahmet C. Koyuncu, Batu Bahat Hospital, Psychiatry, Istanbul University, Istanbul Medical School, Psychiatry Dep., Capa, Istanbul, 34000, 4890, Sibel Cakir

Educational Objectives:
- The participants are going to learn the importance of the manipulative suicidal attempts and psychopathology of self poisoning suicide attempters and draw attention to the seriousness and clinical features of this patient group.

Summary:
Suicidality is one of the most problematic issue which needs emergent effective investigation and care in psychiatry. The heterogeneity of the etiology, different risk factors, type of the suicide attempts and other clinical and psychosocial factors makes the diagnostic and management difficulties. All these variables create complexity to assess the suicidal patients. Seriousness of self poisoning type of suicidality is usually hard to decide about afterwards psychiatric follow up. To clarify the clinical features and psychopathology of suicide attempters we conducted this study among self poisoning suicide patients. 48 patients who treated in Intensive Care Unit (ICU) following suicide attempts by self poisoning were assessed sequentially with Structured Clinical Interview for DSM-IV Disorders (SCID-I). To eliminate the important part of manipulative and impulsive attempt only patients who treated at ICU were included to the study. Other sociodemographics and clinical features were also studied.

Majority of the patient were female (79%) and mean age was 27.68, duration of mean education was 8.1 years. Marriage did not seem as risk or preventive factor; 50 % of patients were married. 78% of patients declared that there were conflicts within the family and close social environment and these provoked the suicide attempts. Emotional problems were notified by 14.6% of the attempts.

81.3 % of patients met at least one DSM-IV diagnosis (66.6 % major depressive disorder) 10.5 % patients have more than one diagnosis. 22.9 % of patients had manipulative suicide attempts and 72.7 % of them did not met any axis I diagnosis.

This study concluded that important amount of the manipulative suicide attempts need a specific care in ICU and may be serious. Other clinical features will be discussed during presentation.

References:

NR421 Tuesday, May 22, 12:00 PM - 2:00 PM The Impact of Care Programs in the Outcome of People With Schizophrenic Disorder in the Community
Maria Fe Bravo-Ortiz, M.D. Hospital Universitario La Paz, Psychiatry, P Castellana 261, Madrid, 28046, 4700, Alberto Fernandez-Liria, M.D., Carlos Gonzalez-Juarez, Maria Alonso-Suarez, Ana Belen Santos-Olmo

Educational Objectives:
- Demonstrate the impact of Clinical Case Management in resource use, quality of life, symptomatology, satisfaction with services and uncovered needs in schizophrenic patients.

Summary:
The present study is about the differential clinical characteristics and their relationship with outcome measures in schizophrenic patients included in three "Clinical Case Management (CCM)" programs in two catchment areas of Madrid (Spain). It's part of an effectiveness study of this case management programs (Project IPSE) in schizophrenic patients that have been attended in three CMHC in two catchment areas in Madrid (Spain). In this areas there exists a Psychiatric Case Register (PCR) since 1985 that includes information about admissions, emergencies and outpatient care.

Objectives: a) To evaluate the effectiveness of Care Programs (PSC) in people with schizophrenic disorders in 2 catchment areas of Madrid after 2 years of follow-up. B) To identify the features that these PSC defines in each one of the studied community CMHC and that they have a bigger impact in the results in the clinical, social state and use of resources.

Method: Prospective study in 2 phases. Retrospective analysis in resource use (emergencies, admissions, consults, rehabilitation). SAMPLE: 267 cases.

Results: 1) Significant reduction of admissions, stays and emergencies in later years to entry in PSC. 2) Significant improvement in 2 years follow-up in quality of life, disability, not covered needs and symptoms. 3) Significant differences between the SSM and the CC in service satisfaction, but not in admissions. 4) When
CRPS is added to PSC they show better results in the use of the emergency and hospitalization.

Conclusions: The PSC turn out to be effective as for the reduction of hospitalization and emergencies, quality of life, reduction of disability and not covered needs. A more detailed analysis is needed to discriminate among those features with major impact in the results.

References:

NR422 Tuesday, May 22, 12:00 PM - 2:00 PM Loneliness and Social Connection in Community Dwelling Elderly
Brian Lawlor, M.D. St. James's Hospital, Psychiatry, St. Patrick's Hospital, James's Street, Dublin, 8, 4190, Jeanette Golden, M.B.Ch.B., Ronan Conroy, Ph.D., Irene Bruce, R.N.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the impact of loneliness and social connection on depression, anxiety and quality of life of community dwelling older people

Summary:
Aims: The aim of this study was to examine the relationship between social network, loneliness, depression, anxiety and quality of life in community dwelling older people living in Dublin.
Methods: 1345 individuals over the age of 65 were recruited through primary care practices and were interviewed in their own homes using GMS- AGECAT. Information on quality of life, loneliness, and social network was obtained using standardized instruments by trained research staff.
Results: Adjusting for age and gender, integrated social networks were associated with a decreased risk of depression. Loneliness was more common in women, increased with age and those with an integrated social network had a significantly lower risk of reporting loneliness. Widowhood significantly increased the risk of loneliness. While widowhood was also associated with an increased risk of depression, this risk was attributable to the effect of loneliness in widowhood. Integrated social network was associated with decreased risk of anxiety and better quality of life. Loneliness and social network type were independent predictors of depression, anxiety and quality of life.
Conclusions: Integrated social network is associated with lower levels of loneliness and a decreased risk of depression and anxiety. The association between network type and loneliness and quality of life are independent of their association with depressive and anxiety disorders. These findings have important implications for the treatment and prevention of mental illness in community dwelling older people.

References:

NR423 Tuesday, May 22, 12:00 PM - 2:00 PM Benzodiazepine Dependency Among Community-Dwelling Seniors
Philippe Voyer, Ph.D. Laval University, Faculty of nursing, Cité universitaire, Quebec City, PQ, G1K 7P4, 1220, Michel Préville, Ph.D., Pamphile Nkogho Mengue, M.S.C.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the typical and atypical symptoms of benzodiazepine dependency among seniors.

Summary:
Benzodiazepines are the type of psychotropic medication most used by seniors (Blazer et al., 2000; Madhusoodanan & Bougurovic, 2004). In 2000, 19.4 % of seniors in Quebec province (Canada) consumed a benzodiazepine (RAMQ, 2001). Benzodiazepine medication is used to relieve symptoms of anxiety and insomnia (Collège des médecins du Québec, 2000). Effectiveness of this medication for treating these symptoms is limited to 30 days of continuous use (Baker & Shaw, 2001; Committee on Safety of Medicines, 1988; Joint Formulary Committee, 2000; Holbrook et al., 2000). Despite this, most seniors use benzodiazepine for longer periods (Bartlett et al., 2004; Isacson et al., 1992; Jorm et al., 2000; Llorente et al., 2000). Consequently, many seniors experience adverse drug reactions having to do with their long-term use of benzodiazepines (Barbone et al., 1998; Berg & Dellasega, 1996; Gray et al., 2003; Lodhi & Shah, 2004; Maxwell et al., 1997; Tamblyn 1998; Verster et al., 2004; Wagner et al., 2004). Drug dependency is one of these potential adverse drug reactions (Mishara et Legault, 2000; Mort & Aparasu, 2002). Benzodiazepine dependency represents a significant public health concern, yet it is insufficiently studied. As far as the authors are aware, there has not been a single Quebec descriptive study to determine the prevalence of this condition among seniors. The goal of this presentation is to determine according to DSM-IV-TR criteria, the prevalence rate of benzodiazepine dependency among elderly people. Results from our population based study conducted in the province of Quebec (n=2402) indicated that 6.9% of elderly users of benzodiazepine are DSM-IV-TR dependent. Typical (DSM-IV-TR) and atypical symptoms of dependency will be discussed. Implications of these results for future research will be discussed (method of data collection). DSM-IV-TR criteria of drug dependency may underestimate the true prevalence of this problem among seniors.

References:

NR424 Tuesday, May 22, 12:00 PM - 2:00 PM Depression in Patients With Dementia: A Community-Based Study Using a National Managed Care Database
Ruby C. Castilla-Puentes, M.D. University of North Carolina, Chapel Hill and Center for Clinical Epidemiology and Biostatistics-School of Medicine, University of Pennsylvania, Psychiatry and Epidemiology, 530 South 2nd St Suite 743, Philadelphia, PA, 19147, 9000, Miguel E. Habeych, M.D.
Educational Objectives:

To demonstrate the high prevalence of depressive disorders in dementia patients
To recognize the significance of the diagnosis of depressive disorder in patients with dementia

Summary:
Background: Comorbid depression is common in all types of dementia. It may, however, appear to be different from classic depression in community based studies.

Objectives: To determine prevalence of depression in patients with a diagnosis of Alzheimer's disease, vascular dementia, and unspecified dementia using the Integrated Health Care Information Solutions (IHCIS) claims database.

Methods: We used the IHCIS claims database to estimate the prevalence of depression in patients with a diagnosis of Alzheimer's disease, vascular dementia and unspecified dementia for the year 2001.

Results: Among the 488,091 patients with full year of eligibility during 2001, 6,440 (1.3%) were identified with a diagnosis of dementia and 63.6% were women. Alzheimer's disease group included 2,947 (45.6%) patients; Vascular Dementia group included 725 (11.8%) patients; and unspecified dementia group included 2,768 (43.0%) patients. The prevalence of depressive disorders was much higher in vascular dementia group (44.1%) and unspecified dementia group (32.4%) compared to Alzheimer's disease group (18.5%). The prevalence of depressive disorders in the controls was 3.4%.

Conclusions: Depressive disorders are common comorbidities or complications of dementia, especially in patients with vascular dementia. Rigorous assessment of depressive symptoms in vascular dementia should be part of good clinical practice.

References:

NR425 Tuesday, May 22, 12:00 PM - 2:00 PM
Risk Factors for Depression in Elderly: The Role of Chemical Mediators, Quality of Life and Religiousity

Claudia Drucker, Sr. Unifesp, Psychiatry, R. Batataes, 391 - cj. 53, Jd. Paulista, San Paulo, 01417-020, 3510, Sergio Luiz Bley, Sr., Ph.D.

Educational Objectives:
Depression in elderly may be associated to several variables that can contribute to the development or maintenance of their state. The present study aims to investigate not only an isolated risk factor but also several clinical and psychosocial variables simultaneously. The objectives are to investigate the chemical mediators roles, clinical and psychosocial factors that can be related to Depression in the elderly.

Summary:
Introduction: Depression in elderly may be associated to several variables that can contribute to the development or maintenance of their state. The present study aims to investigate not only an isolated risk factor but also several clinical and psychosocial variables simultaneously.

Objectives: To investigate the chemical mediators roles, clinical and psychosocial factors that can be related to Depression in the elderly.

Methodology: It is a cross-sectional study whose sample was constituted by 477 elderly, over 60 years-old, living in an institution and in community. Patients having cognitive deficits evaluated with Mini Mental State Examination (MMSE) lower or equal to 13 points and with Clock Drawing Test (CDT-10) lower or equal to 3 points were excluded. Subjects were considered depressed if they presented score higher or equal to 6 points in Geriatric Depression Scale (GDS-15). The chemical mediators analyzed were: reactive C protein (PC-R), cortial; insulin-like growth factor I (Igf1), homocystein and total cholesterol. To assess the functional performance, the instruments used were: Katz and Lawton Scales of Daily Activities and International Physical Activity Questionnaire (IPAQ); religiosity was evaluated by Allport's Frequency Religious Participation Scale and Hoge's Intrinsic Religious Motivation Scale and quality of life by WHOQOL-Brief. The social-demographic, self-referred diseases; physical examination and medication in use data were obtained through structured questionnaires. Statistical analysis was performed through logistic regression.

Results: The results obtained through logistic regression showed that low quality of life in the psychological domain (OR=10.8), use of psychotropic medication (OR=2.0), sleep disturbances (OR=2.7), low Igf1 (OR=2.0), extrinsic and less spiritualized religiosity (OR=2.0) are associated to depression in this sample.

Discussion/Conclusion: Risk factors to depression in this population seem to be related to psychosocial clinical factors and psychopathology ones as well.

References:
medication treatment. Aripiprazole was initiated at 5 mg daily and increased as tolerated. Efficacy outcomes included psychopathology scores (Young Mania Rating Scale/YMRS), Hamilton Depression Scale/HAM-D), extrapyramidal symptom assessments, and level of functioning measurement (Global Assessment Scale/GAS).

Results: Twenty older adults (mean age 59.6 years, range 50-83 years) received aripiprazole therapy. The majority of individuals had bipolar depression. On preliminary analysis, individuals had significant reductions in depression scores (Hamilton Depression Rating Scale/HAM-D base = 13.4, HAM-D end (LOCF) = 7.5, p< 0.001), as well as mania scores (Young Mania Rating Scale/YMRS base= 8.4, YMRS end (LOCF)= 5.6, p< 0.03). There were also significant improvements in functional status as measured by the Global Assessment Scale/GAS (p= .001). Mean daily dose of aripiprazole was 10.26 mg/day SD ± 4.9, range 5-20 mg/day. Overall, aripiprazole was well tolerated in this older adult population.

Conclusion: Aripiprazole appears efficacious and well tolerated in older adults with bipolar disorder. Of particular note, aripiprazole therapy was associated with improvements in bipolar depression in this older population. However, larger, controlled trials are needed to confirm these preliminary findings.

References:

NR427 Tuesday, May 22, 12:00 PM - 2:00 PM
Subjective Memory Complaints and Objective Cognitive Functions of the Elderly Living in the Institution
Jung Sik Lee, M.D. Yongin psychiatric research institute, Psychiatry, Yongin Psychiatric Research Institute, 4 Sangha-ri, Gusan-eup, Yongin, 449-769, 5800, Hongseok Oh, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the association of subjective memory complaints in the elderly with objective cognitive functions, depression and other demographic variables such as sex, age, and education.

Summary:
Objectives: There are inconsistent results about relationships among the subjective memory complaints (SMC), objective memory functions, and depression. The Authors tried to examine the association of subjective memory complaints in the elderly with objective cognitive functions, depression and other demographic variables such as sex, age, and education.

Methods: Total 175 participants living in the asylum for the aged had completed CERAD-K (the Korean version of the Consortium to Establish a Registry for Alzheimer’s Disease) to evaluate neuropsychological function. All of them were evaluated by four specific questions about everyday memory function. Symptomatic of depression were evaluated by SGDS-K (Short Geriatric Depression Scale of Korean version). We divided the elderly into two groups (SMC+ group: SMC- group) to evaluate the differences in cognitive function and depression.

Results: 109 (62.3%) of the subject acknowledged having trouble with their memory. Memory decline and cognitive decline were associated with SMC. SMC+ group scored significantly lower on word delayed recall test than SMC- group, especially. Age, sex and education were significantly associated with SMC in total subject but not education in non-demented subject. Total score of SMC was explained partly by word delayed recall and depression variables in non-demented subject.

Conclusion: This study suggested that association between SMC and objective memory function had clinical implication that SMC was a significant part of MCI criteria associated with early stage of Alzheimer’s Disease.

References:

NR428 Tuesday, May 22, 12:00 PM - 2:00 PM
Cognitive Dysfunction in the Geriatric Depression Living in the Institution
Jung Sik Lee, M.D. Yongin psychiatric research institute, Psychiatry, Yongin Psychiatric Research Institute, 4 Sangha-ri, Gusan-eup, Yongin, 449-769, 5800, Hongseok Oh, M.Ed.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize cognitive dysfunction in the elderly with depression and the association between geriatric depression and demographic variables such as sex, age, and education.

Summary:
Objectives: There is a wide spectrum of cognitive dysfunction in geriatric depression due to heterogeneity. The Authors tried to investigate cognitive dysfunction in the elderly with depression and the association between geriatric depression and demographic variables such as sex, age, and education.

Methods: Total 101 non-demented participants living in the asylum for the aged had completed frontal lobe function test (executive function and conceptualization) and CERAD-K (the Korean version of the Consortium to Establish a Registry for Alzheimer’s Disease) to evaluate neuropsychological function. Symptoms of depression were evaluated by SGDS-K (Short Geriatric Depression Scale of Korean version). We divided the elderly into two groups (depressed, non-depressed group) to evaluate the differences in cognitive function.

Results: 30 (29.7%) of the subjects suffered depression and 50 (49.3%) had cognitive decline. Geriatric depression is not associated with age, sex, and education. Depressed older adults had lower executive function score in total group and cognitive decline group than non-depressed. Within cognitive decline group, subject with geriatric depression had lower scores in word fluency and word delayed recall than non-depressed. There was significant correlation between SGDS-K score and executive function.

Conclusion: Subjects with geriatric depression had significant executive dysfunction. Executive dysfunction in depressed older adults may provide the basis for further investigation of mechanisms of geriatric depression. Timely identification of executive dysfunction fundamental to daily activities of depressed older adults may lead to coping strategies that will improve the prognosis of geriatric depression.

References:
NR429 Tuesday, May 22, 12:00 PM - 2:00 PM

Neuropsychological Prediction of Conversion to Alzheimer's Disease

Inn-Sook Ahn Samsung Medical Center, Samsung Biomedical Research Institute, Department of Psychiatry, Samsung Medical Center, 50 ilwon-dong, Kangnam-gu, Seoul, 135-710, 5800, Doh Kwan Kim, Ji Hae Kim

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to recognize that the individuals who complain subjective memory impairment have an increased risk of future dementia. Thus it is important to evaluate periodically cognitive function and related symptoms using the reliable and objective instrument.

Summary:
- It is well known that Alzheimer's disease (AD) pathology in the brain has appeared before the clinical onset of dementia. The purpose of this study is to explore the cognitive impairment and functional decline among the preclinical AD. 51 non-demented subjects who visited at Geropsychiatry Clinic, Department of Psychiatry were included in the study. Individuals with subjective memory impairment were 25 and individuals with mild cognitive impairment were 26. They completed baseline clinical evaluation and neuropsychological test battery assessing various cognitive functions, activities of daily living, and behavioral problems. 11 subjects were ultimately diagnosed with AD according to DSM-IV 0.5 to 2 years (mean 1.3 years) later and 38 subjects remained non-demented throughout the follow-up period of 4 years. 2 subjects with mixed dementia and vascular dementia were excluded from the analyses. The subjects who subsequently developed AD performed more poorly than non-demented at baseline on the Korean-Rey Auditory Verbal Learning Test (K-AVLT) Word List Delayed Recall, Korean-Rey Complex Figure Test (K-CFT) Delayed Recall, and abstract thinking task. Among the 17 neuropsychological tests, the K-AVLT Word List Delayed Recall (AUC=0.872) discriminated best between subjects diagnosed with AD and non-demented, followed by the K-CFT Delayed Recall (AUC=0.852) and Immediate Recall (AUC=0.830), the K-AVLT Word List Total Learning (AUC=0.793) and Delayed Recognition (AUC=0.785), the abstract thinking (AUC=0.787), and the go-no-go test (AUC=0.724). Our results confirm that cognitive impairment can be detected well before clinical onset of AD. Memory function measures discriminated the most accurately between preclinical AD and subjects who remained non-demented. On the other hand, cognitive functions that decline later in the disease process, such as visuospatial function, would be less useful predictors of early AD. These findings are consistent with the commonly accepted view that some of the earliest brain changes in AD occur in the medial temporal lobe structures.

References:

NR430 Tuesday, May 22, 12:00 PM - 2:00 PM

The Control of Acute Psychosis or Agitation in a Geriatric Population: Use of Intramuscular Ziprasidone

Marijo B. Tamburrino, M.D. University of Toledo, Psychiatry, University of Toledo Health Science Campus, 3000 Arblington Ave., Stop # 1138, Toledo, OH, 43614-2598, 9000, Alina Rais, M.D., Tanvir Singh, M.D., Theodor Rais, M.D.

Educational Objectives:
- At the end of this presentation, the participant should be able to:
  1. list the most common adverse side effects of ziprasidone
  2. describe management of acute psychosis and agitation in geriatric inpatients

Summary:
- The purpose of this open label study was to assess the safety and efficacy of ziprasidone IM in controlling acute psychosis and agitation in geriatric patients. Patients above 60 years old who were admitted to a Geriatric Psychiatry inpatient unit were invited to participate. Exclusion criteria included: history of arrhythmias, recent myocardial infarction, electrolyte imbalance, severe vomiting or diarrhea, and QTc interval > 450. Patients who became acutely psychotic or agitated received ziprasidone IM 10 mg q 6-8 hours, up to a maximum dose of 20 mg/24 hours. Most subjects (79%) received only one 10 mg dose. The Brief Psychiatric Rating Scale (BPRS), Delirium Rating Scale (DRS) and the Behavioral Activity Rating Scale (BARS) were obtained at baseline and at 30 minutes, 2 hours and 24 hours after the first dose of ziprasidone IM. The data were analyzed using paired t-tests comparing individual differences between two variables, and one way repeated measures ANOVA to determine if the means differed over time. Fourteen patients, six male and eight female, mean age 77+ 8 years, participated in this study. Each patient had a diagnosis of dementia, co-occurring with one of the following: delirium, major depressive disorder with psychotic features, schizophrenia, bipolar disorder, or schizo-affective disorder. Physiologic measures, including QTc intervals, remained unchanged pre and post study. Compared with baseline scores, there was significant improvement in BPRS (p<0.001), DRS (p<0.001) and BARS (p<0.001) over time measured at 30 mins, 2 hrs and 24 hours. (BPRS: Baseline=59.6, 30 min=45.7, 2 hrs=37.3 and 24 hrs=49.4, DRS: Baseline=19.1, 30 min=14.8, 2 hrs=12.2 and 24 hrs= 5.6; BARS: Baseline=6.3, 30 min=4.4, 2 hrs=4.4 and 24 hrs=4.9.) This study suggests that ziprasidone IM may be a safe and effective short-term treatment for agitation or psychotic geriatric patients. Larger, double-blind studies are needed to confirm these findings.

References:

NR431 Tuesday, May 22, 12:00 PM - 2:00 PM

Comparative Safety and Tolerability of Alzheimer's Disease Treatments

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand differences in the tolerability and safety profiles of the four medications currently prescribed for Alzheimer's disease.

Summary:

Purpose: Mild to moderate Alzheimer's disease (AD) is currently treated with cholinesterase inhibitors (ChEIs), while moderate to severe AD is treated with the N-methyl-d-aspartate (NMDA) receptor antagonist memantine and the cholinesterase inhibitor donepezil. The purpose of this study is to review the safety and tolerability data for ChEIs and memantine, based upon manufacturers' data found in the prescribing information.

Methods: Prescribing information was obtained from the package inserts of memantine, donepezil, rivastigmine, and galantamine. The safety information from each prescribing information document was extracted and analyzed for trends in safety and tolerability for each medication, compared to placebo.

Results: An inspection of prescribing information data indicated that the ChEIs donepezil, rivastigmine, and galantamine are associated with cholinomimetic effects. Nausea and vomiting were consistently reported across all ChEI trials as the most common reasons for trial discontinuation. Dizziness, anorexia, and diarrhea were also commonly reported adverse events (AEs) in all ChEI trials.

The most frequently reported AEs in memantine trials were dizziness, headache, and confusion. No AEs led to trial discontinuation in >1% of patients at a frequency greater than placebo.

Conclusions: From a regulatory point of view, all currently marketed AD treatments are safe and tolerable, including the co-administration of an NMDA receptor antagonist and a ChEI. Although it is difficult to make comparisons between drugs studied in different trials, available data suggest that AEs most commonly observed in the ChEIs trials (gastrointestinal AEs) are typical of that drug class. Memantine provides an alternative or concomitant therapeutic option with a distinct AE profile.

References:


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Safety and Efficacy of Memantine in the Treatment of Moderate to Severe Alzheimer's Disease: An Updated Meta-Analysis

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Educational Objectives:

At the conclusion of this presentation, participants should be able to recognize the significant benefits of memantine treatment over placebo on measures of cognition, behavior, function and global status for patients with moderate to severe AD. Participants should also recognize that the adverse event profile of memantine is not significantly different from that of placebo, and that discontinuations in clinical trials are significantly lower for patients taking memantine than for those taking placebo.

Summary:

Purpose: Memantine, a moderate-affinity, uncompetitive N-methyl-d-aspartate (NMDA) receptor antagonist, is approved in the US and Europe for treatment of moderate to severe Alzheimer's disease (AD). This updated meta-analysis assesses the overall safety and efficacy of memantine in randomized, placebo-controlled trials in moderate to severe AD.

Methods: Double-blind, placebo-controlled memantine trials of 16-28 weeks duration in patients with moderate to severe AD were collected and analyzed for measures of behavior (Neuropsychiatric Inventory), cognition (Severe Impairment Battery), function (Alzheimer's Disease Cooperative Study Activities of Daily Living-19 item version), and global status (Clinician's Interview-Based Impression of Change plus Caregiver Input). Weighted mean differences and odds ratios with fixed effect models were calculated.

Results: Out of five analyzed trials, two included participants on stable cholinesterase inhibitors. Two new trials have been integrated since the last memantine meta-analysis, one set in US nursing homes and one set in China. Significant effects of memantine were demonstrated on all outcomes, with no evidence that efficacy was driven by outlier trials. Evidence of heterogeneity occurred only on the measure of cognition. Findings were similar using OC or LOCF approaches.

Similar numbers of participants received memantine (n=767) and placebo (n=761). The proportions of all-cause discontinuations and discontinuations due to adverse events (AEs) were significantly lower for memantine than for placebo. The proportion of AEs, SAEs, and deaths were similar between the two groups.

Conclusion: This meta-analysis of five 16-28 week trials in moderate to severe AD shows significant benefits of memantine treatment over placebo on measures of behavior, cognition, function and global status. Memantine was safe and well tolerated.

References:


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A Longitudinal Analysis of Antipsychotic Treatment of Nursing Home Residents with Dementia

Christie Teigland New York Association of Homes and Services for the Aging, Albany, New York Association of Homes and Services for the, 150 State Street, Suite 301, Albany, NY, 12207-1698, 9000, Colene Byrne, Mark Sharp, Gilbert J. L'Italien, A Vickie Tuomari, Robert D. McQuade, Patricia K. Corey-Lisle

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the characteristics of patients with dementia who also have psychiatric disorders or behavioral symptoms and are treated with antipsychotic drugs in nursing homes.

Summary:

Objective: Antipsychotic are commonly used in nursing home residents with dementia who also have psychiatric disorders or behavioral symptoms. We sought to describe the prevalence of antipsychotic treatment and to identify patient characteristics associated with treatment.

Methods: Minimum Data Set (MDS) data from all (n=698) nursing home facilities in New York State (NYS) representing approximately 100,000 long-term residents per year between 1999 and December 2005 were used for this investigation. MDS data were linked to capture all assessments submitted for each resident.
Subjects were limited to long-term residents aged 55 years and older with dementia. Logistic regression was used to estimate the likelihood of treatment based on behavior symptoms.

**Results:** Approximately 33.4% of long-term residents were treated with antipsychotics in 2005 (95% CI 27.0-29.5), an increase from 24.3% treated in 2000. Once treated, residents spent a mean of 15 months on the antipsychotic, or 72% of the total months spent in the nursing home from initiation of medication to discharge or death. Sixty-four percent of residents with psychosis were treated with antipsychotics; 44% of these were also treated with antidepressants. MDS quality indicators associated with treatment were having falls (OR 1.5; 95% CI 1.4-1.6), any behavior symptoms (OR 3.4; 95% CI 3.3-3.6), and delirium (OR 1.6; 95% CI 1.4-1.7). Residents exhibiting specific behavior and psychiatric symptoms were more likely to be treated, including being physically abusive (OR 3.0; 95% CI 2.7-3.4), having hallucinations (OR 2.8; 95% CI 1.4-4.2) and having delusions (OR 2.6; 95% CI 2.0-3.4). Only 24.7% of all treated residents has a diagnosis of psychosis.

**Conclusions:** Long-term residents with dementia who are treated with antipsychotics typically remain on the antipsychotic for most of their nursing home stay. Behavior symptoms are strongly linked to the likelihood of being treated regardless of a co-diagnosis of psychosis.

**References:**


**NR434 Tuesday, May 22, 12:00 PM - 2:00 PM**

**Design Makes a Difference: A Meta-Analysis of Antidepressant Response Rates in Placebo-Controlled versus Comparator Trials of Late-Life Depression**

Joel R. Sneed, Ph.D. Columbia University, Psychiatry, 1051 Riverside Drive, Unit 98, NY, NY, 10032, 9000, Bret R. Rutherford, M.D., David Rindskopf, Ph.D., Harold A. Sackelm, Steven P. Roose, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant will be familiar with all randomized controlled clinical trials in depressed outpatients age greater than 65 in which a placebo or medication comparison condition was used. They will understand that response rates are higher in comparator trials than they are in placebo-controlled trials by approximately 17%. Finally, they will be able to discuss various factors that may affect response rates across different trial designs including patient expectation.

**Summary:**

**Background:** Qualitative reviews of late-life antidepressant clinical trials suggest there is a marked difference in response rates to medication in placebo-controlled versus comparator trials. No quantitative review, however, has been conducted to test this hypothesis.

**Method:** A meta-analysis was conducted of all published articles in peer-reviewed journals from 1985 to the present to identify randomized clinical trials contrasting antidepressant pharmacotherapy to placebo or an active comparator in late-life depressed outpatients. Sixteen studies (9 comparator trials and 7 placebo-controlled trials) were identified. Response rates to medication in both placebo-controlled and comparator trials were extracted and submitted for analysis using mixed effects logistic regression in HLM.

**Results:** We found significant variability in response rates beyond chance. This variability decreased by 30% when we included study type in the model. As expected, response rates to medication in comparator trials were significantly higher (63%) than response to medication in placebo-controlled trials (46%).

**Conclusions:** Response rates are higher in comparator trials compared to placebo-controlled trials. These findings have important implications for clinical trial design, in particular, combined medication and psychotherapy trials that use placebo-controlled medication conditions because the response rates from these conditions are likely to be substantially lower than those from unblinded conditions.

**References:**


**NR435 Tuesday, May 22, 12:00 PM - 2:00 PM**

**Cerebrovascular Disease Risk Factors are not Associated With a Distinct Clinical Profile of Late Life Psychotic Depression**


**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to describe the association between the presence of cerebrovascular risk factors and the clinical presentation of psychotic depression in late life.

**Summary:**

**Objective:** “Vascular depression,” defined by Alexopoulos (1997) as non-psychotic unipolar Major Depression with onset after age 60 and concurrent hypertension, has a different clinical profile (more psychomotor retardation, less insight and guilt, greater impairment of general cognition and executive function) than non-vascular depression. We investigated whether Alexopoulos’ criteria defines a subgroup of elderly subjects with unipolar Major Depression with Psychotic Features (MD-Psy).

**Methods:** Subjects, aged 60 and older, selected from the first 219 participants of the NIMH-sponsored study “Acute Pharmacotherapy of Psychotic Depression,” had a DSM-IV diagnosis of MD-Psy, 17-item Hamilton Depression Rating Scale (HDRS17) score > 21, and at least one delusion. The sample was grouped into “vascular MD-Psy” (defined as presence of hypertension with MD illness onset after age 60) and “non-vascular MD-Psy” (no hypertension with MD illness onset before age 60.) Assessments included the Cumulative Illness Rating Scale-Geriatric version (CIRS-G), Mini-Mental Status Exam (MMSE), Mattis Dementia Rating Scale (MDRS), I-P Scale, and Scale for Assessment of Positive Symptoms (SAPS). We utilized chi-square and t-tests without correction for multiple comparisons.

**Results:** The vascular MD-Psy group (n=39) was older (mean age 75.6 (7) vs. 69.1 (6.5) years, t=-3.84, df=65, p=0.0003) and more medically burdened (CIRS-G total score 8.7 (3) vs. 4.2 (2.5), t=-6.53, df=65, p=0.0001) than the non-vascular MD-Psy group (n=28). The vascular MD-Psy group had worse performance on...
NR436  Tuesday, May 22, 12:00 PM - 2:00 PM
A Comparative Study of the Efficacy With Escitalopram and Paroxetine in Older Depressed Patients With or Without Executive Dysfunction
Kyung phil Kwak, College of Medicine, Dongguk University, Gyeongju, Korea, Department of Psychiatry, Department of Psychiatry, College of Medicine, Dongguk University, Gyeongju, Korea, 780-350, 5800, Kwang Hun Lee, Ji hyun Shin

Educational Objectives:
This was an open-label prospective study to assess the efficacy of escitalopram and paroxetine in older depressed patients (over 60 years old) with or without executive dysfunction.

Summary:
Escitalopram and paroxetine was administered over a 8-week treatment period in 52 nondepressed and depressed elderly patients. Depressive symptoms were measured by Beck Depression Inventory (BDI), Korean Geriatric depression Scale(K-GDS) and Montgomery-Asberg Depression Rating Scale (MADRS). Executive functions were assessed with Controlled oral word association test and the Korean Stroop Color-Word test.

A total of 40 patients completed the study. At endpoint (8 weeks), the mean change from baseline in MADRS total score was -20.2 for patients treated with escitalopram (n = 28) and -19.1 for patients with paroxetine (n = 24), resulting in no difference. The proportion of remitters (MADRS < 12) after 8 weeks was 64% for escitalopram and 61% for paroxetine. Both abnormal Controlled oral word association test and abnormal Stroop Color-Word scores were associated with an unfavorable response of geriatric depression to escitalopram and paroxetine.

There were no significant differences in the efficacy and tolerability between escitalopram and paroxetine. Executive dysfunction increases the risk for poor response of geriatric depression to escitalopram and paroxetine.

References:

NR437  Tuesday, May 22, 12:00 PM - 2:00 PM
M.D. Faculty Salaries in Psychiatry and All Clinical Departments, 1980-2005
Harold Alan Pincus, M.D. Columbia University, Psychiatry, 1051 Riverside Drive, Unit 09, New York, NY, 10032, 9000, Mark G. Haviland, Ph.D., Thomas H. Dial, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize salary differentials between academic psychiatrists and physicians in other clinical specialties as well as increasing salary differentials between department chairs and full professors.

Summary:
Objective: This study compared trends in the salaries of faculty in academic departments of psychiatry with those of faculty in all academic departments.

Method: Data were from the Association of American Medical College's reports on faculty salaries for the years 1980 to 2005. Average Ns for psychiatry for the 26-year span (ranges in parentheses): chair, 91 (74-106); professor, 508 (386-635); associate professor, 536 (347-735); assistant professor, 994 (563-1414); and instructor, 148 (34-336). Total clinical faculty Ns: chair, 1340 (1048-1720); professor, 7913 (4694-11250); associate, 8137 (4327-12685); assistant, 13893 (7189-22946); and instructor, 2132 (541-4352).

Results: Figure 1 shows salaries by position and academic rank for psychiatrists and physicians in all specialties. Salary figures are inflation adjusted (presented in 2005 dollars). The trend lines show increases in salary for physicians in both psychiatry and all departments. Compared with salaries for physicians in all specialties, however, those for psychiatrists were lower and the trend lines were flatter. The large and growing salary differences between chairs and professors that reported for 1980-2001 continued to grow through 2005.

Figure 2 shows inflation-adjusted compound annual growth rates from 1980 through 2005 for faculty salaries by rank, for psychiatry faculty and all faculty. In psychiatry the annual compound growth rate for chairs was 1.5 percent compared with 0.7 percent for professors; for all specialties, those rates were 2.4 percent and 1.2 percent, respectively.

Conclusion: The lower, flatter pay trends in academic psychiatry possibly reflect general inequities and deficiencies in financing for mental health. The recruitment and retention implications of these trends are important because of the widely recognized need for clinician investigators in psychiatry.

Future investigations might examine which factors underlie variation in compensation levels among academic psychiatrists and whether the increasing differentials for chairs of academic departments parallel trends in other sectors.

References:
Summary:
Background: Subthalamic Nucleus Deep Brain Stimulation (STN-DBS) has been shown to significantly improve motor symptoms in advanced Parkinson's disease (PD). In previous reports we have shown that STN-DBS could induce both apathy (Drapier et al, 2006) and fear recognition impairment (Biseul et al, 2006). In regard to these results, we hypothesised that apathy and fear recognition impairment shared the same functional abnormalities so that apathetic patients had an associated fear recognition impairment.

Methods: A consecutive series of 18 patients was assessed three months before (M-3) and three months (M3) after surgery. Mean (± SD) age at surgery was 59.7 (7.6). Mean disease duration at surgery was 12.2 (2.6) years. Apathy was evaluated using the Apathy Evaluation Scale (AES) at both M-3 and M3. Patients were assessed as well using a computerised paradigm of recognition of emotional facial expressions (Ekman & Friesen, 1976), before and after STN DBS. The intact ability to percept faces was firstly assured using the Benton Recognition test.

Results: Apathy significantly worsened at M3 (43.3 ± 9.3 vs. 0.011) after STN-DBS in comparison with M-3 (38.1 ± 6.5). There was a selective reduction of percentages of recognition of facial expressions of fear (54.4 ± 18.8 vs 41.96 ± 22.8, p = 0.049) and sadness (73.78 ± 25.75 vs 55.85 ± 19.9 p = 0.007) after STN DBS. There was a significant correlation between apathy score and fear recognition impairment (r = 0.54, p = 0.019). There was no significant correlation between apathy score and sadness recognition at M3.

Conclusion: As we hypothesised, our results show a correlation between apathy and fear recognition impairment after STN-DBS. Futhermore, we can conclude that apathy and fear recognition networks share same territories in the limbic circuit, particularly in the limbic part of the sub-thalamic nucleus.

References:

NR439 Tuesday, May 22, 12:00 PM - 2:00 PM
Is There a Role of Somatization in the Manifestation of Non-motor Symptoms of Parkinson's Disease?
Harald Murck, M.D. Novartis Pharmaceuticals Corporation, Clinical Development and Medical Affairs - Neuroscience, 1 Health Plaza, East Hanover, NJ, 07936, 9000, Mark Stacy, M.D., Kurt Kroenke, M.D.

Educational Objectives:
At the conclusion of this presentation, participants should recognize the importance non-motor symptoms may play in Parkinson's Disease.

Summary:
Introduction: There is increasing awareness about non-motor symptoms of Parkinson's disease (PD) and recognition that dopamine is also involved in sensory mechanisms, like pain threshold. Somatization is a term which refers to medically unexplained symptoms which may in part be attributable to psychological factors. So called Wearing-Off (WO) occurs when the duration of efficacy of dopaminergic medication shortens in the course of disease progression. Phenomenologically there is an overlap between typical symptoms of patients with somatization and non-motor symptoms of WO, in particular the complex of pain/aching, anxiety and mood changes. Moreover, primarily psychiatric disorders, in particular major depression, have typical "psychomotor" and vegetative expressions, like tremor, bradykinesia, and gastrointestinal complaints.

Method/Results: Recently, we examined the presence of motor- and non-motor symptoms of wearing off using a new 9-question self report screening tool, the WOC-9, in a cohort of PD patients. Of the 216 subjects, 157 reported any symptom benefit from dopaminergic drug therapy. 43 - 50 % of the patients, who reported non-motor symptoms (anxiety, pain, mood-changes), experienced an improvement with the next dose. This was only slightly lower than that of the motor symptoms (slowness, reduced dexterity, which was in the range of 48-66%). However, the report of single non-motor symptoms was much lower (25-48 %) in comparison to motor symptoms (56-80 %). This discrepancy between the reported presence of motor vs. non-motor symptoms, but a similar reported improvement of present symptoms leads to the hypothesis, that non-motor symptoms might be attributed by the patient to motor symptoms, and therefore are not recognized as separate symptoms.

Conclusion: The conceptual framework of PD as a primarily motor disease might conceal the recognition of non-motor symptoms. The importance of these symptoms, independent of the more recognized motor symptoms, requires further emphasis and exploration.

Supported by Novartis Pharmaceuticals.

References:
CPK (obtained in 18/28 episodes within 48 hours of presentation, normal <195) was 4135±999 for NMS [n=3], 311 ± 103 for catatonia with autonomic signs [n=8], and 106±16 for catatonia without autonomic signs [n=7, P<0.05].

Conclusion: Autonomic signs are common in catatonia and may indicate a more severe episode. CPK may be selectively elevated in those catatonic episodes with autonomic signs. These data suggest analysis of autonomic and laboratory indices will support in those catatonic episodes with autonomic signs, catatonia with autonomic signs, and neuroleptic malignant syndrome (NMS).

References:

NR441  Tuesday, May 22, 12:00 PM - 2:00 PM
Handwriting Quantification For Monitoring Drug-Induced Extrapyramidal Side Effects In Patients With Psychoses
Michael Caligiuri, Ph.D. University of California, Psychiatry, 9500 Gilman Drive, 0052, San Diego, CA, 92093, 9000, Hans-Leo Teulings, Ph.D., Charles Dean, M.D., Alexander B. Niculescu, M.D., James B. Lohr, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will have knowledge of a novel approach to the assessment of drug-induced movement disorders in the clinical setting.

Summary:
Clinical trials of new antipsychotic medications often rely on subjective, observer-based ratings of movement abnormalities to evaluate safety and tolerance. Imprecise ratings of these adverse side-effects have often led to inconsistent results from these trials. While there are numerous examples of instrumental procedures for quantifying drug-induced extrapyramidal side effects (EPS), their widespread application in the clinical setting is lacking. The goal of this project is to develop and validate a practical approach to quantifying EPS based on kinematic analyses of handwriting movements for use in the clinical setting.

The instrumentation used to record handwriting movements consisted of a WACOM digitizing tablet and wireless pen. Writing movements were digitized and analyzed using Neuroscript's MoVAlyze software program run on a notebook computer. Schizophrenia subjects with and without clinically observable EPS were instructed to draw loops of different sizes and levels of complexity with each hand. Three variables were extracted from the analysis of pen movements: peak vertical velocity, slope of the velocity x stroke height function (velocity scaling, VS), and a measure of smoothness called normalized jerk. We also collected severity ratings using a variety of standard movement disorder and psychopathology scales and recorded medication histories.

Preliminary results indicate significantly reduced smoothness (p<0.05) for tardive dyskinesia (TD) versus non-TD patients; and significantly lower velocities (p<0.005) and VS slopes (p<0.02) for patients with neuroleptic-induced parkinsonism (NIP) versus non-NIP patients. Medicated patients exhibited lower VS slopes (p<0.05) than unmedicated patients. The handwriting assessment was brief and detected subtle abnormalities not observable with standard ratings.

Findings to date support the validity of our handwriting movement analysis system as a practical tool for monitoring EPS in a variety of inpatient and outpatient neuropsychiatric settings. From an industry and governmental perspective, drug development will benefit from reliable and valid tools for assessing medication-induced side effects.

References:
NR444  Tuesday, May 22, 12:00 PM - 2:00 PM

Are There Any Cognitive Differences Between Patients With Schizophrenia, Schizoaffective Disorder and Delusional Disorder?

Lars Helldin, M.D. Nu Health Care, Psychiatric Department, Department of Psychiatry, NAL, Trollhättan, SE-46185, 4010, Fredrik Hjärthag, B.S.C., Torsten Norlander, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the correlation between cognitive performance, different psychotic disorders and symptom severity

Summary:

Introduction: Despite extensive research into the early detection of schizophrenic psychoses there still do not exist easily applicable or very reliable methods for identifying individuals at risk. The Basel FePsy-study (Früherkennung von Psychosen) therefore tries to contribute to optimising the methods for early risk assessment.

Methods: The project uses a stepwise enrichment strategy for identifying individuals at risk for psychosis. Based on widespread information campaigns 234 individuals at suspected risk were referred to our Early Detection clinic between 3/1/2000 and 2/29/2004. In 54 of these individuals their risk for psychosis could be confirmed using a newly developed screening procedure and the criteria of Yung et al. 1998. These individuals have been examined extensively and 52 of them could be followed up for up to 5 years to detect actual transition to psychosis. Predictors of transition were analysed using logistic regression with backward stepwise elimination (Wald Statistics).
Results: 19 of the 52 individuals at risk have in the meantime made the transition to psychosis. Most transitions occurred during the first two years. Within this population of individuals at risk characteristics such as age, gender, prodromal symptoms or social decline did not further contribute to the prediction of transition, but predictors of transition were certain attenuated psychotic symptoms (suspiciousness), certain negative symptoms (anhedonia/asociability) and certain cognitive deficits (paradigms of disinhibition, planning and problem solving). In an integrated model for predicting transition using these variables the overall predictive accuracy was 76.6 with a sensitivity of 88.2 and specificity of 70.0.

Discussion: At this stage, our approach to early detection of psychosis seems to be promising. Further results from this ongoing study and other studies will hopefully allow to make the prediction of psychosis more reliable in future.

References:

NR446 Tuesday, May 22, 12:00 PM - 2:00 PM
Vardenafil Improves Depression and Quality of Life in Chronic Schizophrenic Outpatients With Erectile Dysfunction
Charalampos I. Mitsonis, M.D. Psychiatric Hospital of Athens, 6th, 7, Metamorfoseos str- Halandri, Athens, 15234, 4840, Nikolaos P. Dimopoulos, M.D., Nikolaos M. Andriotis, M.D., Konstantina E. Stamatooulu, M.D., Fivos E. Tsakiris, M.D., Eleni E. Maragkoudaki, M.D., Maria-Nefeli E. Katsanou, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that vardenafil is not only an effective and safe agent for the treatment of erectile dysfunction in outpatients with chronic schizophrenia but also improves other variables relevant to sexual function such as depressive symptoms and quality of life.

Summary:
Erectile dysfunction (ED) is an important contributing factor for poor quality of life and depression in men with chronic schizophrenia, and a common reason for non-compliance to pharmacological treatment. The aim of this study was to assess the safety and efficacy of vardenafil in chronic schizophrenic outpatients with ED and investigate the effect of vardenafil on depression and quality of life of these patients.

In an open label study, seventeen stabilized outpatients meeting criteria for chronic schizophrenia, who reported ED, were administered vardenafil as needed for 12 weeks, but no more than once a day. The starting dose was 10 mg with possibility to increase the dose to 20 mg. Patients were instructed to take medication one hour before intended intercourse and without regard to food intake. Endpoints included International Index of Erectile Function erection function (IEF) domain, Montgomery-Asberg Depression Rating Scale (MADRS), and Quality of Life Scale (QLS) scores. Blood chemistries, vital signs, and 12-lead electrocardiograms were evaluated at baseline and at weeks 4, 8 and 12. Fourteen patients (82.3%) completed the 12-week study. From the patients who completed the study, 11 (78.5%) needed a dose of 20 mg. There was a statistically significant improvement in the mean scores for EFS (p<0.001), MADRS (p<0.01) and QLS (p<0.05).

NR447 Tuesday, May 22, 12:00 PM - 2:00 PM
Real-World Dosing Patterns of Second Generation Antipsychotics and Adherence
Chi-Chang Chen, Ph.D. Bristol-Myers Squibb Company, Outcomes Research USA, 777 Scudders Mill Road, Plainsboro, NJ, 08536, 9000, Myoung S. Kim, Ph.D., Edward Kim, M.D., Quynh-Van ND Tran, Pharm.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize:
1. Compare real-world dosing patterns of different antipsychotics in patients diagnosed with schizophrenia or schizoaffective disorder
2. The relationship between antipsychotic dosage and treatment adherence in schizophrenia and schizoaffective disorder

Summary:
Purpose: This study compared real-world dosing patterns of second generation antipsychotics (SGAs) with label-recommended dosing ranges. The relationship between dosing and adherence was also examined.

Method: Patients with an SGA claim (aripiprazole, olanzapine, quetiapine, risperidone, or ziprasidone) between July 1, 2003-June 30, 2004, with one year continuous enrollment after index prescription, were extracted from a large claims database (PharMetrics). During one-year follow-up, distributions of average daily dose for each SGA were stratified by the following: psychiatric diagnosis (schizophrenia, bipolar disorder, both schizophrenia and bipolar disorder, and all others); treatment regimen (monotherapy, combination with other atypical, combination with typical, and combination with other atypical and typical); and adherence, defined as having a Medication Possession Ratio (MPR) between 70-110%

Results: A total of 56,414 patients were included; preliminary results for schizophrenia and bipolar patients are reported. Among schizophrenia patients (n=3,042), percentages of prescriptions within the label-recommended dosing range varied from 37.7% (olanzapine) to 93.9% (aripiprazole); olanzapine had the highest rate of below-recommendation dosing (47.0%, significantly higher than aripiprazole, p<0.001) and quetiapine had the highest rate of above-recommendation dosing (20.2%, significantly higher than aripiprazole, p<0.001). Compared to schizophrenia, higher percentages of below-recommendation dosing prescriptions were found in bipolar patients (n=30,102); quetiapine was the highest (88.7%), followed by olanzapine (45.2%), aripiprazole (39.6%), and ziprasidone (38.3%) (all differences were significant, p<0.001). Among SGAs prescribed for schizophrenia patients, olanzapine was associated with the highest adherence (56.5% adherent), risperidone with the lowest (35.2%) (different was significant, p<0.001). Adherence to SGAs was generally lower in...
biological patients than schizophrenia patients, with only 26.4-29.7\% of patients adherent.

Conclusion: This analysis demonstrates the discrepancies between dosing recommended by package inserts and dosing in clinical practice. The degree of difference varied by antipsychotic, psychiatric diagnosis, and treatment regimen. Dosing patterns also appear to be related to treatment adherence.

References:

NR448 Tuesday, May 22, 12:00 PM - 2:00 PM
The Effect of Second Generation Antipsychotic Drugs on Event Related Potentials (ERPs) in Schizophrenia: A Preliminary Study
Albert M. Boxus, M.D. association audoise sociale et medicale, Psychiatrie, ASM Place du 22 Septembre, LIMOUX, 11300, 4279

Educational Objectives:
- At the conclusion of the presentation, the participant should be able to refine the diagnosis of schizophrenia by using cognitive event-related potentials and to evaluate cognitive impact of antipsychotic drugs

Summary:
Background: The effects of the second generation antipsychotic drugs (risperidone, olanzapine, clozapine) on cognitive dysfunction have been investigated by ERPs in schizophrenia. However, at the best of our knowledge, the effect of amisulpride and aripiprazole remain unknown. The aim of this study was to investigate the potential effect of all these drugs on ERPs in schizophrenia.

Methods: Fifty-five individuals (32 males and 23 females; mean age=35.9 [SD=13.8]) meeting DSM-IV criteria for schizophrenia, admitted for an acute relapse, were included in the study and observed within eight months period from 2005/10 to 2006/07. They were treated with the following antipsychotics (mean daily dosage): aripiprazole (13.75 mg), risperidone (5.06 mg), olanzapine (14.12 mg), amisulpride (1000 mg) and clozapine (150 mg). The other psychotropic drugs were prohibited except for cyamemazine (100mg/d during the first week), benzodiazepines, zolpidem and anticholinergic medications. Clinical and electrophysiological evaluations were performed before the start of treatment (T1) and after remission (T2). Psychopathology was measured by the Positive and Negative Syndrome Scale (PANSS) and Brief Psychiatric Rating Scale (BPRS).

Results: The mean follow-up was 5 months.
After treatment, P300 latency was not significantly improved but we observed a significant increase in P300 amplitude (p<0.02). P50 suppression deficit, which was present in 49 subjects at T1, was observed in only 44 patients at T2 (p<0.003). This improvement occurred particularly in patients receiving aripiprazole or risperidone. PANSS and BPRS decreased respectively from 100±12 and 85±8 at T1 to 53±11 and 38±6 at T2 (p<0.01)

Conclusion: The effect of the antipsychotic drugs studied herein are different regarding to the evaluation test used. These results suggest that clinical improvement in response to treatment may be, at least in part, mediated through cognitive change indexed by P300 and P50 suppression in schizophrenia.

References:

NR449 Tuesday, May 22, 12:00 PM - 2:00 PM
Evaluation of Serum Thyroid Hormone Levels in Schizophrenic Patients
Clarissa S. Gama, Ph.D. HCPA, Psychiatry, Rua Ramiro Barcelos, 2350, Porto Alegre/RS, 90035-000, 3510, Fabiano A. Gomes, M.D., Tiago Crestana, M.D., Maria I. Lobato, Ph.D., Paulo S. Belmonte-de-Abreu, Ph.D., Joana A. Palha, Ph.D.

Educational Objectives:
- There has been recent findings in the pathophysiology of schizophrenia about the interaction between external factors such as hormones and vitamins with different nuclear receptors. These receptors interfere in the transcription of several genes that may regulate the disease onset, course and progress, thyroid hormones may be potential candidates for this role (1). The aim of this study is to evaluate the serum levels of TSH, total T4 and total T3 in schizophrenic patients.

Summary:
We included in the study consecutive stabilized adult schizophrenic patients from our outpatient schizophrenia clinic at Hospital de Clinicas de Porto Alegre and healthy controls. We collected demographic, clinical and medication data and the blood samples were drawn in the morning after a 12h fast. Patients, relatives and controls gave informed consent and the project was approved at the local Ethics Committee.
We recruited 68 schizophrenic patients (85.5\% male), mean age of 35.65±8.54 years. The control group consisted of 38 persons (52.6\% male), mean age of 28.84±8.02 years. All patients were taking maintenance antipsychotic therapy (clozapine=28, atypicals = 19, typicals = 21). Six patients presented with hypothyroidism (increased TSH and/or decreased T4 and/or decreased T3) and were excluded from the analysis. There was no case of hypothyroidism in the control group. We found a statistically significant difference (t test) in the total T4 levels of patients (6.18±1.58) and controls (9.54±1.82; p<0.001) and in the total T3 levels of patients (103.78±16.48) and controls (129.08±21.31; p<0.001). There was no significant difference in the TSH levels of patients (2.05±0.98) and controls (1.94±1.20; p=0.64). There was no significant change in the results when we excluded the patients with past or current use of lithium (15 patients).

Our data show significant differences in the levels of thyroid hormones (total T3 and total T4) in schizophrenic patients compared with healthy controls. These results are in line with the hormonal regulation hypothesis of schizophrenia postulated by Goodman (2) and must be replicated in larger samples with additional studies of drug free patients in different stages of the disease, to confirm if it constitutes a vulnerability factor or a trait/state marker. The data suggest that thyroid hormones may be involved in the pathophysiology of schizophrenia with the need of a better understanding of its molecular and biochemical processes.

References:
NR450  Tuesday, May 22, 12:00 PM - 2:00 PM

Comparative effectiveness of rapid acting intramuscular (RAIM) olanzapine and short-acting typical intramuscular (IM) antipsychotics.

Tamas Treuer, M.D. Lilly, Hungaria Kft, H-1075 Budapest, Madách Imre utca 13-14, Budapest, 0000, 4370, Murat Atmaca, Sang Yeol Lee, Peter Pregelj, Mete Saylan, Annu Thakur, Sergio Villasenor

Educational Objectives:

- At the conclusion of this presentation, the participant should be able to demonstrate an understanding of the comparative effectiveness of RAIM olanzapine and short acting typical IM antipsychotics in the acute inpatient setting, and be able to discuss the value of observational studies in providing 'real-life' information.

Summary:

**Objective:** To compare the effectiveness of RAIM olanzapine with that of short acting typical IM antipsychotics as measured by the mean change in the Positive and Negative Syndrome Scale-Excited Component (PANSS-EC) and the Clinical Global Impressions Severity (CGI-S) rating scale at 2, 24, 72 hours and 7 days post initial injection.

**Methods:** This is a prospective, observational study of patients from Africa and the Middle East, Australia, Canada, Central and Eastern Europe, Korea, and Mexico. Inpatients aged >18 requiring >1 injection of a short acting IM antipsychotic, and with a diagnosis meeting the local indication for olanzapine (agitation of acute mania and/or schizophrenia) were included. Comparative analyses were adjusted for potential baseline confounders using linear, logistic or Cox regression. Patient groups were based on the first study injection administered, regardless of subsequent medications.

**Results:** A total of 2011 patients were enrolled from 15 countries; RAIM olanzapine n=1294 (64.3%), other IM antipsychotics n=717. The most commonly prescribed IMs were haloperidol (n=436, 21.7%) and zuclopenthixol acetate (n=107, 5.3%). Baseline agitation scores (mean ±SD) were 24.6±5.88 (PANSS-EC), and 5.4±0.91 (CGI-S). RAIM olanzapine patients experienced a significantly greater decrease in PANSS-EC and CGI-S scores at two hours compared with the other IM group (olanzapine-other IMs, LS mean [95% CI] PANSS-EC: -0.81 [-1.29, -0.34] p<.001, CGI-S: -0.12 [-0.19, -0.04] p=.002). This trend was observed at all assessments (p<.02). Olanzapine RAIM patients also experienced significantly greater symptom improvement at the point of transition to oral medication (PANSS-EC: p=.01, CGI-S: p=.001). In addition, extrapyramidal symptoms were less common for patients in the RAIM olanzapine group (10.0% vs 21.3%, p<.001), as reflected by the prevalence of anticholinergics (13.9% vs 42.5%, p<.001).

**Conclusion:** RAIM olanzapine provided more effective acute control of agitation than other short-acting IM antipsychotics in this trans-regional observational study.

Supported by funding from Eli Lilly.

References:


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NR451  Tuesday, May 22, 12:00 PM - 2:00 PM

Schizoaffective Disorder Prevalence Among Psychosis Patients Using Mini-International Neuropsychiatric Interview


Educational Objectives:

- At the conclusion of the presentation, the participant should be aware of the high clinical prevalence of schizoaffective disorder among patients presenting with psychotic symptoms. They should appreciate the ability of the MINI instrument to quickly and reliably make the diagnosis in these individuals. Geographic differences in concordance between MINI and clinical diagnoses as well as antipsychotic treatment patterns will be discussed.

Summary:

**Background:** Schizoaffective disorder prevalence is 10-30% among patients seeking inpatient hospital care. This ongoing international study evaluated the proportions of patients diagnosed with schizoaffective disorder using MINI, a validated psychiatric structured interview.

**Methods:** Patients between 18-65 years of age with symptoms consistent with acute or chronic psychosis were evaluated clinically and interviewed by the investigator using MINI.

**Results:** To date, 57 patients from 6 US sites and 40 patients from 3 sites in India have been assessed. By MINI, 31.6% (18/57) of US patients were diagnosed with Schizoaffective disorder, 52.6% (30/57) with schizophrenia, 12.3% (7/57) with mood disorder with psychotic features, and 3.5% (2/57) as other. Among the 18 patients diagnosed with schizoaffective disorder by MINI, a clinical diagnosis of schizoaffective disorder was made in 27.8% (5/18); schizophrenia in 55.6% (10/18); and bipolar disorder in 5.6% (1/18); and bipolar disorder in 11.1% (2/18).

By MINI, 30% (12/40) of Indian patients were diagnosed with Schizoaffective disorder, 50% (20/40) with schizophrenia, 7.5% (3/40) with mood disorder with psychotic features or mood disorder NOS, 5% (2/40) with schizoaffective disorder, 5% (2/40) with psychotic disorders, and 2.5% (1/40) with delusional disorder.

Among the 12 patients diagnosed with Schizoaffective disorder by MINI, a clinical diagnosis of Schizoaffective disorder was made in 50% (6/12), schizophrenia in 41.7% (5/12), and psychosis in 8.3% (1/12). Antipsychotic agents combined with antidepressants and/or mood stabilizers were used in more patients enrolled from India (58.3%) than the US (50%).

**Conclusions:** In this convenience sample, the diagnosis of Schizoaffective disorder was more frequently made by MINI than clinical interview, with percentages being comparable to that reported in epidemiologic studies. Further analyses including data obtained from patients enrolled from Eastern Europe and Asian Pacific countries are pending.

References:


NR452  Tuesday, May 22, 12:00 PM - 2:00 PM
Cognitive Effects of Ziprasidone and Clozapine in Treatment-Resistant Schizophrenia: Results From An 18-Week Double-Blind Trial

Philip D. Harvey, Ph.D. Mt. Sinai School of Medicine, Psychiatry, 1425 Madison Avenue, 4th Floor, New York, PA, 10029, 9000, Lewis Warrington, M.D., Antony D. Loebel, Fabio Romeo, M.D., Barbara Gorini, M.D., Allesandro Galluzzo, M.D., Emilio Scahetti, M.D.

Educational Objectives:

At the conclusion of this presentation, the attendee will have acquired the following new information:

Understanding the cognitive benefits of atypical antipsychotic medications in treatment resistant schizophrenia

Understanding the differential cognitive benefits of atypical antipsychotics (clozapine vs. ziprasidone) in treatment resistant schizophrenia

Summary:

Background: Recent data from the CATIE schizophrenia trial has suggested that there may be few differences in cognitive effects of antipsychotic medications. However, assessment of such effects can be complex, due a number of confounds, including subject characteristics and dosage of the treatments. In specific, treatment resistant patients may show a substantial dissociation between clinical and cognitive benefits, with clozapine showing fewer cognitive benefits. This study compared the cognitive and clinical benefits of clozapine and ziprasidone in patients with a history of failure to respond to previous antipsychotic treatments.

Methods: Patients with a documented history of either failure to respond to multiple previous adequate antipsychotic treatments or intolerance of treatment were randomized in double-blind fashion to either clozapine or ziprasidone in a single country (Italy), multi-site trial. Efficacy assessments included the Positive and Negative Syndrome Scale (PANSS) and a cognitive assessment battery examining episodic memory (RAVLT), executive function (Stroop test), and processing speed (Trail-making test Parts A and B).

Results: Analyses of the cognitive variables found statistically significant within group improvements for ziprasidone in learning and delayed recall on the RAVLT and Trail Making Parts A and B. Clozapine treated patients improved on the RAVLT, but not on the trail making test. A composite cognitive score improved in both groups, but the improvements were significantly larger in the ziprasidone group (p=0.029).

Discussion: This study indicated that cognitive functioning improved following treatment with ziprasidone in patients with a history of either treatment resistance or intolerance. While cognitive improvements were only found for a subset of items in the battery, processing speed and episodic memory may be related to functional disability and the overall improvement was larger in the ziprasidone group. These findings are consistent with several prior studies on the cognitive effects of atypical antipsychotics.

References:


NR453  Tuesday, May 22, 12:00 PM - 2:00 PM
Predictors of Long-term Outcome in Schizophrenia: a Double-blind, 196-week Treatment of Ziprasidone versus Haloperidol

Antony D. Loebel Pfizer Inc, US Medical, 235 East 42nd Street, 8th Floor, New York, NY, 10029, 9000, Steven G. Potkin, M.D., Philip D. Harvey, Ph.D., Lewis Warrington, M.D., Cynthia Siu, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to have a greater understanding of the factors associated with the attainment of remission in long-term treatment of schizophrenia.

Summary:

Background: Previous studies have shown a significant longitudinal relationship between remission (1) and quality of life in an almost 4-year, double-blind, schizophrenia study comparing ziprasidone and haloperidol (2). In this paper, we examine potential predictors of remission in that study.

Methods: One hundred and eighty six subjects completed an initial 40-week randomized, double-blind trial and enrolled in a 3-year, double-blind continuation study of ziprasidone or haloperidol. Logistic regression was used to control simultaneously for multiple variables predicting remission (in the final 6 months prior to discontinuation or completion of the trial).

Results: The predictive model found that ziprasidone-treated subjects (N=139) had a 3-fold increase in the likelihood of remission than the haloperidol-treated subjects (N=47) (p=0.03), after controlling for baseline characteristics. The following factors were significantly associated with sustained remission for all treatment groups in the model: better baseline QLS total score (p=0.001), Caucasian race (p=0.006), schizoaffective disorder (OR 3.9; p=0.02), lower baseline symptom severity (p=0.02), younger age (p=0.038), no prior psychiatric hospitalization (p=0.046), and no family history of psychotic illness (p=0.07). Single (never married) subjects were less likely to attain remission (p=0.035). The predictive validity of these findings was confirmed using the area under the receiver operating characteristic curve (ROC) (AUC 0.85, SE=0.03, 95% CI 0.8-0.9).

Conclusions: These findings are consistent with previous reports showing that patients with relatively good prognosis may be less chronically ill and have a schizoaffective diagnosis, lower symptom severity, history of close interpersonal relationship and a favorable global QLS score. Treatment with ziprasidone was a significant predictor for sustained remission. These results suggest the potential for enhanced symptom remission and long-term outcomes among patients treated with a second-generation antipsychotic.

References:


NR454  Tuesday, May 22, 12:00 PM - 2:00 PM
Prevalence of Liver Disease in Medicaid Recipients with Schizophrenia or Bipolar Disorder

Jasmanda H. Wu, Ph.D. Ortho-McNeil Janssen Scientific Affairs, LLC, Outcomes Research, 1125 Trenton-Harbourton

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The true prevalence of liver disease have a higher prevalence of liver disease than Medicaid recipients with schizophrenia or bipolar disorder as compared to non-men-

Educational Objectives:

To understand the relationship between early response to treatment with antipsychotic drugs and the patient’s subsequent treatment outcomes.

Summary:

Objective: To test whether early onset of response to antipsychotic medications accurately predicts subsequent response in the treatment of patients with schizophrenia.

Methods: We used data from 5 randomized, double-blind clinical trials comparing olanzapine with other atypical antipsychotic drugs in the treatment of patients with schizophrenia, schizoaffective disorder, or schizophreniform disorder, who were at least moderately ill at baseline (N=1314). Conditional probabilities (sensitivity, specificity, positive and negative predictive values) were used to characterize the likelihood of “ultimate response to treatment” (defined as at least 20% improvement from baseline on the PANSS total score during treatment for up to 3 months [endpoint of this analysis]), based on achieving at least 20% improvement on the PANSS total score at 2 weeks. In addition, Receiver Operating Characteristic (ROC) curve was generated to predict ultimate response by the magnitude of improvement in PANSS total at 2 weeks.

Results: Using the conditional probabilities approach, 90% of non-responders at endpoint were correctly identified as non-responders at 2 weeks (high specificity). However, only 45% of responders at endpoint were correctly identified as responders at the 2-week time point (moderate sensitivity). The area under the ROC curve (AUC) was 77%, indicating that the magnitude of early symptom improvement at 2 weeks can discern subsequent response at 3 months.

Conclusions: Early non-response to antipsychotic medications appears to be a strong predictor of subsequent lack of response in the treatment of patients with schizophrenia. Further research is needed to determine if early non-responders will benefit from a switch to another antipsychotic agent in order to minimize exposure to potentially ineffective or suboptimal treatment.

References:


NR455 Tuesday, May 22, 12:00 PM - 2:00 PM

Predicting Response to Atypical Antipsychotics Based on Early Response in the Treatment of Schizophrenia

Educational Objectives:

At the conclusion of this presentation, the participant should have a better understanding of the relationship of patient beliefs about antipsychotic medication use and their likelihood of discontinuing treatment prematurely.

Summary:

Background: The objective of this study was to examine the relationship between patient beliefs about medication use and their likelihood of discontinuing treatment prematurely. Associations of patient beliefs about medication with clinical psychopathology and their life satisfaction were also assessed.

References:

2. Kilbourne AM, Cornelius JR, Han Xiaoyan, et al: General-medi-

Methods: This post-hoc analysis used data from a randomized, open-label, 1-year trial of antipsychotics in the treatment of patients with schizophrenia or schizoaffective disorders (N=664). Medication management was at doctors' discretion, reflecting naturalistic treatment in usual clinical care settings. Patient-reported beliefs about medication were assessed by Rating of Medication Influences (ROMI), degree of clinical psychopathology was measured by Positive and Negative Syndrome Scale (PANSS), and patient quality of life was measured by Lehman Quality of Life Interview (LOLI).

Results: Patient perception of medication benefit was the only strong predictor of treatment duration among the 5 underlying dimensions of medication influences. Low level of perceived beneficial effect of medication was associated with greater likelihood of early treatment discontinuation (Hazard Ratio=1.78, 95% Confidence Interval [1.26, 2.51], p=0.001) Patients with greater beliefs in the beneficial effect of treatment also had better clinical psychopathology outcome and were more satisfied with their quality of life and well-being.

Conclusion: Understanding the predictors of early treatment discontinuation in the care of schizophrenia patients is important for the development of interventions to improve treatment adherence. Current findings suggest that patient perception of beneficial effect of medication may be a critical factor in patient motivation for treatment adherence and hence a determinant of a satisfactory treatment outcome.

References:
2. Cramer JA, Rosenheck R. Compliance with medication regi-

NR457 Tuesday, May 22, 12:00 PM - 2:00 PM
Functional, Clinical, and Economic Ramifications of Early Non-Response to Antipsychotics in the Naturalistic Treatment of Schizophrenia

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Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that in the naturalistic treatment of schizophrenia, early non-response to treatment with antipsychotics appears to accurately predict subsequent non-response to treatment. Compared to early responders, early non-responders appear to have poorer clinical and functional outcomes, to perceive their medication as less beneficial, and to incur substantially higher total treatment costs. Findings suggest that early non-responders may benefit from change in antipsychotic regimens to minimize prolonging exposure to sub-optimal or ineffective treatment alternatives.

Summary:
Objective: To compare the functional, clinical, and economic outcomes of patients who did and did not have early response to antipsychotic medication evident at 2 weeks into the naturalistic treatment of schizophrenia.
Methods: This post hoc analysis used data from a 1-year, multi-site, randomized open-label study of antipsychotics in the treatment of schizophrenia, conducted in the U.S. between 5/1998 and 9/2002. “Response” was defined as at least 20% improvement on the PANSS total score from baseline; “Early Response” as at least 20% improvement at 2 weeks. Patients with early response were compared to patients without early response (“early non-responders”) on standard psychiatric outcome measures following 8 weeks of treatment. Systematic abstraction of medical records provided resource utilization data for calculating total direct treatment cost per patient for the first 8 weeks of treatment. Statistical comparisons were made both unadjusted and adjusted for a set of patient characteristics, identified a priori.

Results: Early response/non-response at 2-weeks predicted subsequent response/non-response at 8-weeks with high overall level of accuracy (73%). Almost all (90%) non-responders at 8 weeks were correctly identified at 2 weeks (high specificity). Compared to early responders (N=108, 22%), early non-responders (N=389, 78%) were significantly more likely to experience, at 8 weeks, poorer levels of functioning, were less likely to perceive adherence with medication as beneficial, and incurred significantly higher total treatment costs. Early non-responders were twice as costly as early responders ($4,264 vs. $2,017 following 8 weeks of treatment, p<.01).

Conclusions: In the naturalistic treatment of schizophrenia, early non-responders appear to have poorer clinical and functional outcomes, to perceive medication as less beneficial, and incur substantially higher total treatment costs compared to early responders. Findings suggest that early non-responders may benefit from change in antipsychotic to minimize prolonging exposure to sub-optimal or ineffective treatment alternatives.

References:

NR458 Tuesday, May 22, 12:00 PM - 2:00 PM
Association Between Antipsychotic Dose and Treatment Adherence Among Patients With Bipolar Disorder With Predominantly Depressive Symptoms

Frank D. Gianfrancesco, Ph.D., HECON Associates Inc., Health Economics, 9833 Whetstone Drive, Montgomery Village, MD, 20886, 9000, Martha Sajatovic, M.D., Kritika Rajagopalan, Ph.D., Ruey-Hua Wang, M.S.

Educational Objectives:
At the conclusion of this session, the participants should be able to understand the association between antipsychotic dosing and treatment adherence in patients with bipolar disorder experiencing predominantly depressive symptoms.

Summary:
Introduction: Treatment adherence may be adversely impacted with higher antipsychotic doses, as side effects may be exacerbated. This study evaluated the association between antipsychotic dose and treatment adherence among patients with predominantly depressive symptoms of bipolar disorder.

Methods: Claims data for antipsychotic treatment episodes in commercially insured patients with bipolar disorder and predominantly depressive symptoms (ICD-9-CM) were examined. Adherence was measured by intensity (regularity of prescription refills captured by the medication possession ratio [MPR]) and treatment duration.

Effects of higher doses (in chlorpromazine equivalents) of risperidone, olanzapine, quetiapine, ziprasidone, aripiprazole, and typical antipsychotics on both components of treatment adherence
were evaluated using multiple regression analysis. Dose effects on adherence intensity were evaluated over successive stages of treatment.

**Results:** There were 2597 treatment episodes for patients with bipolar disorder with predominantly depressive symptoms. Olanzapine and the typical antipsychotics showed reduced adherence intensity with higher doses in all stages of treatment, with most achieving significance (P<0.05). Risperidone and quetiapine showed increased adherence intensity with higher doses in the initial stage of treatment (P<0.05), with risperidone showing decreased intensity in a later stage (P<0.05). None of the relationships showed significant changes in weight and weight-related quality of life.

**Conclusions:** For patients with bipolar disorder and predominantly depressive symptoms, higher doses of olanzapine and typical antipsychotics appear to adversely impact adherence intensity during all stages of treatment, possibly reflecting the influence of adverse events. Higher doses of quetiapine and risperidone appeared to promote adherence intensity in the initial stage of treatment, possibly because of greater effectiveness. Higher doses of all atypical antipsychotics, except olanzapine, appeared to encourage longer treatment duration, which may also be related to better symptom control.

Supported by funding from AstraZeneca Pharmaceuticals LP.

**References:**

**NR459**

**Tuesday, May 22, 12:00 PM - 2:00 PM**

**Are Changes in Weight and Weight-Related Quality of Life Meaningful in Community Patients with Schizophrenia Treated With Aripiprazole or Standard of Care?**

Patricia K. Corey-Lisle, Ph.D. Bristol Myers Squibb, Global Epidemiology and Outcomes Research, 5 Research Parkway, Wallingford, CT, 06492, 9000, Ronette L. Kolotkin, Ph.D., Ross D. Crosby, Ph.D., Hong J. Kan, Ph.D.

**Educational Objectives:**
At the conclusion of the presentation, the participant should be able to demonstrate increased knowledge about how clinical meaningful changes in weight-related quality of life can be determined from a validated instrument and how this can be applied in clinical research.

**Summary:**
**Background:** Since weight gain is a distressing side effect of antipsychotic medications in patients with schizophrenia, we assessed changes in weight and weight-related quality of life (QOL) among outpatients treated with aripiprazole and standard-of-care (SOC).

**Methods:** Patients requiring medication changes due to efficacy or tolerability issues (n=544) were randomized to ARI (n=278) or SOC (n=266). Weight and weight-related QOL (using the IWQOL-Lite) were assessed at baseline, and weeks 8, 18 and 26. Weight changes and QOL were evaluated between ARI and SOC using random regression analysis across time points using all available data and controlling for baseline values. Meaningfulness of change in IWQOL-Lite scores was assessed using a published algorithm integrating both anchor-based and distribution-based methods, accounting for baseline severity and regression to the mean. This algorithm allows determination of the percent of participants in each group at each level of baseline severity exhibiting meaningful improvement.

**Results:** Baseline demographic characteristics, BMI, and IWQOL-Lite scores (except Work) were comparable between groups. ARI participants lost an average of 1.5% of their baseline weight in comparison to a gain of 1.4% by SOC participants (P<0.0001). ARI participants experienced significantly greater increases in Physical Function, Self-Esteem, Sexual Life, and IWQOL-Lite total score compared to SOC participants (all P's < .01). Among all participants, 17.6% of ARI experienced clinically meaningful improvements in IWQOL-Lite score compared to 11.3% of SOC participants (P= .046). Among participants who had moderate to severe impairments in weight-related quality of life at baseline, 43.5% of the ARI group (27 of 62) vs. 25.8% of the SOC group (17 of 66) experienced meaningful improvements in IWQOL-Lite total score (P=.049).

**Conclusions:** Compared to patients treated with SOC, aripiprazole treatment was associated with significant reductions in weight and a greater proportion of meaningful improvements in weight-related quality of life.

**References:**
tomatology; upward dose titration in first 60-days and prior antipsy-
chotic monotherapy. Logistic regression identified three factors
related to response: female gender (OR 1.51 95% CI [1.1,2.1],p= 0.02), concomitant benzodiazepine therapy (OR 1.49 95% CI
[1.1,2.1], p=0.02), and upward dose titration (OR 2.0 95% CI
[1.4,2.8], p=0.0001). Response rates did not differ significantly
according to antipsychotic agent, although the newer agents (ari-
piprazole, ziprasidone) trended toward a higher response rate than
the older agents (olanzapine, quetiapine).

Conclusions: In addition to the choice of therapy, there are
relevant patient characteristics that may predicting response to
therapy. Upward dose titration on initiation or change of medica-
tion should be considered as a routine standard of care.

References:
1. Gasquet, I., et al., Pharmacological treatment and other pre-
dictors of treatment outcomes in previously untreated patients
with schizophrenia: Results from the European Schizophrenia
Outpatients Health Outcomes (SO-HO) study. International
Clinical Psy.

2. Van Brunt, D., et al., Statistically determining treatment of
choice for individual patients with schizophrenia. Value in
Health, 2005.

NR461 Tuesday, May 22, 12:00 PM - 2:00 PM
Comparison of Aripiprazole and Haloperidol in Early
Episode Schizophrenia

Edward Kim, M.D. Bristol-Myers Squibb, Neuroscience Medical
Strategy, 777 Scudders Mill Road, Plainsboro, NJ 08536,
9000, James Eudicone, M.S., Kimberly Portland, Ph.D., Andrei
A. Pikalov III, M.D., Quynh-Van Tran, Pharm.D.

Educational Objectives:
At the conclusion of this presentation, the participant should
be able to understand the comparative efficacy and safety of
aripiprazole and haloperidol in the treatment of patients with early
episode schizophrenia.

Summary:
Objective: To assess the efficacy of aripiprazole compared to
haloperidol in patients early episode schizophrenia.
Method: Data from two 52-week double-blind randomized con-
trolled trials (31-98-217 and 31-98-304) comparing aripiprazole
with haloperidol were pooled for posthoc analysis. Patients in the
efficacy sample were classified as “early episode” if they were
less than 40 years of age with a duration of illness less than or
equal to 60 months. All others were classified as “chronic”. Within
each subgroup, we conducted an ANCOVA on the Positive and
Negative Syndrome Scale (PANSS) and Montgomery-Asberg De-
pression Rating Scale (MADRS) baseline to endpoint change
(LOCF) with baseline score, treatment, and protocol as covariates.

Results: The efficacy sample of 1269 patients yielded 360 cases
meeting inclusion criteria (237 aripiprazole, 123 haloperidol). In
this sample, the mean change in PANSS total score was -21.8
(SD 2.4) for aripiprazole and -15.3 (SD 2.9) for haloperidol (p =
0.02). Aripiprazole was also superior on the PANSS negative
and general subscales (p = 0.03 and 0.02, respectively). The mean
change in MADRS total score was -1.2 (SD 0.8) for aripiprazole
and +1.3 (SD 1.0) for haloperidol (p=0.01). In patients with chronic
schizophrenia there were no significant differences between aripi-
prazole and haloperidol on change in PANSS or MADRS scores.

Conclusions: Aripiprazole demonstrated superior efficacy to hal-
operidol in reducing psychotic and depressive symptoms when
administered to patients with early episode schizophrenia in a
posthoc analysis of two 52 week trials. This difference was not
demonstrated in more chronic patients.

References:
1. Sanger TM, Lieberman JA, Tohen M, Grundy S, Beasley C Jr,
2. Schooler N, Rabinowitz J, Davidson M, Emsley R, Harvey PD,
et al: Risperidone and haloperidol in first-episode psychosis: a
long-term randomized trial. Am J Psychiatry. 2005
May;162(5):947-53.

NR462 Tuesday, May 22, 12:00 PM - 2:00 PM
What are the Functional Implications of
Neuropsychological Normality in Schizophrenia?

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Psychiatry, 1425 Madison Avenue, 4th Floor, box 1230, New
York, NY, 10029, 9000, Philip D. Harvey, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should
understand how different degrees of cognitive impairment affect
social and functional deficits in schizophrenia.

Summary:
Cognitive dysfunction is considered a core feature of schizo-
phrenia and is the most robust and stable predictor of functional
disability. Yet, a large minority of patients performs within the
normal range of functioning on neuropsychological instruments.
Little is known about the functional status of these neuropsycho-
logically normal (NN) schizophrenia patients. In this study (N= 245)
of cognitive and functional status in schizophrenia, 16% of
patients performed within 1 SD of the population mean on a cogni-
tive composite score. NN patients had lower negative symptom
ratings but were equivocal in positive symptoms. Ratings from
case managers and performance based measures indicated
greater functional and social skills in the NN patients. However,
they were just as likely to live in restricted environments (NN=
70%, Impaired =60%), be unmarried (NN=64% Impaired=54%),
and be unemployed (NN=91%, Impaired=89%). Stepwise regres-
sion analyses revealed social skills, functional skills, and positive
symptoms as predictors of outcome in the impaired patients (R2=
.25) but only mood dysfunction to predict outcome in the NN
patients (R2=.16). Cognitively intact patients with schizophrenia
have better social and functional skills than those with cognitive
impairment. However, despite better cognitive ability, less severe
negative symptoms, and better functional skills, there was no
increased tendency to live independently, work, or be married.
Mood dysfunction might be a rate limiter for functional recovery
even if cognitive impairments are improved. These findings have
direct relevance to clinical trials. Cognitive enhancement might
be only a small initial step in reducing disability. Functional recov-
er will likely require a comprehensive treatment approach and
systematic changes in service delivery to promote independence.

References:
1. Bowie CR et al: Determinants of real-world functional perform-
ance in schizophrenia subjects: correlations with cognition,
functional capacity, and symptoms. Am J Psychiatry 2006;
2. Harvey PD et al. Improvement in social competence with short-
term atypical antipsychotic treatment: a randomized, double-
blind comparison of quetiapine versus risperidone for social
competence, social cognition, and neuropsychological func-
tioning. Am.
Neurocognitive Dysfunction Correlates with Suicidal Behavior in Schizophrenia
Sung-Wan Kim, M.D. Chonnam National University Hwasun Hospital, Psychiatry, 160, Ileim-ri, Hwasun-up, Hwasun-gun, Jeonnam, 519-809, 5800, Woong-Jang Kim, Sam-yeon Lee, Yo-Han Lee, Dong-Seok Yang, Il-Seon Shin, Jin-Sang Yoon

Chonnam National University Hwasun

Summary:
Introduction: Neurocognitive deficits are regarded as a core feature of schizophrenia. While up to 50% of patients with schizophrenia attempt suicide during their lifetime, only a few studies have investigated the relationship between suicidal behavior and neurocognitive function.

Method: The study population consisted of 110 patients that met the DSM-IV criteria for schizophrenia. Current and past suicidal behaviors were assessed using the item 'suicidality' on the Brief Psychiatric Rating Scale and suicide attempt history, respectively. Neurocognitive function was evaluated using the Mini Mental State Examination (MMSE) and a computerized battery consisting of the Digit Span Test, Verbal Learning Test (VLT), Continuous Performance Test, Wisconsin Card Sorting Test (WCST), Finger Tapping Test, and Trail Making Test parts A and B. The associations between suicidal behavior and neurocognitive function and clinical characteristics were analyzed.

Results: Current and past suicidal behavior correlated very significantly with each other. There were significant positive correlations between current suicidality and the Positive And Negative Syndrome Scale (PANSS), Calgary Depression Scale for Schizophrenia (CDSS), and Barnes Akathisia Scale (BAS) scores. Current suicidality was significantly negatively correlated with the scores on the MMSE and the number of words recalled in the first trial of the VLT, even after controlling for age, and the PANSS, CDSS, and BAS scores. Subjects with a history of a suicide attempt performed significantly worse on the WCST than those without a history.

Conclusion: The results of this study were not consistent with previous studies, which have reported that suicide attempts had better neurocognitive function than non-attempters, or that suicidality did not correlate with neurocognitive function. The findings suggest that suicidality is related to cognitive rigidity or memory impairment. Further study is warranted to examine the neurocognitive correlates of suicidality.

References:
improvement. We examined initial titration rates in pooled data from 2 similarly designed fixed-dose (40, 80, 120, or 160 mg/d) placebo-controlled studies of ziprasidone in patients with acute schizophrenia and schizoaffective disorder (ziprasidone, N=369; placebo, N=171). These dosages were attained by days 1, 1, 3, and 3 for 40, 80, 120, and 160 mg/d, respectively. Efficacy was assessed using PANSS at Weeks 1 and 6 (LOCF end point) of treatment, while tolerability was assessed by discontinuations (all-cause and due to adverse events). At Week 1, least-squares mean PANSS total score decreases from baseline were 6.2, 5.7, 7.8, 9.0 and 0.84 in the 40, 80, 120, 160 mg/d and placebo groups, respectively. A significant linear dose-response relationship between ziprasidone dose and PANSS total score (F = 16.00, P ≤ 0.001) was observed at Week 1. All ziprasidone doses produced a significant improvement in PANSS total score at Week 1 with the largest effect size (0.52) observed for the 160 mg/d group. No significant adverse event discontinuations at Week 1 were infrequent and did not vary by dose. These results indicate that rapid titration of ziprasidone to 160 mg/d in subjects with acute schizophrenic illness is associated with greater efficacy compared with lower doses and is well tolerated.

References:

NR466 Tuesday, May 22, 12:00 PM - 2:00 PM
Annual Healthcare Costs of Schizophrenia Patients Treated with Olanzapine vs. Quetiapine in a Medicaid Population: An Application of Propensity Score Method with Optimal Matching Algorithm
Glenn A. Phillips, Ph.D. Eli Lilly and Company, US Outcomes Research, Lilly Corporate Center, DC 4133, Indianapolis, IN, 46285, 9000, Andrew P. Yu, Ph.D., Pavel Atanassov, B.A., Howard G. Birnbaum, Ph.D., Rym Ben-Hamadi, M.S.C.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to
• understand the fundamental idea of propensity score methodology
• appreciate the advantage of using optimal matching algorithm with propensity score as well as combining propensity score method and regression analysis
• understand the economic burden of treating schizophrenia patients in Medicaid and evaluate the treatment costs components
• recognize that despite the higher acquisition costs, schizophrenia patients treated with olanzapine incurred lower total costs compared to similar patients treated with quetiapine, and the majority of the economic benefits were due to cost reductions in psychiatric hospitalizations.

Summary:
Objective: To compare annual healthcare costs of treating schizophrenia Medicaid patients with olanzapine vs. quetiapine.
Methods: Adult schizophrenia patients were selected from Pennsylvania Medicaid claims database (1999-2003). Included patients were continuously enrolled and initiated with olanzapine or quetiapine monotherapy after a 90-day washout period. Inflation adjusted treatment costs were calculated for one year post-therapy initiation (2003 dollars). To control for selection bias, olanzapine and quetiapine patients were matched using optimal matching algorithm on propensity scores, which were generated using logistic regression with backward selection from 63 baseline (one year pre-initiation) covariates including demographics, prior drug therapy, utilization, and costs. Treatment costs for the matched cohorts were compared directly. Difference-in-difference regression models (one year post-therapy initiation cost minus one year baseline cost) were applied to further control baseline variations between matched cohorts.
Results: 6,929 patients treated with olanzapine and 2,321 with quetiapine met inclusion criteria. Quetiapine patients appeared more severe at baseline. After propensity score matching, 2,321 patient pairs had similar baseline characteristics including total costs. Compared to matched quetiapine patients, for one year post-therapy initiation, olanzapine patients had similar drug costs ($6,131 vs. $6,014, p=0.326), lower medical costs ($9,897 vs. $11,218, p=0.0128) and lower total costs ($16,028 vs. $17,232, p=0.0279). Lower psychiatric hospitalization costs (-$1,071) account for most of the total cost difference (-$1,203). Difference-in-difference regression analysis confirmed olanzapine's economic advantage. Adjusting for additional baseline variations, the total cost advantage of olanzapine patients was $963 (p=0.032), and was mostly due to a psychiatric hospitalization cost advantage of $997 (p=0.004).
Conclusion: Olanzapine patients had lower total costs than quetiapine patients; most of the economic benefit was attributable to significant reductions in psychiatric hospitalization costs.

References:

NR467 Tuesday, May 22, 12:00 PM - 2:00 PM
The Number Needed to Treat (NNT) for All-Cause Medication Discontinuation in CATIE Compared to a Long-Term Observational Study
Baojin Zhu, Ph.D. Eli Lilly and Company, US Outcomes Research, Lilly Research Laboratories, DC 4133, Indianapolis, IN, 46285, 9000, Haya Ascher-Svanum, Ph.D., Douglas E. Faries, Ph.D., Jamie Karagianis, M.D., Marvin S. Swartz, M.D., Jeffrey W. Swanson, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that the NNTs for all-cause medication discontinuation based on an industry-sponsored non-randomized observational study (US-SCAP) was found to be comparable to the NNTs based on an independent randomized double blind study (CATIE) - when comparing among the atypical antipsychotics, but not when comparing to perphenazine. The NNTs for olanzapine therapy were consistently the lowest (best) when compared to each studied atypical antipsychotic and when compared to perphenazine.

Summary:
Objectives: To compare the Number Needed to Treat (NNT) for all-cause medication discontinuation in an industry-sponsored non-randomized observational study (US-SCAP) with NNTs reported for CATIE, an NIMH-sponsored randomized double blind study. NNTs represented the number of patients needed to be treated with one treatment instead of another to prevent one negative outcome, defined as one additional medication discontinuation for any cause.
**Method:** We used data from a 3-year non-randomized observational U.S. study of schizophrenia-related disorders in usual care (US-SCAP) to calculate NNTs for all-cause medication discontinuation and to compare with NNTs reported for CATIE. Comparisons of NNTs were made under similar conditions, using 18-months following medication initiation, and the same comparators (olanzapine, risperidone, quetiapine, ziprasidone, and perphenazine). To account for selection bias occurring in usual practice, logistic models were employed to adjust for group differences at the time of medication initiation. NNTs with 95% confidence intervals were calculated and compared with published NNTs for CATIE (phase 1).

**Results:** NNTs for all-cause discontinuation of olanzapine vs. each studied atypical antipsychotic during the 18 month following medication initiation in US-SCAP were comparable to CATIE: 7 for olanzapine vs. quetiapine (6 in CATIE), 12 for olanzapine vs. risperidone (10 in CATIE); and 6 for olanzapine vs. ziprasidone (6 in CATIE). The NNT for olanzapine vs. perphenazine in US-SCAP (4) was smaller (better) than in CATIE (9). Findings were essentially unchanged when sensitivity analyses included only patients diagnosed with schizophrenia.

**Conclusions:** The NNTs for all-cause medication discontinuation based on an industry-sponsored non-randomized observational study (US-SCAP) were found comparable to NNTs based on an independent randomized double-blind study (CATIE) when comparing among the atypical antipsychotics, but not when comparing to perphenazine. The NNTs for olanzapine therapy were consistently the lowest (best) when compared to each studied atypical antipsychotic and when compared to perphenazine.

**References:**

**NR468**
**Tuesday, May 22, 12:00 PM - 2:00 PM**
**Impact of the Dopamine D2 Partial Agonist Antipsychotic Aripiprazole on Nicotine Use in Smokers with Schizophrenia**

Jonathan M. Meyer, M.D., University of California, San Diego, Psychiatry, 3350 La Jolla Village Dr. (116-A), San Diego, CA, 92161, 9000

**Educational Objectives:**
- At the conclusion of this presentation, the participant should be able understand the impact of dopaminergic agonists on nicotine use in schizophrenia.

**Summary:**
**Background:** Patients with schizophrenia have three times greater smoking prevalence (65%) than the general population (21%). Neurobiological hypotheses to explain this finding focus on central cholinergic and dopaminergic deficits. The development of antipsychotics with intrinsic dopamine partial agonism offers an opportunity to examine the dopaminergic hypothesis. Methods: 15 stable outpatient subjects with schizophrenia (mean age 47.4 years, mean PANSS 62.7) underwent an 8-week open-label switch to aripiprazole, with 8 subjects followed in a 20-week extension. There was no inducement to change one's smoking behavior, and no formal program to support smoking reduction. Primary outcome measures included the Fagerstrom Test for Nicotine Dependence, and measurement of the nicotine metabolite cotinine (t 1/2=16 hours) in saliva at weeks 0, 4, 8 and 28.

**Results:** 15 subjects completed the initial 8-week study, and 8 completed the 20-week extension. Mean endpoint cotinine dose was 15.71 mg for those who completed 8 weeks, and 18.75 mg for those who continued through week 28. Salivary cotinine changed nonsignificantly from baseline (388.6 ± 363.9 ng/ml) to the week 8 endpoint (379.2 ± 347.9 ng/ml) at the initial sample of 15 subjects. Among the cohort of 8 subjects who continued in the 20-week extension, there was a significant decrease in salivary cotinine from baseline (471.9 ± 447.1 ng/ml) to the week 28 endpoint (255.2 ± 105.9 ng/ml) (p=.036), with 3 of 8 subjects experiencing greater than 50% reductions in cotinine levels. Decreases in salivary cotinine did not correlate with changes in PANSS scores, or ratings of akathisia or other measures of extra-pyramidal side effects.

**Discussion:** Dopaminergic mechanisms may be important mediators of the smoking drive in patients with schizophrenia. In this pilot study, the dopamine partial agonist antipsychotic aripiprazole did decrease smoking behavior, and thus may be useful in smoking cessation treatment for schizophrenia patients.

**References:**

**NR469**
**Tuesday, May 22, 12:00 PM - 2:00 PM**
**National Adherence Initiative in Schizophrenia: Assessing the Risk of Partial- and Non-Adherence in Patients with Schizophrenia**

John M. Kane, M.D., The Zucker Hillside Hospital, Dept of Psychiatry, 75-59 263rd Street Kaufmann Boulevard, Glen Oaks, NY, 11004-1150, 9000, Mary Kujawa, M.D., Donna L. Kerney, Ph.D., R. Bruce Simonson, B.S., Larry Martinez, Ph.D., Ramy A. Mahmoud, M.D., Xavier Amador, Ph.D.

**Educational Objectives:**
- At the conclusion of this presentation, participants will be able to understand the utility of a screening tool in identifying treatment non-adherence in patients with schizophrenia.

**Summary:**
**Introduction:** Partial- or non-adherence to medication regimens among patients with schizophrenia is difficult to recognize in clinical practice. A tool was developed to assist clinicians in identifying patients at risk for non-adherence.

**Methods:** The tool consists of a survey of known non-adherence risk factors and was developed through scientific literature review and input from clinicians, researchers, consumers and caregivers. Survey development occurred in 2 phases: a pilot program where physicians evaluated <=5 patients with schizophrenia by indicating "yes" or "no" on the survey as to whether the patient possessed any of 10 attributes associated with adherence issues, and ranked their importance from 1 (most) to 10 (least) for each patient. Prior to national distribution, the survey was revised with pilot program input to include 8 factors, no ranking system, and data for <=10 patients per clinician. No patient-identifying information was collected. The Chi-square test was used to identify regional differences; multiplicity was not adjusted for.
Results: 2821 physicians (134 from pilot; 2687 nationally) enrolled. Sixty-one (46%) pilot program physicians returned surveys. Data from 309 patients collected from these physicians revealed “poor insight into illness” as the most common (74% of patients) and most important attribute associated with non-adherence, followed by “previous discontinuation of medication on own” (68%) and “forgetting medication” (67%). Significant (p<0.05) regional differences were found for these latter two factors along with “stigma about taking medication” and “psychotic symptoms.”

Conclusions: This survey tool provides useful descriptive data about the magnitude of adherence issues among patients with schizophrenia allowing clinicians to intervene appropriately.

References:

NR470 Tuesday, May 22, 12:00 PM - 2:00 PM
Quetiapine Monotherapy for the Treatment of Chinese Patients with Mania: a Randomized, Double-blind, Multicenter Study Comparing Efficacy and Safety of Quetiapine and Lithium
Niufan Gu, Shanghai Mental Health Center, Psychiatric, 600 Wanping South Road, Shanghai, 200030, 5700, Huafang Li, Cui Ma, Gang Wang, Shiping Xie, Xiaoping Xie, Xiufeng Xu, Xin Yu

Educational Objectives:
At the conclusion of this presentation, the participant should understand that treatment with quetiapine in patients experiencing an acute manic episode of bipolar disorder is effective and well-tolerated.

Summary:
Introduction: Previous studies have demonstrated the efficacy and safety of quetiapine for treating bipolar mania (1,2). This randomized, double-blind, multicenter, parallel-group, 28-day study (D1440L00006) compared quetiapine and lithium in Chinese patients hospitalized for an acute manic episode.

Methods: Patients with bipolar disorder hospitalized for the treatment of acute mania (Chinese Classification of Mental Disorders version 3) and a Young Mania Rating Scale (YMRS) total score ≥20 were randomized to receive quetiapine (twice daily up to 800 mg/day; dose titration according to the prescribing information) or lithium (twice daily; Day 1, 250-500 mg/day; Day 4, 500-2000 mg/day). Primary endpoint: change from baseline to Day 28 in YMRS total score for quetiapine-treated patients (last observation carried forward). Secondary endpoints included: response rate (50% reduction in YMRS total score) and between-group differences in efficacy at Day 28, and recording of adverse events (AEs).

Results: 155 patients were randomized: (78, quetiapine; 77, lithium). Mean doses: 642.9 mg/day and 1377.7 mg/day for quetiapine and lithium, respectively. At Day 28, quetiapine-treated patients showed significant improvements from baseline (change in YMRS total score -18.5; p<0.0001). Decrease in YMRS total score was similar between groups (-18.2 vs -15.9 for quetiapine and lithium respectively; p=0.1052). Response rate was significantly higher for quetiapine-treated Chinese patients (77.9% vs 59.7%; p=0.0132). 61% of quetiapine-treated and 53% of lithium-treated patients reported AEs. The most common AEs for quetiapine were constipation, dizziness, and diarrhea; compared with nausea, constipation, and vomiting for lithium. Three lithium-treated patients but no quetiapine-treated patients withdrew due to AEs.

Conclusions: This study confirms previous findings (1,2) and shows that quetiapine monotherapy up to 800 mg/day is effective and well tolerated for treating Chinese patients with bipolar mania.

References:

NR471 Tuesday, May 22, 12:00 PM - 2:00 PM
Predisposition for Psychiatric Disorder: A Comparison of Subjects Treated for Cannabis-Induced Psychosis and Schizophrenia

Educational Objectives:
At the conclusion of this presentation the participant should be able to recognize that the rate of hereditary predispositions for psychiatric disorders are similar in subjects treated for cannabis-induced psychosis and schizophrenia. The two disorders cannot be distinguished based on predisposition, for either psychosis or psychiatric disorders in general, among first degree relatives.

Summary:
Background: Cannabis use has been associated with an elevated risk of schizophrenia. However, the rate of predisposition for psychosis and other psychiatric disorders among subjects experiencing cannabis-induced psychosis has never been established, or compared with the corresponding rate for schizophrenia.

Methods: The rate of predisposition for psychiatric disorders among subjects treated for cannabis-induced psychosis and schizophrenia was compared by use of a competing risk setup analysis. Data was retrieved from registers encompassing information on all treatment provided by Danish psychiatric hospitals. Information on hereditary predispositions was obtained by linking the subjects to the mother, father, and siblings. Subjects were followed from the date that occurred last of their 15th birthday or 1.1.1994, and until first treatment episode for any psychotic disorder, death, disappearance, or 1st of July 2005. Subjects censored for either a cannabis-induced psychosis or schizophrenia were considered cases. Predispositions for schizophrenia, schizophrenia-like psychosis, other psychotic conditions and other psychiatric diagnosis among first degree relatives were compared between the cases.

Results: Predisposition for psychiatric disorder among mothers, showed both a main difference for all comparisons (p=.038), and specifically a lower risk of receiving a diagnosis for cannabis-induced psychosis compared with schizophrenia (p=.029) for those with mothers suffering from schizophrenia. Predisposition for psychiatric disorders other than psychosis among fathers (p=.024) was associated with an increased risk of treatment for cannabis-induced psychoses compared with schizophrenia. Aside from this, all comparisons were of similar magnitude.
Conclusion: The study demonstrates that predisposition, for both psychiatric disorders in general and for psychotic disorders specifically, contributes equally to the risk of later treatment for schizophrenia and cannabis-induced psychoses.

References:

NR472 Tuesday, May 22, 12:00 PM - 2:00 PM
Once-Daily Quetiapine Sustained Release (SR) Is Effective And Well Tolerated In Patients With Schizophrenia Switched From Quetiapine Immediate Release (IR)

Hans-Jürgen Möller Ludwig-Maximilians-University, Dept. of Psychiatry, Nussbaumstrasse 7, Munich, D-80336, 4280, Sunny Johnson, Temenuzhka Mateva, Didier Meulien, Martin Brecher, Ola Svensson, Frank Miller

Educational Objectives:
At the conclusion of this presentation, the participants should understand that clinically stable patients can be switched from quetiapine IR to quetiapine SR without any deterioration or compromise in safety or tolerability.

Summary:
Introduction: Quetiapine IR is effective and well tolerated in patients with schizophrenia and bipolar disorder (1,2). This randomized, double-blind, dual-matched active-controlled study (D1444CC00146) evaluated efficacy and tolerability of switching from quetiapine IR to quetiapine SR, compared with maintaining quetiapine IR treatment in patients with schizophrenia.

Methods: Patients clinically stable on fixed doses of quetiapine IR (400, 600, or 800 mg/day) were enrolled. Patients received quetiapine IR twice daily for 4 weeks and were then randomized (2:1) to a once daily equivalent dose of quetiapine SR or maintained on quetiapine IR for 6 weeks. Primary endpoint: % patients with insufficient efficacy, defined as either discontinuation due to lack of efficacy or >20% increase in PANSS at any visit.

Results: 497 patients were randomized to quetiapine SR (n=331) or quetiapine IR (n=166). In the modified intent-to-treat (MITT) population, the proportion of patients with insufficient efficacy was similar (9.1% and 7.2% for quetiapine SR and quetiapine IR, respectively). However, using the selected non-inferiority margin of 6%, non-inferiority was narrowly missed (difference 1.86%; 95% CI -3.78, 6.57; p=0.0431). Non-inferiority was shown in the per-protocol (PP) population: 5.3% receiving quetiapine SR showed insufficient efficacy versus 6.2% receiving quetiapine IR (difference -0.83%; 95% CI -6.75, 3.71; p=0.0017). LSM changes in PANSS total score were -3.7 (SR) and -4.2 (IR). In both groups, 93% of patients experienced no change or an improvement in CGI-I score. The incidence of adverse events was similarly low for both groups.

Conclusion: Patients stable on quetiapine IR can be switched to once-daily quetiapine SR without clinical deterioration or compromise in safety/tolerability.

References:

NR475 Tuesday, May 22, 12:00 PM - 2:00 PM
Iloperidone, a Novel Atypical Antipsychotic, Is Associated With Improvement, or No Change, in Akathisia Symptoms
Karen McCollough, Ph.D. Vanda Pharmaceuticals Inc., Regulatory Affairs, 9605 Medical Center Drive, Suite 300, Rockville, MD, 20850, 9000, Curt Wolfgang, Ph.D.

Educational Objectives:
At the conclusion of this presentation, participants should be able to understand the relationship between iloperidone and akathisia and recognize the need to select agents based on individual patient needs. Participants should also be able to recognize iloperidone may be an appropriate choice in patients experiencing akathisia while on other agents.

Summary:
Purpose: Iloperidone is an investigational mixed D2/5HT2 antagonist antipsychotic with affinity for 5HT1A, 5HT2A, and 5HT2C receptors. This profile predicts potentially enhanced clinical efficacy against schizophrenia with reduced extrapyramidal side-effect risk. Akathisia is an undesirable effect of antipsychotic treatment that affects functioning, quality of life, and possibly decisions to continue treatment. Additional medications are also often required to treat akathisia symptoms. Consequently, akathisia was assessed as part of a placebo- and risperidone-active-controlled, efficacy and safety study of iloperidone.

Methods: The Extrapyramidal Symptom Rating Scale (ESRS) and Barnes Akathisia Scale (BAS) were used to assess change in akathisia from baseline to 6-week end point for patients in the iloperidone (12-16mg/d, n=228; 20-24mg/d, n=140), risperidone (6-8mg/d, n=148), and placebo (n=154) groups. Categorical analysis was conducted to determine percentage of patients with akathisia that worsened, remained unchanged, or improved from baseline during the treatment period.

Results: A statistically significant greater proportion of patients in the iloperidone 12-16 mg/d treatment group showed improvement or no change in the akathisia subscale score of the ESRS compared with placebo (p<.05). While the iloperidone 20-24 mg/d treatment group showed a numerical improvement, this was not statistically significant. A categorical analysis for total BAS score showed both iloperidone groups had statistically significant greater proportions of patients with improved scores or whose scores remained unchanged compared with placebo.

Conclusion: Iloperidone treatment was associated with improvement, or no change, in akathisia symptoms compared to placebo. A greater proportion of iloperidone patients demonstrated improvement or no change in akathisia symptoms compared to those treated with risperidone. Results indicate iloperidone may be a good treatment option, especially for patients experiencing akathisia on other agents.

References:
Iloperidone Is Well Tolerated by Subjects With Renal or Hepatic Impairment in Single-Dose Clinical Pharmacokinetics Studies

Greg Sedek, M.D., Ph.D. Vanda Pharmaceuticals Inc., Research Consultant, 46 Longview Trail, Denville, NJ, 07834, 9000, Curt Wolfgang, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate understanding of the pharmacokinetics of iloperidone in individuals with impaired renal or hepatic functioning. The participant should also be able to recognize the importance of considering individual patient characteristics in the selection of drug therapy for the treatment of schizophrenia.

Summary:

Purpose: Iloperidone is an investigational mixed D2/5HT2 antag-onist antipsychotic with affinity for 5HT1A, 5HT2A, and 5HT6 receptors. This profile predicts potentially enhanced clinical efficacy against schizophrenia with reduced extrapyramidal side-effect risk. Open-label studies were conducted to determine single-dose pharmacokinetics of synthetically active compounds iloperidone and metabolite P88 in adults with renal or hepatic impairment compared with healthy controls.

Methods: Study 1(S1): Ten adults with chronic severe renal impairment (CrCl<30mL/min) and 13 matched healthy controls (CrCl>80mL/min) received single iloperidone 3mg oral doses. Study 2(S2): Eight adults with mild-to-moderate hepatic impairment and 8 matched healthy controls received single 2mg doses. Assay results for blood and urine samples collected pre-dose, and frequently for 64-65h (S1) and 48h (S2) post-dose were used to determine iloperidone and P88 pharmacokinetics.

Results: Renal impairment vs controls: Iloperidone clearance was reduced by only 19%, and mean maximum plasma concentration (Cmax) was unaltered, although half-life (t1/2) was significantly prolonged (33.7 vs 15.0h; p=0.02). P88 pharmacokinetics including area-under-the-curve (AUC0-t) were not significantly altered. Hepatic impairment vs controls: Iloperidone tmax, Cmax, AUC0-t, and t1/2 were essentially unaltered. P88 Cmax (1.74 vs 1.02ng/mL; 90% Confidence Interval [CI], 1.29, 2.88) and AUC0-t (34.3 vs 22.9ng*h/mL; 90% CI, 1.06, 2.56) were significantly increased in hepatically impaired subjects without altering renal clearance. Protein binding (98%) was unaffected by renal or hepatic impairment (97%). Iloperidone was well tolerated by all subjects in both studies.

Conclusions: Renal dysfunction did not alter iloperidone and P88 pharmacokinetics to clinically significant levels. Iloperidone exposure was unaffected in mild-to-moderate hepatic impairment. P88 exposure moderately increased, suggesting potential increased combined exposure to pharmacologically active moieties (iloperidone + P88). Protein binding was unaffected by renal or hepatic impairment. Iloperidone single doses were well tolerated by all subjects.

References:


Efficacy and Safety Profile of Bifeprunox in Patients with Schizophrenia

David C. Henderson Massachusetts General Hospital, Psychiatry, 25 Staniford Street, Boston, MA, 02114, 9000, Nathan A. Shapiro, Jens Heisterberg, Paul P. Yeung

Educational Objectives:

Evaluate the role of the investigational partial dopamine agonist bifeprunox in maintaining long-term stability and treating acute schizophrenia, while understanding its overall safety and potentially favorable metabolic profile.

Summary:

Objective: Examine bifeprunox efficacy and safety in acute or stable schizophrenia patients.

Methods: Analyze efficacy and safety in 5 randomized, double-blind, placebo-controlled bifeprunox studies. Primary efficacy endpoint in a 6-month trial of stable schizophrenia (20 mg: n=158; 30 mg: n=172; placebo: n=166) was time to deterioration; in four 6-week placebo-controlled studies of acutely exacerbated schizophrenia, it was mean baseline-to-endpoint change in PANSS total versus placebo. Short-term treatment groups comprised bifeprunox 1-40 mg (n=1021), haloperidol 10 mg (n=50), risperidone 6 mg (n=267) or olanzapine 15 mg (n=146). Reference compounds validated assay sensitivity. Treatment-emergent adverse events (TEAEs) and metabolic changes were investigated using descriptive statistics.

Results: Time to deterioration was statistically significantly longer with bifeprunox than placebo (20 mg: P=0.008; 30 mg: P=0.006). In two 6-week studies, bifeprunox (one 20 mg; one 30 mg) produced statistically significantly greater mean change in PANSS total than placebo (P=0.031, P=0.02, respectively), while iloperidone showed larger reductions than bifeprunox. Six-month study showed similar PANSS total changes from baseline (P=0.002 [20 mg], P=0.017 [30 mg]) at week 6 versus placebo. Most common TEAEs (≥2% and ≥2X placebo) were nausea, vomiting, constipation, stomach discomfort, dizziness, akathisia and anorexia. EPS were experienced in 2.5% and 3.2% of patients on bifeprunox and placebo, respectively, at 6 weeks. At 6 months EPS rates were even lower (1.8%, 0% in patients on bifeprunox and placebo, respectively).

Six-week hyperprolactinemia rates were 0.2% for bifeprunox and 1.4% for placebo. In one 6-week study, endpoint fasting-lipid changes favored bifeprunox (total cholesterol: -7.9%; triglycerides: -24.2%; triglyceride/HDL ratio: -23.8%) over placebo (-6.1%, -19.5%, -17.0%). Mean body weight decreased with bifeprunox (-1.1 kg) and placebo (-0.2 kg) over 6 weeks. Six-month bifeprunox-related metabolic advantages were consistent with 6-week studies.

Conclusions: Bifeprunox 20-30 mg demonstrates favorable short- and long-term efficacy/safety versus placebo in acute and stable schizophrenia.

References:


Long-Term Lipid Profile in Patients With Stable Schizophrenia Receiving Bifeprunox

Michel Bourin University of Nantes, Neurobiology of Anxiety and Depression, EA 3256, rue Gaston Vell BP 53508, Nantes,

NR476 Tuesday, May 22, 12:00 PM - 2:00 PM

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Summary:

Objective: Assess long-term lipid profile of bifeprunox in patients with stable schizophrenia.

Methods: In this 6-month, double-blind study of bifeprunox, 497 patients with stable schizophrenia were randomized to receive once-daily, fixed dose bifeprunox 20 mg, 30 mg or placebo. Fasting and non-fasting lipid measures were evaluated at baseline, month 3 and month 6 (or early termination): total cholesterol (TC), low density lipoprotein (LDL), very low density lipoprotein (VLDL), high density lipoprotein (HDL), and triglycerides (TG).

Results: The table summarizes lipid profile at baseline (mean values) and 6 months (mean change from baseline) in fasting and non-fasting patients (observed cases from a subset of the overall randomized set of patients). Mean total and LDL cholesterol decreased from baseline to month 6 in all groups, with the exception of non-fasting placebo patients. In addition, increases in HDL cholesterol (fasting/non-fasting) from baseline to endpoint were shown in all groups. VLDL levels decreased in all groups, except non-fasting bifeprunox 30 mg patients. Bifeprunox 30 mg treatment significantly decreased adjusted mean fasting TG levels from baseline to endpoint versus placebo (−32.7 versus −5.3 mg/dL; P=0.006).

Conclusions: At 6 months of treatment with bifeprunox, lipid levels remained stable and were comparable to those for placebo. The results of this study suggest that bifeprunox may have a lipid-neutral or perhaps a favorable long-term effect on lipids in patients with stable schizophrenia.

References:


NR479  Tuesday, May 22, 12:00 PM - 2:00 PM
6-Month Placebo-Controlled Study of Bifeprunox Efficacy and Safety for Prolongation of Time to Deterioration in Patients With Stable Schizophrenia

Michel Bourin University of Nantes, Neurobiology of Anxiety and Depression, EA 3256, rue Gaston Veil BP 53508, Nantes, 44035, 4279, Daniel E. Casey, Marc Debelle, Jens Heisterberg, Mette Krog Josiassen, Nathan A. Shapira, Paul P. Yeung

Educational Objectives:

At the conclusion of this session, participants should be able to describe the efficacy and safety of the investigational partial dopamine agonist bifeprunox in patients with stable schizophrenia.

Summary:

Objective: Examine efficacy and safety of the investigational, partial dopamine agonist bifeprunox in stable schizophrenia.

Methods: In this 6-month study, 497 patients with stable schizophrenia received once-daily bifeprunox 20 mg, 30 mg or placebo. Primary efficacy measure was time to deterioration from randomization, with deterioration defined as fulfillment of one or more of the following: CGI-Improvement score ≥5, PANSS item P7 (hostility) and/or G8 (uncooperativeness) score ≥5 for 2 consecutive days, or ≥20% increase in PANSS score from baseline. Key secondary measure was change in PANSS total score at week 6. Safety evaluations included AEs, EPS, weight/BMI, laboratory tests and vital signs.

Results: Treatment with bifeprunox resulted in statistically significant longer time to deterioration of schizophrenia (20 mg: P=0.008; 30 mg: P=0.006) versus placebo. Six-month deterioration rates were 41% for bifeprunox 20 mg, 36% for 30 mg and 59% for placebo. Bifeprunox showed statistically significant difference from placebo in PANSS total score as early as week 6, and at every subsequent time point during the 6-month study. There were statistically significant differences between bifeprunox and placebo in positive and negative PANSS subscales and BPRS scores at endpoint. Most common AEs with bifeprunox (incidence ≥5% and ≥2X placebo) included nausea, vomiting, dizziness, anorexia, akathisia, dyskinesia and asthenia. Prolactin levels decreased in all treatment groups. Bifeprunox-treated patients demonstrated a reduction in triglycerides and an increase in HDL. Bifeprunox 30 mg significantly improved fasting triglyceride levels from baseline compared to placebo (P=0.006). At endpoint, weight decreased significantly in the bifeprunox 30 mg group versus the placebo group (P=0.05).

Conclusions: Compared to placebo, bifeprunox significantly prolonged time to deterioration over 6 months and showed statistically significant difference from placebo in PANSS total score at week 6. Bifeprunox may be beneficial for long-term treatment, and has a favorable metabolic profile for patients with stable schizophrenia.

References:

rolled with a history of persistent treatment inefficacy. Similar results were obtained for patients enrolled due to lack of efficacy alone (−22.6 ± 3.5: ziprasidone [n=27] and −20.5 ± 3.8: clozapine [n=30]) or with both lack of efficacy and treatment intolerance (−26.1 ± 2.7: ziprasidone [n=57] and −22.9 ± 2.8: clozapine [n=65]). In the overall analysis, mean (± SE) change in CGI-S scores was −0.6 ± 0.9 in both the ziprasidone and clozapine groups. Similar results were obtained in patients recruited due to lack of efficacy alone (−0.6 ± 0.1: ziprasidone [n=27] and −0.5 ± 0.1: clozapine [n=30]) or with both lack of efficacy and treatment intolerance (−0.5 ± 0.1: ziprasidone [n=57] and −0.5 ± 0.1: clozapine [n=65]). In this study of schizophrenic patients with a history of persistent treatment resistance or intolerance, the efficacy of ziprasidone and clozapine was consistently comparable in both the overall sample as well as subgroups with prior treatment inefficacy.

References:

NR481 Tuesday, May 22, 12:00 PM - 2:00 PM
Long-Term Efficacy of Ziprasidone in Treatment-Resistant Schizophrenia: Results from a 1-Year, Open-label Extension Study
Emilio Sacchetti, M.D. University of Brescia - Spedali Civili, Dept. of Psychiatry, P.zza Spedali Civili 1, Brescia, 25100, 4759, Alessandro Galluzzo, M.D., Fabio Romeo, M.D., Barbara Gorini, Ph.D., Lewis Warrington, M.D.

Educational Objectives:
At the end of this presentation, the participant will understand the potential role and utility of ziprasidone in the long-term treatment of patients with treatment-resistant schizophrenia.

Summary:
Subjects who completed a randomized, double-blind, 18-week trial (MOZART study), designed to compare the efficacy and safety of ziprasidone vs clozapine in treatment resistant and/or intolerant schizophrenic patients, and who responded to ziprasidone treatment (>20% reduction in PANSS total score), were eligible to continue open-label treatment with ziprasidone for up to 1 year. Subjects maintained the same daily dose of ziprasidone received at the completion of the double-blind core study. Dose changes during both the core and extension study were permitted in order to optimize efficacy and tolerability within the range of 80-160 mg/day. The primary efficacy assessment was LOCF change in PANSS total score from the core study baseline to extension study endpoint. A secondary analysis assessed the proportion of patients maintaining >20% PANSS improvement at study endpoint. Of 45 patients who completed the core study, 44 met entry criteria for the extension study, 42 were included in the intent-to-treat analysis. Mean change in PANSS total score from core baseline to extension study endpoint was −32.2 (95% CI, −39.1 to −25.3; p < 0.001, n=42). At the extension study endpoint, 28 patients (70%) maintained ≥ 20% reduction in PANSS total score (achieved after completion of the core study). Twenty-one patients (50%) completed the 1-year extension study. Ziprasidone was well tolerated in both the core and extension study. Schizophrenic reaction was the most common treatment-emergent, treatment-related adverse event reported in the extension study. These results suggest that ziprasidone may be efficacious and well-tolerated in the long-term management of patients with treatment-resistant schizophrenic illness.

References:

NR482 Tuesday, May 22, 12:00 PM - 2:00 PM
Impact of Meal Size and Fat Content on Ziprasidone Absorption
Kuan Gandelman, Ph.D. Pfizer Inc., Clinical Pharmacology, 885 3rd Avenue, New York, NY, 10017, Jeffrey Alderman, Ph.D., Paul Glue, Ph.D., Mark Versavel, Ph.D., Sheldon Preskorn, M.D.

Educational Objectives:
At the end of this presentation, the participant should be able to recognize the separate effects of calorie intake and fat content of food on the bioavailability of oral ziprasidone.

Summary:
Introduction: Studies in healthy volunteers have found that the bioavailability of oral ziprasidone is increased in the presence of food and that pharmacokinetic variability is reduced. This study investigated the separate influences of calorie intake and fat content of food on ziprasidone bioavailability.

Method: A randomized, 6-way crossover study was conducted in 15 patients taking oral ziprasidone 80 mg bid as their standard antipsychotic therapy. Patients took ziprasidone under 6 meal conditions in randomized sequences (fasted, low-calorie/low-fat, low-calorie/high-fat, medium-calorie/low-fat, high-calorie/low-fat, and high-calorie/high-fat). Crossover periods were separated by at least 3 days for washout of the previous meal condition. Serial blood samples were obtained over the 12 hours post-dose.

Results: Highest ziprasidone exposures were observed with medium-calorie (500 calories) and high-calorie (1000 calories) meals, which were about 77-96% greater than those observed under fasting conditions. Medium-calorie meals were associated with mean ziprasidone exposures of 1570 ng

- hr/mL, 229 ng/mL, 74 ng/mL for AUC, Cmax, and Ctrough, respectively, which were within 90% CI equivalence limits of high-calorie meals. Mean exposure after low-calorie meals (250 calories) approached those under fasting conditions, being approximately 3-33% higher than fasting. Mean fasting ziprasidone exposures were 885 ng

- hr/mL, 123 ng/mL, 40 ng/mL for AUC, Cmax, and Ctrough, respectively. Ziprasidone exposures showed little or no change with the fat content (high or low) of a meal. Ziprasidone exposures with medium-calorie and high-calorie meals were also associated with less variability than those of low-calorie and fasting conditions.

Conclusion: A medium-calorie meal produced near maximal exposures to ziprasidone, similar to a high-calorie meal. A low-calorie meal produced ziprasidone exposures approaching those seen after fasting. Fat content (high or low) did not significantly affect exposures.

References:
NR483 Tuesday, May 22, 12:00 PM - 2:00 PM
Coronary Heart Disease and Diabetes Risk in Schizophrenia Patients Treated with Atypical Antipsychotics: An Analysis of Published CATIE Study Data

Henry Nasrallah, M.D. University of Cincinnati, Psychiatry, 231 Albert Sabin Way, Cincinnati, OH, OH 45267, 9000, Brian Cuffel, Ph.D., Ilise Lombardo, M.D., Sonja Sorensen, M.P.H., Dennis Revicki, Ph.D.

Educational Objectives:
At the end of this presentation, the participant should be able to understand differences in risk for CHD and diabetes for different antipsychotics.

Summary:
Metabolic data from the CATIE schizophrenia study enables comparison of coronary heart disease (CHD) risk among patients receiving treatment with antipsychotic agents using Framingham risk equations and national epidemiologic studies of diabetes risk. The present study estimated 10-year rates of diabetes and CHD from exposure-adjusted mean change in metabolic parameters from phases 1 and 2 of the CATIE study. Relative risk (RR) and number needed to harm (NNH) were calculated for olanzapine, quetiapine, and risperidone relative to ziprasidone, and for ziprasidone relative to no treatment. Olanzapine, quetiapine, and risperidone were associated with an increased risk for diabetes and total mortality and secondary CHD when compared with ziprasidone. RR and NNH values in phase 1 were as follows: olanzapine, RR = 1.17 and NNH = 31 for diabetes and RR = 1.10 and NNH = 95 for CHD; quetiapine, RR = 1.06 and NNH = 88 for diabetes and RR = 1.08 and NNH = 120 for CHD; risperidone, RR = 1.06 and NNH = 92 for diabetes and RR = 1.04 and NNH = 233 for CHD. In contrast, treatment with ziprasidone was not associated with an increased risk for diabetes or CHD (RR < 1.00) compared with no treatment. The same model applied to Phase 2T (tolerability arm) CATIE data yielded similar elevated RR and NNH values for olanzapine and quetiapine, but no risk increases were observed for risperidone or ziprasidone. Results of this model suggest differences in risk exist for CHD and diabetes across atypical antipsychotics. These findings have implications for understanding excess mortality in this population.

References:

NR484 Tuesday, May 22, 12:00 PM - 2:00 PM
Long-Term Weight Profile of Patients With Stable Schizophrenia Receiving Bifeprunox

Michel Bourin Faculte de Medecine, Neurobiology of Anxiety and Depression, 1 Rue Gaston Veil, Nantes Cedex 01, 44035, 4279, Daniel E. Casey, Marc DeBelle, Jens Heisterberg, Mette Krog Josiassen, Nathan A. Shapiro, Paul P. Yeung

Educational Objectives:
At the conclusion of this session, participants should be able to describe the beneficial long-term effects of the investigational partial dopamine agonist bifeprunox on the weight profile of patients with stable schizophrenia.

Summary:
Objective: Weight gain increases the risk of cardiovascular disease and diabetes, and has been reported in clinical trials of several antipsychotics. This analysis evaluated the long-term weight profile of the investigational drug bifeprunox in stable schizophrenia.

Methods: In this 6-month, double-blind study, 497 patients with stable schizophrenia were randomized to a once-daily fixed dose of bifeprunox 20 mg, 30 mg or placebo. Weight and body mass index (BMI) were measured at baseline, week 6, month 3 and month 6 (or early termination). Between-group differences were analyzed by ANCOVA, with age, sex, and baseline weight or BMI as covariates.

Results: Bifeprunox 20 mg and 30 mg treatment resulted in greater raw mean decreases in weight (−1.1 kg, and −1.2 kg, respectively) than placebo (−0.4 kg) at endpoint. The adjusted mean weight change in observed cases (OC) at month 6 also showed a decrease in all groups (bifeprunox 20 mg, −0.3 kg; 30 mg, −0.5 kg; placebo, −0.8 kg). Patients in the bifeprunox 30 mg group, at endpoint, showed a statistically significant decrease in body weight and BMI versus placebo (adjusted mean weight change: −1.5 kg versus −0.8 kg, P=0.027; adjusted mean change in BMI: −0.5 kg/m² versus −0.3 kg/m², P=0.024). Although weight decreases occurred irrespective of nausea and vomiting, patients with these side effects experienced greater weight loss (bifeprunox 20 mg, −1.9 versus −1.0 kg; 30 mg, −2.3 versus −1.1 kg; placebo, −1.9 versus −0.6 kg). The most common AEs (incidence ≥5% and ≥2X placebo) included nausea, vomiting, dizziness, anorexia, akathisia, dyskinesia and asthenia. A similar proportion of patients withdrew due to AEs in the bifeprunox 20 mg and placebo groups, while more patients withdrew in the bifeprunox 30 mg group.

Conclusions: In this study, decreases in body weight and BMI were observed over the long-term in patients treated with bifeprunox.

References:

NR485 Tuesday, May 22, 12:00 PM - 2:00 PM
Do Comorbid Metabolic Disorders Influence the Severity of Illness in Patients Hospitalized with Schizophrenia and Schizoaffective Disorder?

Dale A. D’Mello, M.D. Michigan State University, Psychiatry, 4805 Canyon Trail, Lansing, MI, 48917, 9000, Supriya Narang, M.D.

Educational Objectives:
Appreciate the high prevalence of comorbid metabolic disorders in patients hospitalized with schizophrenia and schizoaffective disorder.
Understand the possible biopsychosocial factors that may contribute to dyslipidemia in patients with schizophrenia and schizoaffective disorder.

Summary:
Patients with schizophrenia are susceptible to metabolic disorders such as obesity, dyslipidemia and diabetes. While these comorbid conditions increase disease burden and diminish quality of life, their influence upon severity of illness remains to be elucidated.

Objectives: The purpose of the present study was to examine the prevalence, and clinical correlates of comorbid metabolic dis-
orders in a cohort of patients hospitalized with schizophrenia and schizoaffective disorder.

Method: We recruited patients with schizophrenia and schizoaffective disorder who were consecutively admitted to the adult psychiatric unit of a general hospital in mid-Michigan during calendar years 2004-2006. We gathered demographic, and health related information from the hospital medical records. We then examined statistical correlations between metabolic variables (body mass index, fasting plasma glucose, serum lipid levels, and blood pressure), levels of psychopathology (PANSS: Positive and Negative Syndrome Scale) and treatment outcomes (psychotropic use, years 2004-2006). We gathered demographic, and health related information from the hospital medical records. We then examined statistical correlations between metabolic variables (body mass index, fasting plasma glucose, serum lipid levels, and blood pressure), levels of psychopathology (PANSS: Positive and Negative Syndrome Scale) and treatment outcomes (psychotropic use, and length of hospital stay).

Results: Of the 77 patients who were included in the study, 79% were overweight or obese, 64% had dyslipidemia, 84% were pre-hypertensive or hypertensive, 39% were pre-diabetic or diabetic, and 56% met diagnostic criteria for metabolic syndrome. There was a positive correlation between admission fasting total serum cholesterol levels and PANSS Global Psychopathology Scores (Pearson correlation co-efficient: r=0.367, p=0.028). Patients who achieved higher scores on the PANSS Negative and Total subscales had longer hospital stays. Body mass index, serum lipids and blood pressure levels did not display a significant impact upon PANSS scores or lengths of stay.

Conclusions: Patients hospitalized with schizophrenia and schizoaffective disorder displayed an alarmingly high prevalence of metabolic disorders. There was a positive correlation between serum cholesterol levels and symptom severity. Patients with schizophrenia are prone to sedentary living and make poor nutritional choices. Those who suffer the most severe psychopathology may also carry the heaviest metabolic burden.

References:
2. Saari K, Jokelainen J, Veijola J, et al. Serum lipids in schizophrenia (n=58) or affective psychoses (n=128) and offspring of control parents (n=174) enrolled in the New England Family Study. We chose 54 items measuring EI from the Bayley scales assessed in eight-month-old infants. These items were grouped into three domains characterizing an infant's development: intermodal experience in relation to 1) one's own body, 2) an object, and 3) social interactions. Generalized linear models were used to assess the relationship between the EI scores and the high-risk status of the offspring.

Conclusions: Patients hospitalized with schizophrenia and schizoaffective disorder displayed an alarmingly high prevalence of metabolic disorders. There was a positive correlation between serum cholesterol levels and symptom severity. Patients with schizophrenia are prone to sedentary living and make poor nutritional choices. Those who suffer the most severe psychopathology may also carry the heaviest metabolic burden.

References:

NR486 Tuesday, May 22, 12:00 PM - 2:00 PM
Early Intermodal Integration in Offspring of Parents with Schizophrenia
Franziska Gamma, M.D. Harvard School of Public Health; University of Lausanne, Epidemiology; Department of Psychiatry, Av. Sainte-Luce 10bis, Lausanne, 1003, 4419, Stephen L. Buka, D.Sc, Jill M. Goldstein, Ph.D., Garrett Fitzmaurice, D.Sc, Larry J. Seidman, Ph.D., Ming T. Tsuang, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will have a better understanding of early intermodal integration (EI) abnormalities in children at risk for schizophrenia and be familiar with the study results demonstrating that some of these abnormalities are liability indicators for schizophrenia. The participant will recognize that the study of EI abnormalities adds a developmental perspective to the neurodevelopmental hypothesis of schizophrenia, both at the psychological and at the biological level. Early intermodal integration is necessary for the full development of perceptual and motor skills, cognition and intersubjective abilities, which are affected in people with schizophrenia.

Summary:
Objective: Early intermodal integration (EI) is the infant’s ability to link motility and perception and to relate perception across modalities. Complex mental and motor functions, which are typically disturbed in patients with schizophrenia, rely on EI. The study determined whether EI abnormalities are liability indicators for schizophrenia. To our knowledge, there is no published study on EI and the vulnerability for schizophrenia.

Method: The study sample included offspring of parents with schizophrenia (n=58) or affective psychoses (n=128) and offspring of control parents (n=174) enrolled in the New England Family Study. We chose 54 items measuring EI from the Bayley scales assessed in eight-month-old infants. These items were grouped into three domains characterizing an infant's development: intermodal experience in relation to 1) one's own body, 2) an object, and 3) social interactions. Generalized linear models were used to assess the relationship between the EI scores and the high-risk status of the offspring.

Conclusions: Body-related and object-related EI abnormalities were specific to infants of parents with schizophrenia. This novel approach adds a developmental perspective to the neurodevelopmental hypothesis of schizophrenia, both at the psychological and at the biological level. It is also in line with neuropsychological findings associated with schizophrenia emphasizing on abnormalities in cortical connectivity and impaired sensory binding.

References:

NR487 Tuesday, May 22, 12:00 PM - 2:00 PM
Auditory and Visual Event-Related Potential P300 as a “Trait” and “State” Markers in Patients with Schizophrenia
Yang-Whan Jeon Our Lady of Mercy Hospital, The Catholic University of Korea, Department of Psychiatry, 665 Bupyeong-Dong, Bupyeong-Gu, Inchon, 403-720, 5800, E-Jin Park, Sang-Ick Han

Educational Objectives:
Even though it is well known that the event-related potential P300 is useful for exploring schizophrenia, it is not enough to be studied on the modality effects. This study was designed to examine which modality is appropriate for biological markers.

Summary:
Auditory and visual oddball paradigms were employed for patients with schizophrenia (N=39) and controls (N=40). For the patients, the symptoms severity was assessed by Positive and negative syndrome scale (PANSS). Auditory paradigm was composed of standard (1000Hz, 80%) and target (2000Hz, 20%) tones with 75 dB once every 2 s. Visual paradigm was composed of standard (small circle, 80%) and target (large circle, 20%) once every 2 s. The subjects were asked to press button to the targets. The modality conditions were counterbalanced within across subjects within groups.
P300 in both paradigms was smaller in patients with schizophrenia across electrodes (F=16.2, p<0.001, for auditory; F=7.8, p<0.01, for visual), but not delayed for both modalities. In visual modality, P300 amplitude was correlated with positive symptom scores in fronto-central areas (from r=0.33 to r=0.47, p<0.05), but not in centro-parietal areas. P300 latency was correlated with general psychopathology scores. In auditory modality, P300 was not correlated with symptoms scores.

Auditory and visual P300 could be used for a trait marker and a state marker for exploring schizophrenia.

References:

NR488 Tuesday, May 22, 12:00 PM - 2:00 PM
Improvements in illness severity, functioning and hospitalization in schizophrenic patients switched to Risperidone Long-Acting Injection (RLAI): 12-month interim report from Belgian patients enrolled in the electronic Schizophrenia Treatment Adherence Registry (e-STAR)
Joseph Peuskens, A.A.S. University Psychiatric Centre KU Leuven, campus Kortenberg, psychiatry, leuvensesteenweg 517, Kortenberg, BE-3070, 4231, Jo Van der Veken, J. Diels, Michael Povey

Educational Objectives:
This presentation aims at informing about the advantages of risperidone long acting injectable concerning the clinical and functional outcome in a naturalistic treatment setting

Summary:
Objectives: results of 12 months changes in illness severity (Clinical Global Impression-Severity, CGI-S), functioning (Global Assessment of Functioning, GAF) and hospitalization in Belgian patients with schizophrenia switched to RLAI in a non-interventional setting and followed up for 24 months.
Methods: e-STAR is a non-interventional study collecting data web-based for 2 years pro-and retrospectively. Results refer to schizophrenia patients in study for 12 months, and not continuously hospitalized in the 6 months preceding enrolment. Baseline of the mirror design for patients hospitalized at start of RLAI was day of discharge from hospital; for ambulatory patients day of start with RLAI treatment. Data were collected in 39 psychiatric hospitals.

Results: Of 410 patients enrolled, 57 % were hospitalized. Until now, 163 patients (62% males) reached 12 months follow-up, of which 84% still continued treatment with RLAI after 1 year. Mean (SD) age was 41.6 (13.6) years, mean (SD) duration of illness 9.8 (9.3) years. Most frequent reasons for switch to RLAI were poor compliance (38.2%) and need for maintenance therapy (23.5%). Mean (SD) CGI score changed from 4.6 (1.0) to 3.5 (1.1) (p<0.001) and scores of very mild/mild illness from 12.6% of patients to 46.3%, moderate illness from 31.8% to 36.4% and marked/severe/very severe score from 55.6% to 17.3% (p<0.001). GAF increased from 43.1 (12.6) to 57.9 (13.6) (p<0.001). Compared to 12 months retrospectively, full hospitalizations mean length of stay decreased by 28 days (p< 0.004) and number of stays decreased by 0.62 (p<0.001). RLAI was generally well tolerated; 1 patient discontinued treatment for adverse events (AEs).

Conclusions. These interim data show that patients switched to RLAI exhibit significant improvements from baseline in clinical and functional outcome after 12 months of continuous treatment. Hospitalization duration and number of hospitalizations decreased significantly. Follow-up is ongoing until 24 months.

References:
1. none.
2. none.

NR489 Tuesday, May 22, 12:00 PM - 2:00 PM
Metabolic Changes Following 24 Weeks’ Treatment with Quetiapine, Olanzapine or Risperidone in Patients with Schizophrenia
John W. Newcomer Washington University School of Medicine, Department of Psychiatry, 660 South Euclid Avenue, Box 8134, St. Louis, MO, 63110-1002, 6000, Robert E. Ratner, Jan W. Eriksson, Robin Emsley, Didier Meulien, Frank Miller, Julia Leonova-Edlund

Educational Objectives:
At the end of this presentation, participants should be able to recognize that commonly prescribed atypical antipsychotics may be associated with differential changes in glucose, insulin, and lipid parameters in patients with schizophrenia.

Summary:
Objective: Metabolic changes following antipsychotic treatment are of interest (1). This randomized, 24-week, flexible-dose study (D1411C00125) compared the effects of quetiapine, olanzapine, and risperidone on glucose metabolism.

Methods: Primary endpoint: changes (baseline to Week 24) in AUC 0-2h plasma glucose following oral glucose tolerance test (OGTT); primary analysis: quetiapine versus olanzapine. Secondary analyses included between- and within-group mean changes, with additional endpoints: fasting plasma insulin, AUC 0-2h plasma insulin, insulin sensitivity index (ISI), insulinogenic index (IGI, descriptive analysis only), fasting lipids and lipid ratios (post hoc analyses).

Results: 395 patients completed the study: quetiapine n=115 (mean dose 607 mg/day), olanzapine n=146 (15.2 mg/day), risperidone n=134 (5.2 mg/day). In the primary analysis population, AUC 0-2h plasma glucose was significantly lower for quetiapine compared with olanzapine (-12.8 mg/dL, p=0.048). Fasting plasma insulin increased by 3.3% (quetiapine), 8.5% (olanzapine), and 11.9% (risperidone). AUC 0-2h plasma insulin increased significantly with olanzapine (+24.45%; CI, 11.46,38.96), but not quetiapine (+13.15%; CI, -0.14, 28.22) or risperidone (+10.74%; CI, -1.2, 24.13). Changes in ISI were significant with olanzapine (-19.1%, CI -27.9, -9.33) and risperidone (-15.8%, CI -25.1, -5.41) but not quetiapine (-10.8%, CI -21.9, 1.85). Median relative changes in IGI were -0.20% (quetiapine), -9.15% (olanzapine), and -3.27% (risperidone). Total cholesterol and LDL increased significantly with olanzapine, but not quetiapine or risperidone. Triglycerides, cholesterol/HDL and triglycerides/HDL ratios also increased significantly with olanzapine, but not quetiapine or risperidone.

Conclusion: Significant reductions in glucose tolerance were seen with olanzapine but not with quetiapine. Similar to other studies (2), olanzapine treatment was associated with insulin resistance and adverse changes in plasma lipids. Changes in plasma lipids with quetiapine were not associated with insulin resistance.
NR490  Tuesday, May 22, 12:00 PM - 2:00 PM
The Association between Antipsychotic Treatment and Unintentional Injury in Patients Diagnosed with Psychiatric Disorder

Qayyim Said University of Utah, Pharmacotherapy Outcomes Research Center, 421 Wakara Way, Room 208, Salt Lake City, UT, 84108, 8000, Elaine M. Gutterman, Myoung S. Kim, Gilbert J. L’Italien, Diana I. Brincker, Richard Whitehead

Educational Objectives:
At the conclusion of this presentation, the participant should be able to evaluate somnolence levels and physical safety risks associated with second-generation antipsychotics.

Summary:
Objective: This study examined the relationship between antipsychotic use, categorized by published somnolence adverse event rates, and unintentional injury (UI).
Method: In a large healthcare claims database, eligible patients (aged 18-64 years) had E-claims for selected Uls (e.g. falls or non-passenger vehicle accidents), with the first injury designated as the index date between January 2001 and December 2004 and diagnoses of schizophrenia or affective disorder (ICD-9 295-296). A nested case-control design was used. Controls had no injury claim and a randomly selected medical claim as the index date. Both groups had a prescription for either a first- or second-generation antipsychotic agent (FGA/SGA) prior to the index claim date. Both groups were within 120% of the prescription days supply. Patients treated with clozapine, depot or more than one antipsychotic were excluded. Somnolence categories were defined as low (aripiprazole or zolpidem), medium (risperidone), high (olanzapine or quetiapine) and any single FGA. A logistic regression model estimated adjusted odds ratios (AOR) with 95% confidence intervals (CI).

Results: 649 cases and 5215 controls, diagnostic groupings were 8.7% schizophrenia, 68.1% affective disorder, and 23.3% both. Antipsychotic somnolence classifications were: 7.9% low, 25.4% medium, 55.6% high, and 11.1% FGA. Relative to low, high somnolence SGAs had an AOR of 1.41; CI (1.03-1.9) for risk of UI, while medium and FGAs had AOR’s of 1.17; CI (0.83-1.64) and 1.19; CI (0.80-1.77), respectively. In a model where olanzapine and quetiapine were disaggregated, the AOR for quetiapine was 1.61 CI (1.15-2.25) and significant, while the effect for olanzapine was not (AOR 1.25; CI [0.89-1.75]).

Conclusion: High somnolence SGAs were associated with a 41% increase in risk of unintentional injury relative to low somnolence SGAs. In disaggregated analyses, quetiapine had a 61% increased risk, while olanzapine risk was not significant. Clinicians should consider somnolence potential and possible physical safety effects when prescribing antipsychotics.

References:

NR491  Tuesday, May 22, 12:00 PM - 2:00 PM
Efficacy of Once-Daily Quetiapine Sustained Release (SR) in Patients with Acute Schizophrenia

Charles Schulz University of Minnesota Medical School, Department of Psychiatry, 2450 Riverside Avenue, Minneapolis, MN, 55454, 9000, René Kahn, Venesil Palazov, Efren Reyes, Didier Meulien, Martin Brecher, Ola Svensson

Educational Objectives:
At the conclusion of this presentation, participants should be able to demonstrate an understanding of the efficacy of the once-daily quetiapine SR formulation.

Summary:
Introduction: Quetiapine immediate release (IR) is effective and well tolerated in patients with schizophrenia and bipolar disorder (1,2) and has recently been approved in the USA for bipolar depression. Nonadherence to medication is common in patients with schizophrenia and may negatively affect long-term outcomes. Less frequent dosing regimens may improve adherence. This 6-week, double-blind, randomized, placebo-controlled study (D1444C00132) evaluated the efficacy and safety of once-daily quetiapine SR; key efficacy data are reported here.

Methods: 588 patients with acute schizophrenia (PANSS total score ≥70; CGI-S >4) received quetiapine SR 400, 600, or 800 mg/day (dose escalation to 400 and 600 mg/day by Day 2; 800 mg/day by Day 3), IR 400 mg/day (5-day dose-escalation schedule: 200 mg twice-daily), or placebo. Primary endpoint: change from baseline to Day 42 in PANSS total score (LOCF). Secondary endpoints included: % patients responding at Day 42 (≥30% reduction in PANSS; CGI-I score ≤3); changes from baseline to Day 42 in PANSS subscale scores and CGI-S. AEs and safety assessments were recorded.

Results: At Day 42, least-squares mean PANSS total score decreased significantly with quetiapine SR (-24.8, p<0.05; -30.9, p<0.001; -31.3, p<0.001; for 400, 600, 800 mg/day, respectively) and quetiapine IR (-26.6, p<0.01) versus placebo (-18.8). PANSS and CGI response rates for quetiapine SR (all doses) and quetiapine IR were significantly higher than for placebo (p<0.05). Improvement in PANSS subscale and cluster scores were also observed for quetiapine SR versus placebo. CGI-S improved significantly with quetiapine SR 600 mg/day (p<0.001), 800 mg/day (p<0.001), and quetiapine IR (p=0.033) versus placebo. The 3-day dose escalation of quetiapine SR was well tolerated; there were no unexpected AEs.

Conclusions: Once-daily quetiapine SR (400-800 mg/day) was effective versus placebo in patients with acute schizophrenia, and was well tolerated.

References:

NR492  Tuesday, May 22, 12:00 PM - 2:00 PM
Effects of Aripiprazole and Olanzapine on Serum Triglyceride: High Density Lipoprotein Ratios in Patients With Schizophrenia (Studies CN138-002, CN138-003 and CN138-047)

Jonathan M. Meyer University of California, Department of Psychiatry, 3350 La Jolla Village Dr. (116-A), San Diego, CA,
Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate that aripiprazole treatment is associated with an improvement in the ratio of triglyceride-high density lipoprotein cholesterol, a marker of insulin sensitivity, in patients with schizophrenia. Participants should also appreciate that olanzapine treatment is not associated with any improvement in this parameter over 26 weeks of treatment.

Summary:

Background: Insulin resistance, a core feature of the metabolic syndrome, is associated with future risk for type 2 diabetes. Recent evidence in non-diabetics suggests that a ratio of serum triglyceride-to-high density lipoprotein cholesterol (TG:HDL-C) greater than 3.0 detects insulin-resistant individuals with greater sensitivity than criteria proposed by the Adult Treatment Panel III to diagnose metabolic syndrome. The objective of this post-hoc analysis was to compare TG:HDL-C ratios in patients treated with olanzapine or aripiprazole for 26 or 52 weeks.

Methods: An exploratory post-hoc analysis of pooled data from 3 randomized, 26- or 52-week, double-blind controlled clinical trials of olanzapine versus aripiprazole. Blood samples from fasting subjects were used to calculate TG:HDL-C ratios, and within and between-group statistical comparisons were made using an observed case approach.

Results: At baseline, TG:HDL-C ratios for subjects randomized to aripiprazole (3.79, n=272) and to olanzapine (3.73, n=274) were similarly high, and not significantly different. In the aripiprazole group, significant improvements were seen compared with the baseline TG:HDL-C ratios at week 26 (3.03, p<0.001) and 52 (3.07, p=0.007). In the olanzapine group, TG:HDL-C ratios were numerically higher than at baseline at week 26 (4.02, p=0.06) and 52 (4.18, p=0.12). The TG:HDL-C ratios were significantly lower in the aripiprazole group than in the olanzapine group at weeks 26 (p<0.0001) and 52 (p<0.004).

Conclusion: At week 26 and 52, TG:HDL-C ratios were significantly lower in the aripiprazole group compared with the olanzapine group. TG:HDL-C ratios improved to near normal in aripiprazole-treated patients at week 26, an effect that was maintained to week 52. Results suggest that long-term aripiprazole treatment may reverse the adverse metabolic effects of other antipsychotic medications, and thereby improve metabolic parameters in patients at high risk for insulin resistance.

References:

1. Mclaughlin T et al: Use of metabolic markers to identify overweight individuals who are insulin resistant. Annals of Internal Medicine 2003;139:802-809.

Summary:

Objectives: Two-year naturalistic study investigating the effects of LAIR and other OA on treatment adherence and tolerability in 400 patients with recently diagnosed schizophrenia (1-5 years since diagnosis).

Methods: This prespecified interim-analysis comprised 179 patients after one year of treatment. Visits were at baseline, after 3, 6, 9 and 12 month. Treatment adherence was defined as continuous treatment with the initial antipsychotic as monotherapy at one year. Clinical symptoms were rated using PANSS, extrapyramidal symptoms with the Extrapyramidal Symptom Scale (EPS).

Results: 89 patients started treatment with LAIR, 90 with one of six OA (olanzapine 11, quetiapine 16, amisulpride 11, ziprasidone 16, aripiprazole 18, oral risperidone 18). Mean age ±SD at baseline was 32.7±10.5 for LAIR and 34.6±11.6 years for OA. Mean duration of schizophrenia was 2.7±1.6 years for both groups. Other demographic variables were comparable between the two groups. There were baseline differences between LAIR and OA with regard to reasons for treatment initiation (non-compliance 56% vs 18%; lack of tolerability 22% vs 31% and symptom severity (baseline total PANSS 94±25 vs 87±27). With regard to treatment adherence, there was a tendency towards higher retention rates and mean duration in the study with LAIR (56% vs 47%, p=0.23; 395±216 vs 342±204 days). PANSS scores improved significantly for both groups (LAIR -17±27 vs OA -16±26, p<0.001 vs baseline). EPS scores improved similarly in both groups from baseline to endpoint (p<0.01). Overall, disease-related AEs (psychosis 14%; agitation 9.5%) were most common, followed by weight gain (9.5%) and fatigue (9%).

Conclusion: In this prospective non-interventional study, patients with newly initiated LAIR or OA treatment demonstrated comparable improvement of psychopathology and EPS and a tendency towards higher treatment adherence with LAIR. This may be of clinical relevance, in particular when considering the higher proportion of non-compliant patients in the LAIR group at baseline.

References:


NR494 Tuesday, May 22, 12:00 PM - 2:00 PM
Evidence of Antipsychotic Treatment Selection Based on Metabolic Risk Factors Among Community-based Schizophrenia Patients (The STAR Trial)
Gilbert J. L’Italien Bristol-Myers Squibb, Wallingford, 5 Research Parkway, Wallingford, CT, 06492, 9000, Linda Hanssens, Ronald N. Marcus, Robert D. McQuade
Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the importance of considering metabolic adverse events associated with certain atypical antipsychotics when selecting an antipsychotic agent for the treatment of patients with schizophrenia.

Summary:

Objectives: Recent metabolic treatment guidelines suggest changing the antipsychotic regimen when patients present with metabolic abnormalities, as such abnormalities may contribute to increased risk of cardiovascular disease.1,2 The naturalistic Schizophrenia Trial of Aripiprazole (STAR) provided the opportu-
nity to assess treatment selection based on metabolic risk factors among patients treated with atypical antipsychotics.

Methods: Patients with schizophrenia included in the study were considered eligible for a change in their previous medication owing to tolerability problems and/or suboptimal control of clinical symptoms. 555 patients were equally randomized to open-label treatment with atypical antipsychotics. The standard-of-care agent was selected by investigators according to patients’ treatment history; patients were not to receive the antipsychotic prescribed just prior to study entry, or one not previously tolerated/effective. Baseline levels of total-, HDL- and LDL-cholesterol, triglycerides, glucose, and weight were compared among the standard-of-care agents (using ANOVA) to determine whether the subsequent selection of standard-of-care agent was associated with metabolic risk.

Results: Mean ± standard error baseline (pre-drug assignment) total-cholesterol levels (mg/dl) were significantly higher (p<0.05) for risperidone (214±5.7) versus olanzapine (201.6±6.2) and quetiapine (206±5.2) patients. LDL-cholesterol levels (mg/dl) were also significantly higher for risperidone (129±3.4) versus olanzapine (118±5.1) and quetiapine (119±5.2) patients. Similarly, baseline triglyceride levels (mg/dl) were significantly higher (p<0.05) for risperidone (185±20) versus olanzapine (161±11) and quetiapine (177±12) patients. There were no between-agent differences in weight or HDL-cholesterol at baseline.

Conclusions: The pattern of lipid levels preceding selection of the standard-of-care agent suggests that clinicians in community practice are following the major metabolic guidelines when choosing an atypical antipsychotic, with risperidone perceived to present a lower metabolic risk versus quetiapine or olanzapine.

References:

NR496 Tuesday, May 22, 12:00 PM - 2:00 PM
Rates of Metabolic Syndrome and Non-High-Density Lipoprotein-Cholesterol Among Overweight Patients Switched From Olanzapine to Aripiprazole (Study CN138-122)
Gilbert J. L’Italien Bristol-Myers Sqiib Company, Department of Psychiatry, 5 Research Parkway, Wallingford, CT, 06492, 9000, John W. Newcomer, Robert Berman, Ronald N. Marcus, Wendy Kerselaers, Robert D. McGuade

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the effects of switching overweight patients with schizophrenia/schizoaffective disorder from olanzapine to aripiprazole on the rates of non-high-density lipoprotein cholesterol and metabolic syndrome.

Summary:
Objectives: To evaluate the rates of metabolic syndrome (MetSyn) and non-high-density lipoprotein-cholesterol (non-HDL-C) among overweight patients switched from olanzapine to aripiprazole.

Methods: In total, 173 overweight patients (BMI ≥27 kg/m²) with schizophrenia or schizoaffective disorder previously treated with olanzapine were randomized to double-blind treatment with aripiprazole or continued olanzapine monotherapy for 16 weeks following a 2-week, open-label, observation period during which subjects continued to receive olanzapine. MetSyn was prospectively defined according to ATPIII criteria to occur within a 7- or 70-day follow-up time window. MetSyn rates at 16 weeks (OC), were compared using a CMH General Association Test, controlling for treatment. Percentage change in non-HDL-C from baseline at 16 weeks was estimated with ANCOVA, adjusting for duration of prior olanzapine exposure, treatment, and log baseline fasting non-HDL-C.

Results: MetSyn rates with aripiprazole versus olanzapine were 60.0% versus 80.3% in the 70-day window (136 evaluable patients in the safety sample [n=164]; RR=0.75; 95%CI: 0.61-0.92; p=0.006) and 36.4 versus 55.0% in the 7-day window (n=115; RR=0.66; 95%CI: 0.44-1.00; p=0.046). Non-HDL-C rate at 16 weeks was significantly (p<0.001) reduced in patients switched to aripiprazole versus those continuing olanzapine (LOCF: -10.9%,
Conclusions: MetSyn rates were 20-30% higher in olanzapine-treated patients versus those switched to aripiprazole, depending on the time window used to define occurrence. Patients switched to aripiprazole demonstrated a clinically relevant decrease in non-HDL-C levels in a short time period versus those continuing on olanzapine. Thus, important risk factors associated with cardiovascular disease and myocardial infarction were decreased in overweight patients with schizophrenia/schizoaffective disorder switched from olanzapine to aripiprazole.

References:


NR498  Tuesday, May 22, 12:00 PM - 2:00 PM
Metabolic Outcomes, in Terms of Weight, Glucose and Lipid Profiles, in Patients with Schizophrenia Treated with Paliperidone Extended-release Tablets for 52 Weeks
Michelle Kramer, M.D. Johnson & Johnson Pharmaceutical Research and Development, CNS, 1125 Trenton Harbortoun Road, Titusville, NJ 08560, 9000, Manüelle Eerdekens, M.D., Rosanne Lane, M.S., Pillar Lim, Ph.D., Jay Sherr, Pharm.D., Joseph Palumbo, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should have an understanding of the tolerability of paliperidone ER in terms of metabolic parameters over a 52-week open-label extension study of the three 6-week double-blind studies.

Summary:
Objective: Increased risk of diabetes associated with some atypical antipsychotics has increased interest in the metabolic effects of these agents. Paliperidone extended-release tablets (paliperidone ER) has been shown to be efficacious and well tolerated in three 6-week double-blind (DB) trials of patients with schizophrenia. Evaluated here are the effects of paliperidone ER on metabolic parameters during the long-term open-label extension (OLE) phases of these DB studies.

Methods: Analyses included pooled data from three international, 52-week, OLE studies in patients with schizophrenia (n=1083, aged ≥18 years) with flexibly dosed paliperidone ER (3, 6, 12 or 15mg; starting dose=9mg). Assessments included changes from OLE baseline to end point in fasting glucose, insulin and lipid levels, glucose-related AEs, body mass index (BMI) and body weight. All samples were collected under standardized fasting conditions.

Results: The population (n=1083), mean±SD age=37.6±10.9 had the following OLE baseline laboratory values: glucose=5.3±1.1mmol/L, insulin=11.0±15.5μu/ml, cholesterol=4.9±1.0mmol/L, high density lipoprotein (HDL)=1.2±0.3mmol/L, low density lipoprotein (LDL)=3.0±0.9mmol/L, triglycerides (TAG)=1.5±0.9mmol/L, BMI=26.4±6.2kg/m² and bodyweight=76.4±19.7kg. Mean±SD duration in OLE was 231.8±145.68 days. The total mean modal dose of paliperidone ER during the pooled OLE was 10.1mg. Mean end point change in serum glucose was 0.2±3.3mmol/L. Five patients in the OLE had glucose levels outside the range 2.22-16.65mmol/L (4 high, 1 low). Mean end point change in insulin levels was 2.8±37.0μu/ml. No increases in mean total cholesterol, TAG, LDL or HDL were observed at end point. Mean end point changes in bodyweight and BMI were 1.1±5.5kg and 0.4±2.0kg/m², respectively. No patients discontinued study medication due to glucose-related AEs or weight increase. The incidence of glucose-related and weight increase AEs were low (<1% and 5%, respectively).

Conclusion: Data from 1-year treatment with paliperidone ER continue to support the favorable metabolic profile observed in the short-term DB studies.
References:


NR499 Tuesday, May 22, 12:00 PM - 2:00 PM
Remission in Schizophrenia: Results From a 12-Month Analysis of Long-Acting Risperidone in Patients With First-Episode Psychosis
Robin A. Emsley University Stellenbosch, Faculty of Health Sciences, PO Box 19063, Tygerberg Cape Town, 7505, 7910, Piet Oosthizen, Liezl Koen, Dana Niehaus, Alice Lex, Rossella Medori

Educational Objectives:

At the conclusion of this session, participants should have an understanding of the remission status of patients with first-episode psychosis after 12 months of treatment with long-acting risperidone.

Summary:

Objectives: Assess rate of remission and relationship with outcomes and examine the association between baseline clinical parameters and early treatment with later remission in a prespecified, 12-month interim analysis from an ongoing 2-year, open-label trial with long-acting risperidone (LAR).

Methods: Eighteen women and 33 men with recent onset psychosis were enrolled. After 1 week of risperidone oro-dispersible tablets (1–3mg), patients received 25mg LAR every 2 weeks for 6 weeks, with flexible dosing thereafter (LAR 25–50mg). Remission status was defined by Andreasen et al., 2006. For all assessments, data at 12 months are presented.

Results: Fifty patients (mean baseline age=25.3±7.3 y) received LAR. Overall, 25 patients (50%) achieved remission by 12 months. Median time to remission was 213 days. Significant baseline clinical and early treatment associations with later remission were female sex (14 (78%) women vs. 11 (34%) men, p=0.007), lower baseline Parkinsonism scores (0.2±0.8 vs. 2.7±3.7, p=0.001) and early treatment response (improvements in PANSS total scores at Week 2 (−17.5 vs. −8.2, p=0.007), Week 4 (−25.7 vs. −15.8, p=0.0122) and Week 6 (−30.2 vs. −20.0, p=0.0374). At 12 months remitted patients had significantly lower PANSS total scores at Week 2 (-17.5 vs. -8.2, p=0.007), Week 4 (-25.7 vs. -15.8, p=0.012) and Week 6 (-30.2 vs. -20.0, p=0.0374).

Conclusions: In this interim analysis of first-episode psychosis, 50% of patients treated with LAR achieved remission at 12 months. Remission was associated with greater improvements in all symptom domains, and a trend towards improved function, health status, productivity and lower resource use.

References:


NR500 Tuesday, May 22, 12:00 PM - 2:00 PM
A Randomized, Open-label, Single-center, Crossover Study of the Potential Effects of Paroxetine on the Pharmacokinetics of a Single Dose of Paliperidone Extended-release Tablets in Healthy Subjects
Adriaan Cleton, Ph.D. Johnson & Johnson Pharmaceutical Research and Development, Global Clinical Pharmacology & Experimental Medicine, Turnhoutseweg 30, Beerse, 2340, 4231, Joris Berwaerts, M.D., Iris van de Vliet, Isung Chang, Ph.D., John Prosscos, Paul van Hoek, M.D., Marielle Eerdekens, M.D.

Educational Objectives:

At the conclusion of the presentation, the reader should understand that paroxetine does not have a clinically significant effect on the pharmacokinetics of a single dose of paliperidone ER and appreciate that initiation or discontinuation of treatment with a CYP2D6 inhibitor does not warrant an adjustment in the dose of paliperidone ER.

Summary:

Objective: Paliperidone undergoes limited hepatic metabolism and in vitro studies suggest a limited role for cytochrome P450 (CYP) 2D6. CYP isoenzymes are involved in the metabolism of certain drugs that are frequently used together, hence potential for drug-drug interactions should be considered. For example, the metabolism of some atypical antipsychotics is subject to inhibition by selective serotonin re-uptake inhibitors. Therefore, paliperidone extended-release tablets (paliperidone ER) may be useful in patients receiving such concomitant medications or those with hepatic impairment. The study assessed the effect of paroxetine, a potent CYP2D6 inhibitor, on the pharmacokinetics of a single dose of paliperidone ER.

Methods: Healthy male subjects received, in random order, each of the following 2 treatments separated by a wash-out period of at least 14 days: 1 tablet of paliperidone ER 3mg (Day 1), or 20mg of paroxetine daily (Day 1-13) with 1 tablet of paliperidone ER 3mg on Day 10. Pharmacokinetic measurements were taken over 96 h after paliperidone ER administration for calculation of C max (ng/mL) and AUC (ng.h/mL) of paliperidone ER.

Results: Sixty subjects were enrolled; 83% completed the study. A very slight and clinically insignificant increase in exposure, reflected by a ratio of 1.09 for C max (CI 1.04-1.30) and a ratio of 1.16 for AUC (CI 1.04-1.30) was observed when paliperidone ER was administered concomitantly with paroxetine compared with paliperidone ER alone. There were no serious AEs or clinically important individual mean changes in clinical laboratory values, vital signs, or ECG parameters.

Conclusion: Co-administration of paliperidone ER and paroxetine compared with paliperidone ER alone caused a minimal increase in paliperidone exposure that was not considered clinically relevant. Thus, the initiation or discontinuation of treatment with a CYP2D6 inhibitor does not warrant a dose adjustment of paliperidone ER.

References:

NR501  Tuesday, May 22, 12:00 PM - 2:00 PM  
Aripiprazole as an Adjunctive Therapy in Patients With Major Depressive Disorders: Impact on Patient-Reported Functional Disability  
Patricia K. Corey-Lisle Bristol-Myers Squibb, Wallingford, 5 Research Parkway, Wallingford, CT, 06492, 9000, Robert Berman, René Swanink, Robert D. Quade, Gilbert J. L'Italien  

Educational Objectives:  
At the conclusion of this presentation, the participant should be able to understand the importance of recognizing and treating functional disability associated with psychiatric disorders. The participant should also be aware of recent evidence showing the benefits of adjunctive aripiprazole to standard antidepressant therapy with regard to family life and social functioning in patients who showed an incomplete response to standard antidepressant therapy.

Summary:  
Objectives: Functional disability or impairment is considered a hallmark of psychiatric disorders¹. We assessed the functional impact of adjunctive aripiprazole in patients with major depressive disorder who showed an incomplete response to ≥1 historical and one prospective standard antidepressant therapy (ADT) using the Sheehan Disability Scale (SDS)² in a multicenter, randomized, double-blind, placebo-controlled trial.

Methods: This 6-week study assessed the safety and efficacy of aripiprazole as an adjunctive treatment to ADT in depressed patients who showed an incomplete response to a prospective trial of ADT. The key secondary endpoint was the change in SDS mean score from baseline. The SDS is a validated, 3-item measure of disability associated with psychiatric disorders. Treatment comparisons of SDS mean score and sub-scale scores (social, family, work) were carried out using ANCOVA, including the baseline evaluation as covariate and with treatment and study center as main effects.

Results: In the last observation carried forward (LOCF) analyses, the mean change in SDS score in patients receiving aripiprazole was -1.11 versus -0.65 for placebo (p=0.055). In the OC analysis, mean change in total scores were -1.17 for aripiprazole vs -0.65 for placebo (p=0.037). Item scores for family life and social disability favored aripiprazole (p=0.030 and 0.017, respectively; LOCF). Work disability item differences were non-significant between groups.

Conclusions: Clinical measures of symptom-severity are widely used in treatment trials. The SDS provides an additional perspective: patient-reported functional impairment. This study demonstrates that treatment with adjunctive aripiprazole plus ADT in patients who showed an incomplete response to standard antidepressant therapy is associated with patient-perceived benefits relating primarily to family life and social functioning.

References:  

NR502  Tuesday, May 22, 12:00 PM - 2:00 PM  
Negative Symptoms of Schizophrenia and Their Impact on Functioning in US and European Patients  
Oscar Leeuwenkamp, Ph.D. NV Organon, Department of Global Health Economics & Strategic Pricing, Molenstraat 110, Oss, 5342 CC, 2771, Robert Morlock, Ph.D., Jason Shepherd, M.S., Richard Perry, B.S.  

Educational Objectives:  
At the conclusion of this presentation, the participant should be able to:  
1. Demonstrate familiarity with standard measures of functional outcome in patients with schizophrenia.  
2. Recognize the relationship between functional impairment and negative symptoms in patients with schizophrenia.  

Summary:  
Background: Negative symptoms are reported in nearly one third of patients with schizophrenia. We assessed survey data on functional outcomes in patients from the US and Europe who exhibited predominantly negative symptoms of schizophrenia.

Methods: Physicians from the US and Europe who prescribed antipsychotics for ≥15 patients with schizophrenia during the preceding 3 months were invited to complete a questionnaire concerning their patients' clinical and functional status.

Results: Surveys on 2591 patients from the US and 6569 patients from Europe (France, n=1492; Germany, n=1439; Italy, n=1002; Spain, n=1310; United Kingdom, n=1326) were completed. Physicians classified symptoms as being predominated by or with a high level of positive symptoms (US, 47%; Europe, 38%), predominated by or with a high level of negative symptoms (US, 24%; Europe, 32%), or not dominated by either symptom type (US, 20%; Europe, 22%). Symptom ratings were not obtained from 9% of US patients and 8% of European patients. US physicians' ratings on the Global Assessment of Functioning Scale and scales rating overall and cognitive function and patients' ability to meet their own needs did not vary notably with symptom classification. In contrast, European physicians' ratings showed significantly greater functional impairment in patients with predominant negative symptoms. In both the US and Europe, patients with predominant negative symptoms were more likely to require caregivers (US, 51%; Europe, 57%) than patients in all other symptom categories (US, 41%-48%; Europe, 49%-50%).

Conclusions: In this large multinational cross-sectional survey of physicians from the US and Europe, patients with predominant negative symptoms of schizophrenia were functionally impaired to a degree that matched or surpassed the impairment associated with predominant positive symptoms. These findings suggest that improving the treatment of negative symptoms of schizophrenia could enhance overall functionality in patients with schizophrenia.

References:  

NR503  Tuesday, May 22, 12:00 PM - 2:00 PM  
Neuropsychological Impairment in Treatment-Resistant Depression: A Normative Comparison  
Philip D. Harvey Mt. Sinai School of Medicine, Department of Psychiatry, 1425 Madison Avenue, 4th Floor, New York, NY, 10029, 9000, Gahan J. Pandina, Carla M. Canuso, Mary J. Kujawa, Stephen C. Rodriguez, Ramy A. Mahmoud  

Educational Objectives:  
At the conclusion of this presentation, participants will be able to characterize the profile and severity of cognitive impairments in patients with treatment resistant depression (TRD). This will include an understanding of the different ability areas impaired and their relative disturbance compared to demographically similar healthy comparison subjects.

Summary:  
Background: Treatment-resistant depression (TRD) is a psychiatric condition with substantial morbidity and mortality, but little information is available about its determinants, especially cogni-
tive impairments. This is the first study of cognitive impairment in TRD using normative reference data.

Methods: A structured and computerized baseline cognitive assessment was performed on a large sample of patients with TRD (N=497) from a multinational study of atypical antipsychotic augmentation of antidepressant therapy. Patients met DSM-IV criteria for major depressive disorder, had evidence of nonresponsive depression from a single or recurrent episode with or without psychotic features, and scored ≥20 on the Hamilton rating scale for depression. Baseline cognitive tests performed included Auditory Number Sequencing (working memory), Continuous Performance Test (executive functioning), Face Memory Test (secondary memory), Set-Shifting Test (processing speed, executive function, procedural learning), and Tapping Speed Test (simple motor speed). Data for healthy comparison subjects were collected in the US. Subjects were selected for similarity to the TRD patients on age, education, and gender.

Results: Baseline cognition data were available for 272 subjects with TRD and 63 healthy controls. With the exception of two Set Shifting Test reaction time (RT) variables (Mean imitation RT, Mean reversal RT), there was significantly poorer performance in TRD subjects vs healthy controls in all cognitive tests (P<0.05). Impairments were greatest in domains of motor speed, episodic memory, and attention, with large effect size differences (d>0.5). Changes in some cognitive measures were observed and will be discussed further.

Conclusions: Patients with TRD performed consistently more poorly than healthy controls across assessments. Impairments were slightly more severe than those in currently depressed patients with non-resistant major depression. Evaluating cognitive impairment and response to treatment in TRD will be a substantial step in understanding the determinants of disability in this condition.

Supported by Janssen L.P.

References:

NR504 Tuesday, May 22, 12:00 PM - 2:00 PM
Evaluating the Four-Item Negative Symptom Assessment (NSA-4) Scale in Schizophrenic Patients With Predominant Negative Symptom
Larry Alphs, Ph.D. Pfizer Inc., Global R&D, 2600 Plymouth Road, B003/1018, Ann Arbor, MI, 48105, 9000, Cheryl Hill, Ph.D., Pilar Cazorla, Ph.D., Jacquelyn Wilson, Ph.D., Robert Morlock, Ph.D.

Educational Objectives:
The at the conclusion of this presentation, the participant should be able to:
1. Demonstrate familiarity with the clinical instruments used to assess the negative symptoms of schizophrenia.
2. Describe the methods by which the validity of the NSA-4 was documented.

Summary:
Background: The 16-item Negative Symptom Assessment scale (NSA-16), which includes a separate Global Rating, is a validated measure of negative symptoms in schizophrenia. A 4-item version has been designed for raters with minimal training to provide quick assessment of patients with negative symptoms. We evaluated the psychometric properties of the NSA-4 for comparison with the NSA-16.

Methods: The NSA-16 was administered at randomization in clinical trials in patients (n=561) with predominant negative symptoms. Coadministered measures included the Positive and Negative Syndrome Scale (PANSS), Clinical Global Impression-Severity of Illness scale (CGI-S), and Level of Functioning (LOF) assessment. The NSA-4 and NSA-16 were compared for their ability to predict the NSA Global Rating and CGI-S. Convergent and divergent validity were assessed using correlations between the NSA-4 and NSA-16 and other outcome measures. Internal consistency and test-retest reliability of the NSA-4 and NSA-16 were also compared.

Results: NSA-4 showed high correlation with NSA-16 (r = 0.85, P<0.0001). Both instruments showed high correlation with the NSA Global Rating (r=0.71 for NSA-16 and r=0.70 for NSA-4, both P<0.0001), PANSS negative factor (Marder) score (r=0.63 and r=0.57, P<0.0001), PANSS negative symptoms subscale score (r=0.59 and r=0.52, P<0.0001), and LOF (r=0.51 and r=-0.47, P<0.0001). Both the NSA-4 and NSA-16 were predictive of severity classifications as determined by the NSA Global Rating and CGI-S (P<0.0001). Internal consistency was 0.85 for NSA-16 and 0.64 for NSA-4 (decrease expected for a 4 item scale measuring multiple domains). The test-retest intraclass correlation coefficient was 0.87 for NSA-16 and 0.82 for NSA-4 (both adequate).

Conclusions: The NSA-4 and NSA-16 both demonstrate acceptable psychometric properties for assessing the impairment associated with negative symptoms in patients with schizophrenia. The NSA-4 is an easy-to-use tool that can be used in clinical practice for quick assessment and tracking of negative symptoms.

References:

NR505 Tuesday, May 22, 12:00 PM - 2:00 PM
Effect of Risperidone Long-Acting Injectable on Hospitalizations: 12-Month Interim Analysis of the Schizophrenia Outcomes Utilization Relapse and Clinical Evaluation (SOURCE)
Chris Kozma, University of South Carolina, Adjunct Professor, 112 Fox Hollow Circle, West Columbia, SC, 29170, 9000, Susan Vallow, Lian Mao, Stephen C. Rodriguez, Mary J. Kujawa

Educational Objectives:
At the conclusion of this presentation, participants will be able to recognize the clinical characteristics of patients with schizophrenia who have been initiated on risperidone long-acting injectable. They will also be able to identify the healthcare resource utilization patterns of these patients based on our interim results.

Summary:
Objective: To evaluate mental health-related hospitalizations and emergency room visits in the 12 months prior to and following initiation of risperidone long-acting injectable (RLAI) in an ongoing, 2-year observational study of schizophrenia patients.
Methods: Adult schizophrenia patients requiring RLAI treatment were eligible. Patient demographics, treatment history, healthcare utilization, functioning, quality of life, antipsychotic satisfaction, and medication use were analyzed. This interim analysis reports
on patients who completed >12 months of the trial. Percentages of patients hospitalized and numbers of patients with mental health-related hospitalizations and ER visits in the 12 months prior to baseline (pre-period) were compared to that during the 12 months following RLAI initiation (post-period). McNemar’s tests were utilized for pre to post comparisons of categorical data, and paired t-tests were utilized on continuous measures.

Results: 108 patients met inclusion criteria; mean±SD age was 48.8±10.4 years and 64.2% were male. In the pre-period, 28.4% were hospitalized, vs 17.4% in the post-period (P=0.046). Mean hospital days per patient across all patients decreased from 8.2±23.7 in the pre-period to 4.2±24.5 in the post-period (P=0.023), while among those hospitalized in either period (n=43), mean hospital days decreased from 20.3±34.4 to 10.1±38.5 (P=0.023). Similarly, the percentage of patients incurring ER visits decreased, from 19.6% in the pre-period to 9.8% in the post-period (P=0.050). Mean number of ER visits decreased from 0.38±1.0 in the pre-period to 0.16±0.6 in the post-period (P=0.033).

Conclusions: Fewer patients were hospitalized and incurred emergency room visits in the 12-month period following initiation of RLAI compared to the pre-period. Further analyses will examine factors contributing to relapse and hospitalization.

Funded by Ortho-McNeil Janssen Scientific Affairs, LLC

References:

NR507 Tuesday, May 22, 12:00 PM - 2:00 PM
A Pharmacokinetic (PK)-Pharmacodynamic (PD) Relationship Exists for Efficacy of Iloperidone: A Novel Investigational Atypical Antipsychotic Agent
Pablo Baroldi, M.D., Ph.D. Vanda Pharmaceuticals Inc., Management, 9605 Medical Center Drive, Suite 300, Rockville, MD, 20850, 9000, Curt Wolfgang, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that a PK/PD relationship exists for the efficacy of iloperidone and apply that knowledge to understand the importance of this relationship in the management of patients with schizophrenia.

Summary:
Purpose: Iloperidone is an investigational mixed D_{2}/5HT_{2A} antagonist antipsychotic with affinity for 5HT_{1A}, 5HT_{2A} and 5HT_{3} receptors. This profile predicts potentially enhanced clinical efficacy against schizophrenia with reduced extrapyramidal side-effects. We investigated the exposure-response relationship for iloperidone through PK-PD modeling analysis.

Methods: Iloperidone plasma levels were randomly obtained at steady-state after dose administration during two phase 3 trials. Only patients reaching target dose who were maintained at that dose level >6 days (reaching steady state) were included in PK-PD analysis. Trial data was combined with a previous PK study, finding iloperidone dose-proportionality (2-12mg bid), to build a population PK model. C_{avg}=0 was assigned to placebo-treated patients as baseline for comparison. After modeling, predicted or simulated values of C_{avg} at last steady state dose for patients from the two phase 3 studies were made and correlated with last available efficacy measurements using multiple regression analysis.

Results: Schizophrenia symptom improvement was associated with higher iloperidone C_{avg} after baseline adjustment (study drug ranges, 12-24mg/d). Statistically significant greater proportions of responders (>20% improvement from baseline) in iloperidone-treated patients in one study had C_{avg}>5ng/mL (n=43) compared with those with C_{avg}<5ng/mL (n=224) for four out of five efficacy scales (p=.05) (Positive and Negative Syndrome Scale [PANSS] during the preceding year. Differences between patients with predominant negative symptoms versus those with predominant positive symptoms were seen in the frequency of outpatient visits (US, 8.9 vs 8.1; Europe, 8.2 vs 6.7), frequency of ED visits (US, 0.42 vs 1.0; Europe, 0.46 vs 0.83), and mean length of hospital stay (US, 25.7 vs 35.5 days; Europe, 53.0 vs 57.3 days). In contrast, the mean number of current medications was similar for patients with predominant negative symptoms versus those with predominant positive symptoms in both the US (2.1 vs 2.0) and Europe (1.5 vs 1.6).

Conclusions: In this retrospective survey, US and European patients with predominant negative symptoms of schizophrenia had more frequent outpatient visits but fewer ED visits and a shorter mean length of hospitalization compared with patients with predominant positive symptoms.

References:

NR506 Tuesday, May 22, 12:00 PM - 2:00 PM
Impact of Positive and Negative Symptoms of Schizophrenia on Resource Use in the United States and Europe
Robert J. Morlock, Ph.D. Pfizer Inc., None, 235 East 42nd Street, New York, NY, 10017, 9000, Oscar Leeuwenkamp, Ph.D., Jason Shepherd, M.S., Richard Perry, B.S.

Educational Objectives:
1. Demonstrate familiarity with the positive and negative symptoms of schizophrenia.
2. Summarize the impact of positive and negative symptoms on utilization of clinical services.

Summary:
Background: Patients with schizophrenia may experience positive (e.g., hallucinations) or negative (e.g., social withdrawal, blunted affect, apathy) symptoms. The objective of this research was to assess the impact of negative versus positive symptoms on clinical resource use.

Methods: Physicians in the United States and 5 European countries who prescribed antipsychotics for 15 or more patients with schizophrenia within the preceding 3 months completed a questionnaire regarding their patients’ clinical status (relative prominence of negative vs positive symptoms) and resource use during the preceding year (mean values for psychiatric outpatient and emergency department [ED] visits, length of last completed hospitalization, and number of current medications taken).

Results: Data were collected from 7962 patients (US, 1709; Europe, 6253). In the US and Europe, similar percentages of patients had at least one psychiatric hospitalization (48.8% and 50.7%) and at least one psychiatric ICU stay (7.3% and 9.6%)
Total, PANNS-Positive, PANNS-Negative, and PANNS-General Psychopathology). This result was not observed in the second study because relatively fewer patients in the second study had C_{avg}<5ng/mL, leading to higher percentage of patients showing clinical response and resulting lower response variation.

Conclusions: Iloperidone showed an exposure-response relationship, suggesting minimal effective exposure level for iloperidone is 5ng/mL. Therefore, full therapeutic iloperidone benefit should be assessed once steady-state is achieved. Therapy with iloperidone should be patient individualized though consideration of this PK-PD relationship while balancing tolerability/adverse effects.

References:

NR508  Tuesday, May 22, 12:00 PM - 2:00 PM
Genotyping Facilitates Individualized Prediction of Pharmacokinetic Response to Iloperidone in Extensive and Poor CYP2D6 Metabolizers

Curt Wolfgang, Ph.D. Vanda Pharmaceuticals Inc., Clinical Program Head, Vanda Pharmaceuticals Inc., 9605 Medical Center Drive, Suite 300, Rockville, MD, 20850, 9000

Educational Objectives:
At the conclusion of this presentation, the participant should be able to demonstrate awareness of the pharmacokinetics of iloperidone in genotyped extensive and poor CYP2D6 metabolizers. The participant should also be able to recognize the potential utility of this information and the importance to individualizing drug therapy to the patient in the management of schizophrenia.

Summary:
Purpose: Iloperidone is an investigational mixed D_{2}/5HT_{2} antagonist antipsychotic with affinity for 5HT_{1A}, 5HT_{2A}, and 5HT_{2C} receptors. This profile predicts potentially enhanced clinical efficacy against schizophrenia with reduced extrapyramidal side-effect risk. Iloperidone metabolism involves P450 enzyme CYP2D6 and 3A4, resulting in major metabolites P88 (contributes to efficacy) and P95 (non-contributory). A study was conducted characterizing iloperidone pharmacokinetics in genotyped poor (PM) and extensive (EM) CYP2D6 metabolizers. Iloperidone interaction with dextromethorphan, a CYP2D6 prototype substrate, was assessed.

Methods: A two-cohort study was completed in healthy subjects genotyped as CYP2D6 EM (Cohort 1, n=18) or PM (Cohort 2, n=8). All subjects received single 3mg dose iloperidone in Period 1. In Periods 2 and 3, subjects received either 80mg dextromethorphan or 3mg iloperidone + 80mg dextromethorphan in random order. Iloperidone plasma samples were collected for 72 hours after administration of iloperidone and iloperidone + dextromethorphan. Dextromethorphan serum samples were collected for 24 hours after administration of dextromethorphan and 72 hours after administration of iloperidone + dextromethorphan.

Results: Iloperidone and P88 exposures were significantly increased (57% and 95%, respectively) in PM, while P95 exposure was significantly decreased (80%). Elimination half-life was prolonged 88% for iloperidone and 46% for P88. In contrast, CYP2D6 substrate did not influence pharmacokinetic parameters of iloperidone: C_{max} of iloperidone alone (2.7ng/ml) and in combination with dextromethorphan (2.75ng/ml) appeared at the same median time (T_{max}=2.5h). In general, pharmacokinetic parameters of iloperidone were similar in the presence, or absence, of dextromethorphan.

Conclusions: Genotyping of patients as poor or extensive CYP2D6 metabolizers facilitates individualized prediction of pharmacokinetic profile to iloperidone. Although iloperidone was well-tolerated by poor and extensive CYP2D6 metabolizers, the ultimate clinical goal of achieving best balance of efficacy/tolerability/side-effects can be better realized considering CYP2D6 status.

References:

NR509  Tuesday, May 22, 12:00 PM - 2:00 PM
Reach of Benchmark Psychiatric Trial Results to Community-Based Providers: A Case Study of CATIE

Anthony Q. Weiss, M.D. Massachusetts General Hospital, Psychiatry, Building 149, 149 13th St., Charlestown, MA, 02129, 9000, Timothy J. Petersen, Ph.D., Mark A. Blais, Psy.D., Jeff Huffman, M.D., Robert J. Birnbaum, M.D.

Educational Objectives:
1. At the conclusion of the presentation, the participant should be able to recognize the extent to which results of a recent benchmark psychiatric trial have reached the knowledge base of community-based providers.
2. At the conclusion of the presentation, the participant should demonstrate an understanding of the impact of intensive continuing medical education on community-based providers' knowledge of the findings of a recent benchmark psychiatric trial.
3. At the conclusion of the presentation, the participant should be able to identify factors that may mediate this learning process, and geographical differences in pre and post activity knowledge levels.

Summary:
Background: Recent publication of findings from benchmark psychiatric trials has added immensely to the field's knowledge base of optimal methods to treat and manage major psychiatric disorders. The extent to which these findings have been disseminated to front-line, community-based providers is largely unknown. The objective of this study was to examine, as part of a nationwide, academic-based CME program, participant knowledge levels of the CATIE trial, both before and after an educational activity.

Methods: Responses from 1463 audience members at Massachusetts General Hospital Psychiatry Academy (MGH-PA) CME events, held in nine cities across the United States, were used for our analyses. The focus of this report is on pre and post-educational activity questions that pertain to results of the CATIE trial. Descriptive statistics were utilized to calculate response patterns and knowledge change.

Results: Of those audience members actively treating patients with schizophrenia, 48% indicated, prior to program delivery, that CATIE trial results had no impact on their practice. In addition, prior to the lecture, on average only 29% of audience members were able to accurately identify the clinical endpoint used in this landmark trial. Robust knowledge increase of CATIE trial results
was evidenced following the activity. An analysis of geographic variance revealed a consistent result across all nine cities. 

**Conclusion:** Despite its status as a pivotal, benchmark clinical trial, CATIE appears to have had minimal impact on the practice of community-based providers in this sample. This may in part relate to limited awareness of even the basic aspects of the study, despite over thirty high-profile publications regarding CATIE over the past year. As evidenced by post-lecture testing, this CME activity showed a substantial impact on knowledge. Whether this type of lecture-based CME program increases utilization of this information in clinical practice remains to be seen.

**References:**


**NR510**

**Tuesday, May 22, 12:00 PM - 2:00 PM**

**Continuity of Care in Schizophrenia**

Susan Vallow Ortho-McNeil Janssen Scientific Affairs, LLC, Scientific Affairs, 1125 Trenton-Harbourton Road, Titusville, NJ, 08560, 9000, Patricia Russo, Joseph J. Parks III, Marcos Memran, Lee Stern

**Educational Objectives:**

At the conclusion of this presentation, participants will recognize the importance of continuity of care in the treatment of patients with schizophrenia. They will also know the factors that influence continuity of care in the treatment of these patients.

**Summary:**

**Background:** Transfer of care from inpatient to the community is a critical phase in the treatment of patients with schizophrenia; however, failures to achieve first post-discharge appointments continue to persist. Lack of patient insight and discontinuity of primary provider involvement have been cited as negative contributing factors to continuity of care.

**Purpose:** This qualitative study describes the current protocols for inpatient to outpatient transfer, and identifies those with the greatest influence on continuity of care.

**Methods:** Literature and internet searches were performed to compile state-specific guidelines, clinical practice guidelines, and algorithms related to facilitating continuity of care. Structured phone interviews were conducted with care managers in a variety of geographically-dispersed treatment settings (rural, suburban, urban). Relative importance of factors was rated from low to high (0-10).

**Results:** Searches of state guidelines revealed great disparity in the level and type of guidelines that are followed. Results of the interviews revealed eight factors that influenced continuity of care. Availability of medications between settings had the greatest influence (9.3). Individualized treatment approach (8.3), access to care (8.3), family involvement (7.8), insurance coverage (7.6), schizophrenia-related effects on behavior (7.5), and communication between managers (7.4) followed. Discharge instruction clarity had the least influence (6.5). Influence ratings varied according to inpatient vs outpatient setting: health coverage, 8.7 vs 6.5; communication between settings, 6.8 vs 8.2; and clarity of discharge instruction, 6.0 vs 7.0. Insurance coverage was most influential in inner-city settings (7.5 urban, 9.0 inner-city, 7.1 suburban).

**Conclusions:** Medication availability had the greatest influence on continuity of care. Further research is needed to study the consequences of levels of continuity, and to identify programs that improve continuity and patient outcomes.

Source of Funding: Ortho-McNeil Janssen Scientific Affairs, LLC

**References:**


**NR511**

**Tuesday, May 22, 12:00 PM - 2:00 PM**

**Antiviral Therapy Completion and Response Rates Among Hepatitis C Patients With and Without Schizophrenia**

Alex Mitchell, B.S. Portland VA Medical Center, Mental Health, Portland VA Medical Center, P3MHDC, 3710 SW US Veterans Hospital Rd., Portland, OR, 97239, 9000, Marilyn S. Huckans, Ph.D., Samantha Ruimy, B.S., Jennifer Loftis, Ph.D., Peter Hauser, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to: 1) Recognize that patients with serious mental illness are at increased risk for hepatitis C (HCV) and that patients with HCV have increased rates of psychiatric comorbidities. 2) Demonstrate an increased understanding of the neuropsychiatric side effects associated with antiviral therapy for HCV.

**Summary:**

**Objective:** To compare antiviral therapy completion and sustained viral response (SVR) rates between hepatitis C (HCV) patients with- versus those without schizophrenia (SCHZ).

**Methods:** We conducted a retrospective medical record review of all patients with SCHZ who received antiviral therapy for HCV between 1998 and 2006 at facilities in the Veterans Integrated Service Network 20 of the Veterans Healthcare Administration. Patients confirmed to have SCHZ and to have had antiviral therapy (n=50) were compared to a control group of demographically (age, HCV genotype, race, gender, and period of military service) matched patients with no history of SCHZ (n=50) on the following rates: antiviral therapy completion, end of treatment response (ETR), SVR, psychiatric/ medical side effects, and emergency room visits/ inpatient hospitalizations during antiviral therapy. Patients were subgrouped by genotype for analyses because standard of care includes six months of antiviral therapy for genotypes 2/3, versus twelve months for genotype 1.

**Results:** The total sample (n=100) was predominantly male (96.7%), Caucasian (91.7%), and middle-aged (50.4±4.9 years). 46.7% (n=28) had genotypes 2/3, 46.7% (n=28) had genotype 1, and 6.7% (n=4) had unknown genotypes. For genotypes 2/3, antiviral therapy completion rates were not significantly different between SCHZ+ and SCHZ- Groups (76.9% vs. 80.0%); the SCHZ+ Group was significantly more likely to achieve an ETR (100% vs. 66.7%, $\chi^2=5.3, p=0.044$) and an SVR (76.9% vs. 40%, $\chi^2=3.9, p=0.049$). For genotype 1, antiviral completion (42.9% vs. 57.1%) and response (ETR: 42.9% vs. 28.6%, SVR: 35.7% vs. 21.4%) rates did not significantly differ between groups. For patients in either genotype subgroup, there were no significant differences between the SCHZ+ and SCHZ- groups in other response variables.

**Conclusions:** Our retrospective chart review suggests that patients with SCHZ complete and respond to antiviral therapy for HCV at rates similar to those without SCHZ.

NR512 Tuesday, May 22, 12:00 PM - 2:00 PM
Effect of Ziprasidone on Weight and Metabolic Parameters at Various Fixed Doses in Patients With Schizophrenia or Schizoaffective Disorder
David Gibson Folks, M.D. Maine General Medical Center, Psychiatry, Maine General Medical Center, 6 East Chestnut St, Augusta, ME, 04330, 9000, Ilise D. Lombardo, M.D., Ruoyong Yang, Ph.D., Antony D. Loebel, M.D.

Educational Objectives:
At the end of this presentation, the participant will understand the effects of ziprasidone on weight and metabolic parameters at varying fixed doses.

Summary:
Ziprasidone has consistently displayed a favorable metabolic profile in short- and long-term studies. The question whether ziprasidone is associated with any dose-related effects on weight and other metabolic parameters has not been fully explored. We conducted a meta-analysis of patients with schizophrenia or schizoaffective disorder who received fixed doses of oral ziprasidone (daily dose ≤ 40 mg, n = 226; 80 mg, n=147; 120 mg, n = 120; 160 mg, n = 104; 200 mg, n = 85) during 4 short-term, fixed-dose, placebo-controlled clinical trials. We assessed the change from baseline to last visit for non-fasting total cholesterol, triglycerides, glucose, weight, and body mass index (BMI). Dose response was determined by using orthogonal polynomial contrasts. In an ANCOVA analysis, the LS mean changes from baseline for the 5 dose groups ranged from: total cholesterol (mg/dL), -3.7 to -12.1; triglycerides (mg/dL), -0.84 to -12.7; glucose (mg/dL), -1.5 to 2.2; weight (kg), 0.55 to 1.2; BMI, 0.18 to 0.43. There was no significant dose-related effect for any of these metabolic variables, weight, or BMI. These results indicate that in short-term placebo controlled trials, ziprasidone at doses of ≤ 40 to 200 mg/d is not associated with dose-related effects on weight, lipid, or glucose measures.

References:
1. Bruce Parsons, Antony Loebel, Kathryn Williams, et al. Weight effects associated with dose-related effects on weight, lipid, or glucose measures.

NR513 Tuesday, May 22, 12:00 PM - 2:00 PM
Asenapine Improves Cognitive Function In Acute Schizophrenia: A Placebo- and Risperidone-Controlled Trial
Steven Potkin, M.D. University of California, Irvine Medical Center, 101 City Drive South, Route 88, Orange, CA, 92668, 9000, Kirsten Fleming, Ph.D., Brendon Binneman, Ph.D., David S. Keller, Ph.D., Larry Alphs, Ph.D., John Panagides, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
1. Demonstrate familiarity with the cognitive effects of schizophrenia.
2. Demonstrate familiarity with standard measures of cognitive function in patients with schizophrenia.

Summary:
Background: Asenapine, a novel psychopharmacologic agent in development for the treatment of schizophrenia and bipolar disorder, was compared with placebo and risperidone in a previously presented clinical trial in patients with acute schizophrenia. Here, we present the results of cognitive function testing performed during that trial.

Methods: Cognitive function in patients with acute exacerbation of schizophrenia symptoms was assessed in a 6-week, randomized, double-blind, placebo- and risperidone-controlled study. Patients were randomized to fixed doses of asenapine (5 mg BID), risperidone (3 mg BID), or placebo. A battery of neurocognitive tests administered at baseline, week 3, and week 6 or last visit (with last observations carried forward in patients not completing the study) assessed speed of processing (Category Fluency, Letter Fluency, Trails A and B, Digit Symbol Substitution Test [DSST]), working memory (Letter-Number Span Test), verbal learning and memory (Rey Auditory Verbal Learning Test, which includes immediate and delayed recall and delayed recognition); visual learning and memory (Benton Visual Retention Test), and reasoning and problem solving (Wisconsin Card Sorting Test [WCST]). Dunlap’s D >0.25 denoted moderate or greater effect size.

Results: Asenapine improved verbal learning and memory (Dunlap’s D 0.45, 0.38, and 0.25 for immediate and delayed recall and delayed recognition, respectively) and processing speed (0.43, 0.34, and 0.31 for Trails A time, DSST, and Letter Fluency) but decreased performance in Trails B errors (-0.26). Risperidone improved processing speed (Dunlap’s D 0.31 and 0.24 for Trails A time and DSST) but decreased performance in reasoning and problem solving (-0.35 and -0.31 for WCST percentage of perseverative errors and total number correct).

Conclusions: In patients with acute schizophrenia, treatment with asenapine was associated with improved cognitive function in the domains of processing speed and verbal learning and memory, which are considered relevant to functional outcome.

References:
NR514  Tuesday, May 22, 12:00 PM - 2:00 PM

Insight in Alcoholic Schizophrenic Patients: Comparison with Nonalcoholic Schizophrenic Patients Using SUMD, WCST, and MMPI Profile

Jin Hun Kim, M.D. Seoul National Hospital, Psychiatry, Department of Psychiatry, Seoul National Hospital, 51 Neungdong-Ro, Gwangin-Gu, Seoul, 143711, South Korea, Jin Hak Kim, Ph.D., Daeho Kim, Ph.D.

Educational Objectives:
- Through this presentation, the audience will know the degree of insight impairment in patients with alcoholic schizophrenia, especially compared with non-alcoholic schizophrenics.

Summary:
Background: Schizophrenic patients with alcohol use disorder (dual diagnosis, DD) showed more frequent hospitalization and poorer compliance compared to schizophrenic patients without alcohol use disorder (single diagnosis, SD). This showed that DD subjects could have the lower level of insight than SD subjects. However, the degree and pattern of impairment of insight between DD and SD have rarely been compared, especially when subjects are psychiatrically stable.

Methods: Using SUMD-K (insight), WCST (prefrontal functioning), and MMPI-LK profiles (psychological defense), we compared stable DD patients (n = 34) and SD patients (n = 39).

Results: Stable DD subjects demonstrated impairments in current insight across two domains of SUMD compared with stable SD subjects. WCST preservation errors significantly correlated with unawareness of illness in SD while psychological defense was significantly correlated with unawareness of illness in DD. Unawareness of illness in DD was significantly correlated with duration of alcohol use disorder.

Conclusion: Relatively stable DD subjects differed from SD subjects in several aspects of insight. The degree of impairment of insight was greater in DD patients compared with SD subjects. Impairment of insight in DD subjects, unlike SD subjects, reflected psychological defense rather than prefrontal functioning.

References:

NR515  Tuesday, May 22, 12:00 PM - 2:00 PM

The Relationship Between Clinical Efficacy and Quality of Life: A Randomized, 40-Week, Double-Blind Study of Ziprasidone versus Haloperidol Followed by a 3-Year, Double-Blind Extension Phase

Stephen M. Stahl, M.D. Neuroscince ED Institute, Psychiatry, 5857 Owens Avenue, Suite 102, Carlsbad, CA, 92008, 9000, Ashok K. Malla, M.D., John W. Newcomer, M.D., Antony D. Loebel, M.D., Lewis Warrington, M.D., Eric Watsky, M.D., Cynthia Siu, Ph.D.

Educational Objectives:
- At the conclusion of this presentation, participants will be able to describe the efficacy and tolerability of the atypical antipsychotic risperidone vs placebo in acutely ill adolescent patients with schizophrenia.

Summary:
Background: Conflicting evidence exists regarding whether second-generation antipsychotics (SGAs) lead to a greater improvement than conventional agents in negative, cognitive, and mood symptoms associated with schizophrenia. We conducted a longitudinal analysis to evaluate long-term treatment with ziprasidone versus haloperidol (up to 196 weeks), as assessed by PANSS negative and GAF scores (primary efficacy measures) and their association with quality-of-life (QLS) (2) improvement.

Methods: The study included two treatment periods: (i) a 40-week, randomized, double-blind phase comparing ziprasidone (ZIP 80-160 mg/d given BID, N=227; ZIP 80-120 mg/d given QD, N=221) versus haloperidol (HAL 5-20 mg/d, N=151), followed by (ii) a 3-year, double-blind extension phase on the same double-blind medications. Of the 220 subjects who completed the 40-week phase, 186 (84.5%) (ZIP BID N=72, ZIP QD N=67, and HAL N=47, respectively) consented to participation in the extension study. Longitudinal changes in the primary efficacy measures and their associations with QLS outcomes were analyzed using Generalized Estimating Equations (GEEs) with adjustments for the effects of dropout.

Results: In the randomized, double-blind, 40-week core study, ziprasidone was associated with greater improvement in efficacy and QLS outcomes than haloperidol, but the differences were not statistically significant. Longitudinal trajectories of these outcomes observed in the extension phase indicated differential treatment effects favoring the higher dosage group of ziprasidone (80-160 mg/d given BID, vs. haloperidol) (p<0.05 for PANSS negative, GAF scores, and QLS). A similar pattern was observed for the ziprasidone QD group (80-120 mg/d given QD, vs. haloperidol), but differences were not statistically significant. A significant, longitudinal association between improvement in efficacy and quality-of-life was found for all treatment groups (p<0.05, all measures).

Conclusions: In this long-term, double-blind study, ziprasidone treatment (80-160 mg/d given BID) was associated with greater clinical improvements than haloperidol. These results demonstrate the potential for enhanced long-term outcomes in using a second-generation antipsychotic.

References:
1. Davis JM, Chen N, Glick ID: A meta-analysis of the efficacy of second-generation antipsychotics. Arch Gen Psychiatry. 2003;60:553-564.

NR516  Tuesday, May 22, 12:00 PM - 2:00 PM

Efficacy and Safety of Risperidone in Adolescents with Schizophrenia

Magali Haas, M.D. Johnson & Johnson Pharmaceutical Research and Development, CNS, 1125 Trenton-Harbor Court Road, Titusville, NJ, 08560, 9000, Alan S. Unis, M.D., Margaret Copehaver, Ph.D., Jorge Quiroz, M.D., Stuart Kushner, M.D., Vivek Kusumakar, M.D.

Educational Objectives:
- At the conclusion of this presentation, participants will be able to describe the efficacy and tolerability of the atypical antipsychotic risperidone vs placebo in acutely ill adolescent patients with schizophrenia.

Summary:
Objective: To evaluate the efficacy and safety of two dose ranges of risperidone in the treatment of adolescents with schizophrenia.
Methods: This randomized, placebo-controlled, double-blind, multicenter study included adolescents aged 13-17 years with a DSM-IV diagnosis of schizophrenia who were experiencing an acute exacerbation. Patients received risperidone 1-3 mg/day, 4-6 mg/day, or placebo for six weeks. The primary efficacy assessment was Positive and Negative Syndrome Scale (PANSS) total score change at endpoint. Secondary efficacy assessments included PANSS factor scores, clinical response rates, Clinical Global Impressions scales, and Children's Global Assessment Scale (CGAS). Safety assessments included AE reporting and scores on extrapyramidal symptom rating scales.

Results: A total of 160 patients were randomized to placebo (n = 54), risperidone 1-3 mg/day (n = 55), or risperidone 4-6 mg/day (n = 51); 78% completed the study. Improvement in mean±SD PANSS total scores at endpoint was significantly (P<0.001) greater in the risperidone groups (1-3mg: −21.3±19.6; 4-6 mg: −21.2±18.3) vs placebo (−8.9±16.1). A significantly higher percentage of patients in the risperidone groups achieved the clinical response vs placebo. Risperidone was associated with rapid and significant improvement in symptoms, global illness ratings, and psychological and social functioning at both dosage levels vs placebo. The most common AEs were somnolence, agitation, and headache in the risperidone 1-3 mg group, and extrapyramidal disorder, dizziness, and hypotension in the risperidone 4-6 mg group. There were no prolactin-related AEs, or adverse reactions related to glucose or lipid metabolism. EPS severity was low. There were no unexpected safety or tolerability findings.

Conclusions: Daily doses of risperidone 1-3 mg and 4-6 mg were well tolerated and superior to placebo in adolescents experiencing acute exacerbation of schizophrenia. A daily dose of 3 mg demonstrated the best benefit-risk ratio.

Supported by J&JPRD.

References:

NR517 Tuesday, May 22, 12:00 PM - 2:00 PM
Antipsychotic Medications and the Monitoring of Metabolic Side Effects: Can We Improve?
Robert E. Socherman, Ph.D., Portland VAMC, Mental Health, 2634 NE Jarrett Street, Portland, OR, 97211, 9000, Lisa F. Engleman, N.P., Alex Linke, B.S., Peter Hauser, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to identify the current guidelines and recommendations for the monitoring of metabolic side effects for patients who are prescribed antipsychotic medications. In addition, the participant will be able to appreciate the current rates of monitoring of metabolic side effects within a large healthcare system.

Summary:
Objective: To present the level of prescriber monitoring of metabolic side effects for patients who are prescribed antipsychotic medications.
Methods: A retrospective chart review was conducted of all veteran patients who were prescribed antipsychotic medications during the year 2005 to determine the rate of monitoring of metabolic side effects. The primary outcome measure was if any/all of the tests were performed within 6 months after the start of at least one antipsychotic medication. The tests were as follows: blood pressure, cholesterol, glucose, weight, and girth.

Results: Out of 2,460 patients who were prescribed at least one antipsychotic medication in 2005, 1,905 of these patients (61 different Mental Health prescribers) received their prescription from their Mental Health prescriber. During the year 2005, 73.6% (1,399) of patients had their blood pressure monitored at least once, 71% (1,349) had their weight measured, 1.3% (24) had their girth measured, 73.6% (1,402) had their glucose checked, and 72.7% (1,385) had their cholesterol checked. 56.3% (1,071) of patients had all tests except for girth performed, at least once within six months of a medication start, and 84.3% (1,605) of patients had at least one of these tests performed during this period of time.

Conclusion: It is clear that antipsychotic medications have significant adverse effects on weight, girth, blood pressure, lipids, and glucose metabolism which often lead to life-threatening diseases. These study results suggest that the monitoring for metabolic side effects varies significantly based on the test (weight, girth, glucose, blood pressure) and that there are at least 25% of patients who appear to not be monitored at all for metabolic side effects. Early identification of these adverse metabolic effects can minimize and prevent the development of chronic disease.

References:

NR518 Tuesday, May 22, 12:00 PM - 2:00 PM
Early Onset of Antipsychotic Action and Time Course in the Treatment of Acute Bipolar Mania
Terence A. Ketter, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will gain understanding of the time course of antipsychotic action in the treatment of acute bipolar mania.

Summary:
Background: Previous studies have demonstrated the efficacy of ziprasidone in improving symptoms of mania and global illness severity from Day 2 onward in patients with acute bipolar mania (1). Recent research indicates intramuscular ziprasidone produces a significant, early (within 24 hours) improvement in psychotic symptoms (2). In this analysis, we evaluated the potential for an early antipsychotic response to oral ziprasidone in subjects with acute bipolar mania.

Methods: We conducted a pooled analysis of two 3-week, randomized, double-blind, placebo-controlled studies of ziprasidone (40-160 mg/d) in hospitalized patients (N=415) with bipolar I disorder, and a current manic (N=257) or mixed episode (N=158). Efficacy assessments included the Mania Rating Scale (MRS), derived from the SADS-C) and CGI-I-S which were administered at baseline and Days 2, 4, 7, 14, and 21 (or early termination). Improvement in psychosis was evaluated by the SADS-C psychosis subscale (delusions, hallucinations, and suspiciousness). MMRM analysis was used to estimate the time course of response.

Results: Significant improvement in the SADS-C psychosis subscale was observed in the ziprasidone group (versus placebo) as early as Day 4 (p<0.007) in all subjects, and the magnitude of improvement increased with time (p<0.002 Weeks 1, 2 and 3; p<0.003 treatment-by-visit interaction).
Discussion: Ziprasidone is associated with a rapid onset of response in psychotic symptoms associated with acute bipolar mania. These findings support the hypothesis that onset of antipsychotic action can occur early in treatment, with the magnitude of response increasing over time.

References:

NR519 Tuesday, May 22, 12:00 PM - 2:00 PM
Prevalence and Validity of Depression in Schizophrenia
Eran Chemerinski, M.D. Mount Sinai School of Medicine, Psychiatry, 1425 Madison Ave, New York, NY, 10029, 9000, Christopher Bowie, Ph.D., Hannah Anderson, B.A., Philip D. Harvey, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that depressive symptoms are independent features frequently present in patients with schizophrenia.

Summary:
Affective symptoms are common in schizophrenia, though rarely a focus of research or treatment. Depressive symptoms have definitional and methodological overlap with negative symptoms, complicating studies of its prevalence and treatment response. We performed a convergent/divergent validity study of depressive symptoms in schizophrenia. In this study (N=212) of the course of depress in schizophrenia subjects, correlations with cognition, functional status. Schizophr Res. 2006 Jul;85(1-3):12-9. capacity, and symptoms. Am J Psychiatry. 2006 Mar;163(3):418-25.

NR522 Tuesday, May 22, 3:00 PM - 5:00 PM
Protective Effect Against Alcohol Dependence of the Thermolabile Variant of MTHFR
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NR521 Tuesday, May 22, 3:00 PM - 5:00 PM
Neuropsychological Performance of Current and Former Users of MDMA (Ecstasy) and Cannabis
Michael Lyvers, Ph.D. Bond University, Psychology, Dept. of Psychology, Bond University, Gold Coast, Qld, 4229, 8021, Jodie Bradam, M.A.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to identify some of the psychopathological correlates of heavy use of MDMA (Ecstasy) or cannabis (marijuana).

Summary:
Controversy has raged over whether the popular illegal drug MDMA (Ecstasy) may act as a serotonergic neurotoxin at typical doses, leading to memory and cognitive deficits in human Ecstasy users. Our investigation aims to overcome limitations of previous research on this issue. Recently (2 weeks) abstinent Ecstasy users, former (long-term abstinent) Ecstasy users, Ecstasy-naive cannabis user controls, and Ecstasy-naive alcohol user controls are matched on age, gender, education, and premorbid intelligence (estimated by National Adult Reading Test scores). Measures include the Wisconsin Card Sorting Test; Wechsler Memory Scale (WMS-III) immediate and delayed tests of visual and verbal memory; Brief Symptom Inventory (BSI); Impulsiveness Venturesomeness and Empathy Questionnaire; Everyday Memory Questionnaire; and Prospective Memory Questionnaire. Findings thus far (using MANOVA, N = 75) indicate that memory scores were significantly worse in Ecstasy users than controls. However, cannabis use was correlated with memory scores and Ecstasy use. When cannabis use was taken into account by covariate analysis (MANCOVA), the specific association of Ecstasy use with memory impairment disappeared. Ecstasy users scored significantly higher than controls on two BSI subscales, obsessive-compulsiveness and phobic anxiety, both of which have been related to serotonergic system functioning. Ecstasy use was negatively correlated with depression scores, suggesting a possible antidepressant-like action of MDMA. A larger sample is anticipated by the time of the conference, which is likely to lead to additional findings. Such findings are important because earlier work indicating the presence of MDMA-related memory impairments in Ecstasy users did not take cannabis use into account, hence deficits attributed to use of Ecstasy may actually reflect residual effects of cannabis use, or correlates of drug/alcohol use in general. Heavy use of Ecstasy may be associated with specific psychopathology as distinct from heavy use of cannabis or alcohol.

References:
Identifying new biological marker of alcoholism and of severity of alcoholism dependance.

Summary:

Objective: Hyperhomocysteinemia is frequently observed in alcohol-dependent subjects, in particularly in those with marked withdrawal symptoms. The common C677T transition on the Methylenetetrahydrofolate reductase (MTHFR) gene influences homocysteinemia. Our objective was to study the prevalence of the MTHFR C677T polymorphism in alcohol-dependent subjects and the influence of this polymorphism on symptoms associated with alcoholism.

Method: MTHFR C677T polymorphism was determined in 93 control subjects and 242 alcohol-dependent subjects. Serum homocysteine, folate and vitamin B12 levels together with hepatic biological parameters were determined in the control and alcohol-dependent subjects.

Results: Hyperhomocysteinemia is frequently observed in alcohol-dependent subjects, particularly in those with marked withdrawal symptoms. Alcohol-dependent subjects showed a significant decrease in MTHFR 677TT prevalence (9%, 21/242) compared to controls (18%, 17/93) (p<0.02). The relative risk estimated as an odds ratio for alcoholism in subjects with the TT genotype is 0.42 (Odd Ratio 95% confidence interval, 0.21-0.83).

Moreover, drinkers to alcohol, they seem to constitute a subgroup of alcoholic patients with a decreased risk for developing neurotoxic withdrawal symptoms and hepatic toxicity.

References:

titude of scores on the VASs was ranked (lowest-to-highest) as
with Visual Analog Scales (VASs) and Addiction Research Center
tobacco use had lower self-esteem than other polysubstance us-
pharmacodynamic effects are lower in a formulation (OROS MPH) in which slow rate
to the high rates of comorbidity or psychological distress in this
had greater sensation seeking (p<0.001), lower harm avoidance
smallest); simi-
derivatives). PK-PD correlations were higher for IR MPH versus OROS MPH, although all correlations were modest. The correlations for OROS MPH 108 mg were consistently lower than correlations for the other 3 treatments.

Conclusion: Smoking among polysubstance users is often viewed as relatively harmless compared to the use of more illicit substances. However, the present study found important correlates of this substance that underscore its potential contribution to the high rates of comorbidity or psychological distress in this population.

References:

NR525 Tuesday, May 22, 3:00 PM - 5:00 PM
A Double-blind, Placebo-controlled, Randomized, Crossover Study to Assess the Pharmacokinetics and Pharmacodynamics of Abuse Potential for OROS® Methylphenidate versus Immediate-release Methylphenidate

Dolly A, Parasrampuria, Ph.D., McNeil Pediatrics, Division of McNeil-PPC, Inc., Drug Development & Safety, 420 Delaware Drive, Fort Washington, PA, 19034, 9000, Kerri Schoedel, Ph.D., Reinhard Schuller, M.S.C., Patrick E. Ciccone, M.D., Steven A. Silber, M.D., Edward Sellers, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant will recog-
nize that at comparable methylphenidate (MPH) doses and plasma exposure (AUC), abuse-related pharmacodynamic effects are lower in a formulation (OROS MPH) in which slow rate of delivery results in a pharmacokinetic profile of lower early exposure compared with an immediate-release MPH formulation.

Summary:
Objective: To determine if the pharmacokinetic (PK) differences of different formulations alter abuse-related pharmacodynamic (PD) effects of methylphenidate (MPH).
Methods: In this single-dose, double-blind, crossover study, healthy, occasional stimulant-abusing adults (n=49) received single placebo; 50 and 90 mg immediate-release (IR) MPH (Ritalin®); and 54 and 108 mg OROS® MPH doses. PD were assessed with Visual Analog Scales (VASs) and Addiction Research Center Inventory (ARCI) Morphine-Benzodrine Group scales (MBG). Correlations between PK and PD parameters were examined.
Results: IR MPH produced greater early exposure to MPH versus OROS MPH, which had a slow ascending PK profile. Magnitude of scores on the VASs was ranked (lowest-to-highest) as placebo < OROS MPH 54 mg < OROS MPH 108 mg < IR MPH 50 mg < IR MPH 90 mg. OROS MPH 54 mg responses for VAS Drug Liking were significantly lower than IR MPH 50 mg (P<0.05), and OROS MPH 108 mg was consistently lower than IR MPH 90 mg. For VAS Good Effects and VAS High, both OROS MPH doses had significantly lower scores than comparable IR MPH doses (P<0.05 and P<0.0001, respectively). IR MPH produced higher responses for VAS Take Drug Again (significant for low dose comparison [P<0.05]). VAS Alertness demonstrated the highest responses at 1.5 hours postdose. VAS Bad Effects responses were similar to the other VASs, while VASs for Feeling Sick and Dizziness demonstrated little change from baseline. IR MPH 50 mg produced greater subjective effects than both OROS MPH doses on the ARCI MBG. PK-PD correlations were higher for IR MPH versus OROS MPH, although all correlations were modest. The correlations for OROS MPH 108 mg were consistently lower than correlations for the other 3 treatments.

Conclusions: For comparable IR MPH and OROS MPH doses, PK differences of different formulations altered abuse-related subjective PD effects.

References:

NR526 Tuesday, May 22, 3:00 PM - 5:00 PM
OROS MPH®: A Methylphenidate Formulation with a Low Potential for Abuse

Patrick E. Ciccone, M.D., McNeil Pediatrics, Division of McNeil-PPC, Inc., 420 Delaware Drive, Fort Washington, PA, 19034, 9000, H. Lynn Starr, M.D., John J. Coleman, M.A., Thom Mrazik, Robert L. DuPont, M.D., Peter B. Bensinger

Educational Objectives:
At the conclusion of this presentation, the participant will recognize that among various ADHD medications, OROS methylphenidate (MPH) has a low potential for abuse as evidenced by a low frequency of emergency department (ED) reports of abuse compared to other MPH formulations and to non-MPH stimulants (eg, amphetamines, mixed amphetamine salts [MAS]). Atomoxetine (ATX) also had a low frequency of reports. The abuse-resistant design of OROS MPH may account for its relatively low frequency of abuse reports compared with other MPH formulations.

Summary:
Objective: To evaluate the relative abuse potential of OROS® MPH and other ADHD treatments using the Drug Abuse Warning Network (DAWN).
Methods: DAWN is a national health surveillance system that monitors drug-related emergency department (ED) visits. DAWN data cannot estimate prevalence of drug abuse, but they measure related health consequences. Using DAWN, we tracked ED visits resulting from abuse of ADHD medications, including OROS MPH, other MPH formulations, non-MPH stimulants (eg, amphetamines, mixed amphetamine salts [MAS]), and the nonstimulant atomoxetine (ATX), from January 2003-July 2006. To compare DAWN reports of abuse ("Other" category: drug dependence, abuse, withdrawal, suicidal ideation/gesture, recreational use, reason unknown) to medical use, a ratio of reports of abuse was calculated by dividing ED visits for abuse by number of prescriptions filled for each product/category (data from IMS Health, Inc.).
Results: The number of ED reports of abuse for ADHD medications surveyed was 1102: OROS MPH, 69; ATX, 61; other MPH formulations, 301; non-MPH stimulants, 651. The number of prescriptions for OROS MPH and other MPH treatments was similar (~28 vs 25 million), yet OROS MPH accounted for 23% of DAWN reports while other MPH formulations accounted for 77%. The ratio of abuse reports to prescribed use for OROS MPH (3.2x10^5) was lower than that of other MPH formulations (12x10^6); similarly, this ratio was low for ATX (3.5x10^5). Non-MPH stimulants had the highest ratio of DAWN abuse reports to prescribed use (14x10^6).
Conclusions: OROS MPH had a low frequency of ED reports of abuse compared to other MPH formulations. The unscheduled nonstimulant ATX also had a low frequency of reports. Of all ADHD treatments, non-MPH stimulants (eg, amphetamines, MAS) had the most ED reports of abuse. Disparity between abuse ratios of OROS MPH and other MPH formulations may result from the abuse-resistant design of OROS MPH.

References:

NR527 Tuesday, May 22, 3:00 PM - 5:00 PM Morphometric Changes of Corpus Callosum in Chronic Alcoholics: A Magnetic Resonance Imaging Study -
jin hee choi, M.D. seoul veterans hospital, psychiatry, 6-2 dunchon-dong,kangdong-gu, seoul, 134-791, 5800, tae yong kim, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to know the finding of neuroimazing in chronic alcoholics.

Summary:
Objectives: The purpose of this study determines difference on corpus callosum between chronic alcoholic patients and controls, and relationship between severity of ethanol intake and the degree of this atrophy.
Methods: Clinicoradiologic study was carried out in 20 chronic alcoholics and age-matched controls. All subjects were male and right-handed. To estimate alcohol habits for subjects, structured interview have been made. Measurement of the midsagittal corpus callosum area and thickness (genu, truncus and splenium), as well as the frontal lobe index (FLI) and the width of the cortical sulci (SWS) on T1-and T2-weighted Magnetic Resonance Images were performed.
Results: Compared to controls, alcoholics had significantly decreased corpus callosum area and thickness (mainly in genu), and significantly increased FLI and SWS. The callosal area negatively correlated with the cortical atrophies and the area of genu of the corpus callosum negatively correlated with the frontal atrophies. Moreover, the reduction of corpus callosum correlated with the total lifetime dose of ethanol consumed.
Conclusions: In chronic alcoholics, atrophy of the corpus callosum is common finding and may reflect the severity and pattern of cortical damage. And the degree of callosal atrophy correlated with the severity of ethanol intake as well.

References:

NR529 Tuesday, May 22, 3:00 PM - 5:00 PM Psychopathology and Eating Behavior in Female Adolescents With Smoking and Drinking Problems -
Joung-Sook Ahn, M.D. Wonju College of Medicine, Yonsei University, Department of psychiatry, Ilsan-dong 162., Wonju Christian Hospital, Wonju, Gangwon-do, 220-701, 5800, Min-Hyuk Kim, M.D., Jong-ho Shin, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that female adolescents with smoking and/or drinking problems are likely to have externalizing behavioral problems, and their eating pattern is mainly related to drinking problem rather than smoking problem.

Summary:
Objectives: Female adolescents with drinking and smoking problems have shown a sharp increase recently, and they are liable to show abnormal eating behaviors. The objects of this research are 1) to estimate the rate of smoking and drinking among female adolescents, and 2) to invest the association of smoking, drinking, the related psychopathology, and eating behavior.
Method: We conducted a survey of 864 girls at one junior high school (n=405) and one high school (n=459) with questionnaires of the general information related to smoking and drinking behaviors, the Strengths and Difficulties Questionnaire for psychopathology, and the Three Factor Eating Questionnaire for eating pattern. In addition, the BMI and the discrepancy of perceived and ideal body image were calculated.
**Results:** The prevalence of drinking and smoking were 35.1% and 11.5%, respectively. Hyperactivity and conduct problems were found in smoking and drinking female adolescents. Smoking girls at high school got a low disinhibition score and high BMI score, and showed considerable discrepancy between perceived and ideal body image. Drinking girls at high school got a high score in both disinhibition and hunger patterns and a low score in dietary restraint. For the junior high schoolgirls, the lower disinhibition score is, the higher the risk of smoking and drinking is, but for the high schoolgirls, the lower dietary restraint score is, the higher the risk of drinking is. And, disinhibition/hunger measures and psychopathology are positively correlated.

**Conclusion:** Smoking and drinking behavior in female adolescents is closely associated to externalizing behavioral problems, and their eating pattern is mainly related to drinking rather than smoking.

**References:**

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**NR530**

**Psychiatric Disorders in Cannabis Abusers Versus Cannabis Dependant Subjects**

Arkaitz Aguerretxe-Colina
Univ. of Bordeaux, Psychiatry, Association Bizia /MIM, CHCB, BP 08, Bayonne, 64109, 4279, Jean-Pierre Dauloude, M.D., Marc Auriaicombe, M.D., Virginie Beltran

**Educational Objectives:**
At the conclusion of this presentation, the audience should understand co-morbid conditions associated with marijuana abuse and dependence.

**Summary:**

**Objective:** Compare prevalence of psychiatric disorders in cannabis abusers and cannabis dependent subjects.

**Methods:** all subjects who went for a cannabis use problem to addiction clinic Bizia, Bayonne were administrated the Mini International Neuropsychiatric Interview for DSM-IV (MINI) current and lifetime to determine cannabis use status (cannabis abuse CA vs. cannabis dependence CD) and co-occurring psychiatric disorders. Comparisons were made by #2 and Student tests (I±=0.05, StatviewA®). Results: 218 cannabis users were assessed and 176 were included: 93 met criteria for dependence, 83 for abuse. No statistical difference between groups was found on age (21.4, SD=6.8), sex ratio (85% men) and in both groups, over 50% met alcohol abuse criteria. Both groups differed (p=0.05) on alcohol dependence criteria (12% of CD; 2% of CA). CA subjects met significantly more anxiety (30%), mood (37%), psychotic (10%) and antisocial personality (25%) disorder criteria than CA subjects (respectively 2%, 12%, 7% and 8%).

**Conclusion:** Compared to cannabis abusers, Cannabis dependant subjects had a significantly higher prevalence of alcohol dependence and a higher prevalence of anxiety, mood, psychotic and antisocial personality disorders. There is a need for a thorough clinical assessment of psychiatric disorders in subjects seeking treatment for cannabis addiction. The level of co-morbidity supports the concept that marijuana dependence represents greater severity than marijuana abuse.

**References:**

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**NR531**

**Tuesday, May 22, 3:00 PM - 5:00 PM**

**Association Between Stage of Change and Outcomes of Smoking Reduction in Chronic Schizophrenic Inpatients With 8-Week Nicotine-Replacement Therapy**

Bo-Jian Wu, M.D. Yu-Li Hospital, PSYCHIATRY, 448 Chung-Hwa Road, Yu-Li Hualien, Taiwan 981, 448 Chung-Hwa Road, Yu-Li Hualien, Taiwan 981, Yu-Li township, Hualien county, TAIWAN, 981, 5830, Tsuo-Hung Lan

**Educational Objectives:**
To examine the association between stage of change and smoking-reduction outcomes among schizophrenic patients receiving transdermal nicotine patches.

**Summary:**
**Objectives:** To examine the association between stage of change and smoking-reduction outcomes among schizophrenic patients receiving transdermal nicotine patches.

**Method:** The researchers enrolled 110 chronic inpatients with schizophrenia or schizoaffective disorder. They were randomly assigned to a low-dose NRT (20.8mg) or a high-dose NRT (30.2mg). At baseline, the participants were categorized into advanced stage of change (preparation, contemplation) and early stage of change (precontemplation) based on their readiness to change smoking behaviors. Smoking behaviors, stage of change and Positive and Negative Syndrome Scale (PANSS) were assessed at baseline and smoking behaviors were reassessed at 2-months postbaseline.

**Primary outcomes:** Daily cigarettes consumption was more than 25% after 8-week clinical trial. Logistic regression model were used to analyze the association between stage of change (advanced stage vs. early stage) and composite variable consisting of stage of change and different dose of NRT. There were 4 matches of composite variable: high-dose NRT plus early stage, low-dose NRT plus early stage, high-dose NRT plus advanced stage and low-dose NRT plus advanced stage.

**Results:** OR of stage of change on smoking reduction was 7.71 (p = 0.003) Compared with composite variable of high-dose NRT plus early stage, OR of high-dose NRT plus advanced stage was 16.9 (p = 0.009); OR of low-dose plus advanced stage was 17.1 (p = 0.007); OR of low-dose NRT plus early stage was 3.7 (p = 0.22).

**Conclusions:** Stage of change has a predictive value on smoking-reduction outcome. It seems to be rational to choose a low-potency adjuvant on patients with advanced stage of change in a smoking-reduction program based on consideration of cost and side effect. For patients in the stage of precontemplation about to receive upcoming smoking-reduction program, a high-potency adjuvant is the choice of pharmacological agents for reducing smoking.

**References:**
**NR532**
**Tuesday, May 22, 3:00 PM - 5:00 PM**

**Very Low-Dose Naltrexone in the Treatment of Opioid Detoxification**

Paolo Mannelli, M.D., Duke University, Psychiatry, 2213 Elba Street, Suite 159A, Durham, NC, 27710, 9000, Ashwin A. Patkar, M.D., Kathleen Prentil, Ph.D., Neena Ajwani, B.A., Seth Preminger, B.A., Andrea Sada, M.D., Bob Hubbard, M.D.

**Educational Objectives:**
At the conclusion of this presentation, the participant should be able to recognize the use of different techniques of opiate antagonist administration in the treatment of opioid dependence.

**Summary:**

**Introduction:** New opioid detoxification methods are needed to improve treatment efficacy and benefits at follow up. Interesting animal data on the efficacy of very low-dose naltrexone suggest to explore the use of this approach in humans.

**Objective:** To investigate safety, and initial efficacy of very low-dose naltrexone administration during methadone detoxification.

**Methods:** 177 opioid addicts received naltrexone 0.125 or 0.250 mg/day in a double blind, randomized, placebo-controlled design, during methadone based, 6-day inpatient detoxification at 2 different community treatments. Subjects received behavioral and physiological assessments, during treatment and 1 and 7 days upon discharge.

**Results:** No naltrexone related adverse event were recorded. Withdrawal intensity during treatment was not significantly different among conditions. However, drug related craving differed between naltrexone and placebo groups, controlling for baseline and drug use severity (F= 7.720, p=0.001). In particular, significantly lower craving was associated with negative drug screens 7 days after discharge among subjects previously treated with naltrexone.

**Conclusion:** The use of very low-dose naltrexone during opioid detoxification was safe and was associated with reduced craving and drug use at short-term follow up. Further studies will explore other applications of this methodology in the treatment of drug dependence.

**References:**

**NR533**
**Tuesday, May 22, 3:00 PM - 5:00 PM**

**Substance Use Disorders and Overweight/Obesity in Bipolar I Disorder: Preliminary Evidence for Competing Addictions**

Roger S. McIntyre, M.D. University Health Network, Psychiatry, 399 Bathurst Street, Toronto, ON, M5T 2S8, 1220, Susan L. McElroy, Jakub Z. Konarski, Joanna K. Soczynska, Saulo Castel, Kathryn Wilkins, Sidney H. Kennedy

**Educational Objectives:**
This investigation was undertaken to explore the relationship between alcohol/illicit drug dependence and overweight/obesity in individuals with bipolar I disorder in a large population-based survey. The impetus for this endeavor was provided by the need to elucidate factors which predispose and portend comorbidity in bipolar disorder, and the putative pathoetiological similarities between these two comorbidities.

**Summary:**

**Objective:** This investigation was undertaken to explore the relationship between alcohol/illicit drug dependence and overweight/obesity in individuals with bipolar I disorder.

**Methods:** The data for this analysis was procured from the Canadian Community Health Survey: Mental Health and Wellbeing (CCHS) conducted by Statistics Canada in 2002. Bipolar I disorder was defined as persons screening positive for a lifetime manic episode using the World Mental Health of the Composite International Diagnostic Interview (WMH-CIDI). Overweight and obesity were defined as a BMI of 25.0-29.9 and ≥30.0 kg/m², respectively.

**Results:** The total sample was comprised of 36,984 individuals (≥15 years old: Mean age of the weighted sample=44.0 years; SD=19.3) with 2.4% (n=938 mean age of the weighted sample=37.3 years; SD=13.4) screening positive for a lifetime manic episode. Subgroup analysis indicated that overweight/obese bipolar individuals had a significantly lower rate of substance dependence (13% vs. 21%; p<0.01). Conversely, bipolar individuals who screened positive for substance dependence had a lower rate of overweight/obesity when compared to non-dependant bipolaris (39% vs. 54%; p<0.01). The inverse association between the presence of these two comorbid conditions in bipolar I disorder continued to be statistically significant after multivariate analysis (OR=0.57, 95% CI=0.34-0.95, p<0.05).

**Conclusions:** Individuals with bipolar I disorder, manifest an inverse relationship between the presence of comorbid overweight/obesity and substance use disorders. These results suggest that comorbid addictive disorders (i.e. substance use and compulsive overeating) may compete for the same brain reward systems.

**References:**

**NR534**
**Tuesday, May 22, 3:00 PM - 5:00 PM**

**Bupropion Reinstates Cocaine Seeking Behavior in Rats**

C.S Ahn, M.D. Duke University, Psychiatry, 2213 Elba St, Room 159A, Durham, NC, 27710, 9000, Rupa Gopalan, M.D., Paolo Mannelli, Ashwin A. Patkar, M.D., D. Weese, M.D., Tong Lee, M.D., Everett Ellinwood, M.D., Colin Davidson, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to recognize the different effects of antidepressants and their use in drug dependence treatment.

**Summary:**

**Objective:** We tested BUP and 2 other common antidepressants with different profiles, for their potential to reinstate cocaine use in a rat relapse model.

**Methods:** Adult male rats were trained to nose-poke for cocaine for 10 days. Rodents were subsequently withdrawn for a week, and then underwent the following daily schedules: no injection and saline (extinction phase), desipramine (DMI), clomipramine (CLO), BUP and COC. Other rats received only saline, or saline...
for the first 3 days, then BUP and finally COC. Nose-poke rates were recorded every day.

Results: Extinction decreased responding by 65%. DMI and CLO had no effect on responding. BUP and COC both reinstated nose-poke behavior, whether or not they were preceded by DMI and CLO. Conclusion: While DMI and CLO may be used safely in the treatment of cocaine abuse, BUP use may be more problematic for its potential to facilitate relapse. However BUP dosing regimen and route of administration may have influenced results and these effects need to be further examined.

References:
1. Hsiao SY, Cheng CF, Yang YK, Yeh TL, Yu L.
2. Cryan JF, Bruijnzeel AW, Skjei KL, Markou A.

NR535 Tuesday, May 22, 3:00 PM - 5:00 PM
Extended-Release Naltrexone (XR-NTX) Reduces Holiday Drinking in Alcohol-Dependent Patients
Michael J. Bohn, M.D. Aurora Psychiatric Hospital, Behavioral Health Center, 1220 Dewey Ave, Wauwatosa, WI, 53213.
9000, Mark Alexander, Ph.D., Sandra Lapham, M.D., M.P.H., Qunming Dong, Ph.D., Robert F. Forman, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize how extended-release naltrexone may greatly impact public health by significantly reducing drinking during holidays as well as non-holiday periods.

Summary:
Objective: Holiday drinking profoundly impacts public health and, in particular, traffic fatalities. Extended-release naltrexone (XR-NTX) has been shown to reduce drinking in alcohol-dependent patients not only on weekdays, but also on weekends when drinking rates are typically higher. This analysis evaluated whether XR-NTX reduced drinking on major holidays that are historically strongly associated with increased rates of highway fatalities.

Methods: In a 6-month, randomized, 24-site, double-blind, placebo-controlled study, 624 alcohol-dependent adults were randomized to receive once monthly injections of XR-NTX 380 mg (n = 205) or 190 mg (n = 210), or placebo (n = 209) in combination with low-intensity psychosocial support. Patients were evaluated in a post-hoc analysis (Wilcoxon test) on four measures of alcohol consumption during holidays and non-holidays over the course of the study. Holidays were defined as the aggregate of ten holidays monitored from July 2002 through July 2003 for alcohol-related traffic fatalities by the National Highway Traffic Safety Administration.

Results: In the subset of patients who were abstinent for at least 4 days before the onset of treatment, XR-NTX 380 mg (n = 27) significantly reduced heavy drinking (p = 0.014), 'risky' drinking (p = 0.012), any drinking (p = 0.034), and drinks per day (p = 0.010) during holidays compared to placebo (n = 27). XR-NTX 380 mg also significantly reduced drinking during non-holiday periods in this same population.

Conclusion: These results indicate that XR-NTX 380 mg, in combination with counseling, effectively reduced drinking on major holidays, as well as non-holidays, in alcohol-dependent patients with lead-in abstinence. Thus, XR-NTX 380 mg may have important public health impact by maintaining its effectiveness during holiday periods associated with increased rates of alcohol-related highway fatalities.

References:

NR536 Tuesday, May 22, 3:00 PM - 5:00 PM
Influence of the Short Allele of the Serotonin Transporter Promoter Polymorphism on Relapse in Alcohol Dependent Patients
Emmanuel B. Pinto, M.D. Universite de Liege, Psychiatry, Chu Sart Tilman B35, Liege, 4000, 4231, Jean Reggers, Psy.D., Philip Gorwood, M.D., William Pitchot, M.D., Gaby Scantamburlo, M.D., Marc Ansseau, M.D.

Educational Objectives:
At the beginning of this presentation the participant should be aware that relapse to alcohol drinking may be influenced by genetic differences in abstinent alcohol dependent patients.

Summary:
Introduction: As shown in many genetic studies, allelic variation in the promoter region of the serotonin transporter (5-HTTpro) contributes for the risk of alcohol dependence. The short allele (S) of this polymorphism has been associated with co-occurring clinical features in severe alcohol dependence such as depression, early onset or impulsivity. We studied the putative link between this allele and relapse in abstinent male alcohol dependent patients.

Methods: 60 male alcohol dependent patients were followed for 3 months after withdrawal. Persistent abnormalities in lab tests (GGT and CDT) or failure to show up at scheduled interviews were considered as relapse. PCR amplifying the 5-HTTpro polymorphism from genomic DNA were performed. Depressive symptoms (Carroll Depression Scale), anxiety (STAI) as well as daily number of drinks or typology were also evaluated as possible relapse factors.

Results: 67.27% of the patients relapsed during the three-month follow-up. The S allele of the 5-HTTpro was significantly associated with relapse (χ² = 7.66; p < .006) while no other factor such as depression, anxiety or daily number of drinks influenced relapse. Furthermore, typology as defined according to age of onset of alcohol-related problems didn’t influence the occurrence of relapse in our sample.

Conclusions: Responsible for a 5-HT hypo-functioning, the S allele of the 5-HTTpro may be associated with relapse in abstinent alcohol dependent patients, possibly through intermediate phenotypes such as personality features or lack of behavioral inhibition.

References:

NR537 Tuesday, May 22, 3:00 PM - 5:00 PM
Appetite Regulating Peptides in Alcohol Craving: An Investigation in Respect to Subtypes of Alcohol Dependence
Thomas Hillemecher, M.D. University of Erlangen, Psychiatry and Psychotherapy, Schwabachanlage 6, Erlangen, 91054, 4280, Thomas Kraus, M.D., Anja Schanze, M.D., Helge Frieling, M.D., Johannes Kornhuber, M.D., Stefan Bleich, M.D.
Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the differences between various subtypes of alcohol dependence regarding the importance of appetite regulating peptides like leptin and ghrelin in alcohol craving. This helps to better evaluate the importance of the appetite regulating system in the neurobiology of alcohol dependence.

Summary:

Introduction: The neurobiological role of appetite regulating peptides like leptin and ghrelin has been shown in various recent investigations. Aim of the present analysis was to search for differences regarding an association between these peptides and alcohol craving in respect to different subtypes of alcohol dependence.

Methods: A sample of 188 patients admitted for alcohol detoxification was analyzed in respect to leptin and ghrelin serum levels. While leptin was measured in all patients, ghrelin was available in 117 subjects. The Obsessive Compulsive Drinking Scale was used to assess alcohol craving in early withdrawal. All patients were classified according to Lesch's typology of alcohol dependence. For statistical analysis, leptin and ghrelin levels were corrected for BMI.

Results: Using general linear models to analyze a possible interaction between subtyping and leptin/ghrelin levels in respect to craving, we found a significantly positive association for leptin in patients of Lesch's Type 1 (p=0.005) and 2 (p=0.001). Ghrelin levels were associated with craving on a significant level in patients of Lesch's Type 1 (p=0.030). In the other subgroups we found no significant results.

Conclusion: The present results show that appetite regulating peptides may be of special importance regarding alcohol craving in specific subtypes of patients with alcohol dependence.

References:


NR538 Tuesday, May 22, 3:00 PM - 5:00 PM
Cocaine Use as a Risk Factor for Alcohol Dependence in Heavy Drinkers: A 4-Year Follow-up Study
Gabriel Rubio, Ph.D. Mental Health from Madrid, Psychiatry, Lope de Rueda, 43, Eboli,24,4,a, Madrid, 28050, 4700, Monica Jiménez-Giménez, Psy.D., Jorge Manzanoares, Pharm.D., Isabel Martínez-Gras, Ph.D., Miguel Angel Jiménez-Arriero, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize risk factors for developing cocaine dependence in heavy drinkers.

Summary:

Background: Alcohol and cocaine are frequently used together. Cocaine use disorders are very frequent in clinical samples with alcohol dependence but little is known about the role of cocaine in the development of alcohol dependence.

Objectives: To examine the influence of cocaine use on the development of alcohol dependence in non-dependent drinkers during a 4 year-follow-up period. Also, the role of impulsivity as risk factor for alcohol dependence was assessed.

Design and measurements: We recruited 471 (non-dependent) heavy drinkers, aged 18-55 years, who were sent from primary care centres for treatment. They were assessed at 2 years and at the end of the 4 year follow-up period.

Participants and setting: Participants were recruited from primary care centres. At baseline were classified as heavy drinkers (HD, N=280) and as heavy drinkers and cocaine users (HD+Co, N=191).

Results: At 4-year follow-up assessment, 67.9% of HD+Co group met criteria for alcohol dependence versus 13.6% of HD group. Clinical and psychological variables related to impulsivity and amount of cocaine used during follow-up were associated with the development of alcohol dependence. Odds ratios for alcohol dependence were 12.3 and 7.0 for male and female cocaine users, respectively. Also, amount of cocaine used during follow-up was associated with a more rapid progression to alcohol dependence and with the severity of alcohol dependence. Baseline variables related with impulsivity were associated with severity of alcohol dependence.

Conclusions: Cocaine use in heavy drinkers increased risk for alcohol dependence. Our findings agree with previous findings supporting the relationship between impulsivity and risk for alcohol dependence.

References:


NR539 Tuesday, May 22, 3:00 PM - 5:00 PM
Review of Prescribing Trends for Buprenorphine Treatment of Opioid Addiction
Penny K. Randall, M.D. Quintiles, Inc., Medical and Scientific Services, 10201 Wateridge Circle, Building B, San Diego, CA, 92121, 9000, Amir H. Kalali, M.D., Elisa Cascade

Educational Objectives:

At the conclusion of this presentation, the participant should be more aware of changes in prescribing trends for the treatment of opioid dependence.

Summary:

Introduction: The Drug Addiction Treatment Act of 2002 (DATA) permitted for the first time office-based treatment of opioid dependent patients with scheduled narcotics for either detoxification or long-term maintenance therapy. Before passage of this revolutionary legislation, medical treatment for heroin addiction only could be provided through centralized clinics rather than in the private office of qualified physicians. Many of the estimated one-million heroin dependent individuals in the U.S. were thought to have avoided treatment due to stigma associated with clinic treatment. Approved in 2002, buprenorphine and buprenorphine in combination with naloxone were the first narcotic drugs available for office-based treatment of opioid dependence.

We examined buprenorphine and buprenorphine in combination with naloxone prescription trends to determine whether new legislation and approval of these medications has resulted in increases in patients receiving treatment and whether a shift in treatment focus from clinics to physician practices has occurred.

Methods: We used two different data sources from Verispan to examine prescription trends for buprenorphine and buprenorphine in combination with naloxone: 1) quarterly total retail prescriptions from Vector One National (VONA) which captures nearly half of all prescription activity in the US and 2) Prescription Drug & Diagnosis Audit (PDDA) database which captures data on disease state and associated therapy including location of service.
Results: Buprenorphine has experienced significant growth from over 12,000 total prescriptions in 1st Quarter 2003 to nearly 300,000 in 3rd Quarter 2006. Buprenorphine in combination with naltxone was responsible for this growth. In 2006, office-based treatment comprised 87.1% of these prescriptions compared to 23.7%, p=0.003) and dependence (Fisher's exact test p=0.03), drug onset of their symptoms in adolescence are at very high risk for especially adolescent onset, is a clinically significant risk factor abuse (HR=14.6 95% Cl = [1.91 111.1], p=0.01) and dependence that juvenile onset bipolar disorder (BPD) is associated with an elevated risk for cigarette smoking (Cox proportional hazards model: HR=10.0 95% Cl = [2.75 23.1], p<0.001), alcohol abuse (HR=6.7 95% Cl=[1.87 23.7], p=0.003) and dependence (Fishers's exact test p=0.03), drug abuse (HR=14.6 95% Cl=[1.91 111.1], p=0.01) and dependence (HR=10.0 95% Cl=[1.25 79.7], p=0.03) and other psychiatric and elevated risk for cigarette smoking and substance use disorders which were from 0.05 - 1.17 µkat/g protein. Our research has been done on 142 healthy subjects and 113 alcoholics, aged from 18 to 65, having consumed alcohol within last 48 hours. Mean catalytic activity in healthy subjects was 0.5649 µkat/g protein. Mean catalytic GLDH activity in alcoholics increased from 0.5042 µkat/g to 0.6696 µkat/g after 24 - 48 hours to 0.6974 µkat/ g after 48 - 72 hours of abstinence. Using nonparametric Mann-Whitney U Test we found a statistically significant increase (Z = -2.500, p = 0.012) in GLDH activity after 48-72 hours of abstinence. It is possible to conclude that under the influence of alcohol the leukocyte GLDH activity in alcoholics is lower than in healthy subjects. Cessation of alcohol consumption has resulted in a statistically significant increase in leukocytes GLDH activity. Therefore, alcohol consumption results in reduction in GLDH activity as well as protein production and consecutively leads to diminished leukocytes protective ability.

References:
NR542  Tuesday, May 22, 3:00 PM - 5:00 PM
Effects of Binge Drinking and Mental Problems on Adherence to Treatment for Asthma: A California Population Study

Donald L. Anderson, M.D. Loma Linda University, Psychiatry, 11374 Mountain View, Loma Linda, CA, 92354, 9000, Mark G. Haviland, Ph.D., Jim E. Banta, Ph.D., Leonard S. Werner, M.D., Sumner L. Williams, M.A., Kelly B. Haskard, M.A., M. Robin DiMatteo, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the factors associated with adherence to asthma medications and address in practice those that are modifiable.

Summary:
Objective: Our objective was to determine the effects of excessive alcohol use and poor mental health on the use of asthma medications among individuals who had been told by a doctor that they had asthma.

Method: This was a secondary analysis (logistic regression) of a population-based survey. Data were from the 2003 California Health Interview Survey (original N = 42,044, but the data are weighted to represent all Californians). Subjects were respondents who had been told by a doctor that they had asthma and (b) symptomatic during the course of the year prior to the survey. The binary dependent variable was taking versus not taking asthma medications (i.e., adherence versus non-adherence). The main independent variables were binge drinking (five or more drinks at one time in the past 30 days) and mental problems (number of days with poor mental health in the past 30 days). Covariates included age, sex, race/ethnicity, language, income, health status, body mass index, insurance coverage, and social support.

Results: Binge drinking was a significant predictor of non-adherence (p = .025; odds ratio = .685; 95% confidence interval = .492 to .952), whereas mental problems was not. Factors associated with non-adherence (p < .05, odds ratios < 1) included being young and otherwise in good health, English not being one’s first language, and having no usual source of medical care. Factors associated with adherence (p < .05, odds ratios > 1) were being older and in poor health, African American, not working, on Medic aid and having quit smoking.

Conclusion: Respondents reporting binge drinking were significantly less likely to be taking medications for asthma symptom management. This finding, coupled with the known adverse effects of alcohol on asthma symptoms, underscores the importance of clinicians addressing alcohol use, and particularly excessive use, among their patients with asthma.

References:

NR543  Tuesday, May 22, 3:00 PM - 5:00 PM
Predictors of Relapse to Heavy Drinking During a 24-week Follow-up Trial of Korean Patients with Alcohol Dependence

Sung-Gon Kim, M.D. Pusan National University, Psychiatry, 1-GA 10, Ami-dong, Seo-gu, Pusan, 602-739, 5800, Jeong-Hyun Park, M.D., Cheol-Joong Kang, M.B., Young-Myo Je, M.D.

Educational Objectives:
Alcohol drinks per drinking day for the last year were the single best predictor of relapse to heavy drinking at the 24-week follow-up trial. At the conclusion of this study, it is recognized that the more a Korean male patient with alcohol dependence drinks per drinking day, the more attention he will require from a clinician during treatment.

Summary:
Objective: This study provides prevalence estimates of non-medical use (NMU) of methamphetamine in the United States among various demographic groups.

Methods: 4,297 adult (aged 18-49) members of an Internet panel in the US were surveyed regarding NMU of abusable stimulants, some of which are treatments for attention-deficit/hyperac-
tivity disorder (ADHD). A weighting methodology was employed using information from the National Survey on Drug Use and Health and the US Census to derive representative prevalence estimates of NMU of various ADHD medications as well as methamphetamine. This analysis presents a subset of data from the survey pertaining specifically to methamphetamine NMU.

Results: Lifetime and past-year prevalence estimates [% (standard error)] of methamphetamine NMU among adults 18-25 years old were 1.94 (1.34) and 1.79 (0.83) respectively and among adults 25-49 years old were 9.46 (1.94) and 0.36 (0.14). Lifetime and past-year estimates for those not completing high school were 20.64 (7.42) and 0.25 (0.19), for high school graduates were 6.12 (1.50) and 0.80 (0.27), and for college graduates were 5.31 (1.33) and 0.95 (0.33). Lifetime and past year estimates for 18-25 year old college students were 4.36 (1.59) and 0.79 (0.25) and for 18-25 year old non-college students were 7.13 (1.37) and 2.44 (0.61). Lifetime and past year estimates for those with private insurance were 6.25 (1.26) and 0.49 (0.14), for those with public insurance were 9.54 (4.36) and 1.23 (0.66), and for the uninsured were 14.86 (4.65) and 1.06 (0.33).

Conclusions: Methamphetamine NMU is common in the US among several demographic groups with rates ranging among those of other psychotherapeutic drugs used nonmedically. Past year use is common among young adults, particularly non-college students. This analysis is limited by the use of internet panel methodology, which may limit generalizability despite the care taken to calibrate for this selection bias.

References:

NR545 Tuesday, May 22, 3:00 PM - 5:00 PM
Women and Alcoholism: An Individual Patient Data (IPD) Meta-Analysis of Outcome Predictors Based on 935 Female Patients in 16 Acamprosate Clinical Trials
Barbara J. Mason, Ph.D. The Scripps Research Institute, Committee on the Neurobiology of Addictive Disorders, 10550 North Torrey Pines Road, TPC-5, La Jolla, CA, 92037, 9000, Philippe Lehert, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participants will be able to recognize the predictors of treatment outcome and the factors associated with recovery among female patients with alcohol dependence.

Summary:
Background: Recent research has identified important ways in which the clinical characteristics of alcoholic women differ from men (eg, increased rates of comorbid depression and anxiety), but considerably less is known about factors influencing their recovery. The current meta-analysis utilizes a large clinical trial database to identify predictors of treatment response in female alcohol-dependent patients.

Methods: A database consisted of 4457 alcohol-dependent patients receiving acamprosate (n=2383) or placebo (n=2074) who participated in 16 randomized, double-blind, placebo-controlled clinical trials conducted in Europe and the US. A meta-analysis of outcome predictors based on individual patient data (IPD) of 935 female participants was carried out to identify factors that may meaningfully influence treatment outcome. Study duration ranged from 3-12 months. The primary outcome variable was percent days abstinent over the treatment duration.

Results: Baseline assessment showed women to have accelerating dependence symptom severity over time relative to men, including higher amounts of alcohol consumed and higher concentrations of liver transaminases, as well as higher lifetime (not current) rates of suicide attempts, anxiety, and depression. However, these baseline characteristics were not found to significantly influence alcoholism treatment outcome. Clinical characteristics found to significantly increase abstinence duration were baseline motivation to be abstinent, abstinence of at least 2 days at baseline, family support, and treatment with acamprosate. Further analyses showed a highly significant interaction of compliance with treatment, and an advantage for studies of 1 year duration relative to 6 months or less.

Conclusions: Despite greater severity of past psychiatric problems and current alcohol dependence symptoms at baseline compared to male patients, females responded comparably to treatment. Results suggest abstinence duration in women may be significantly influenced by prescribing acamprosate when patients are abstinent at treatment initiation and in conjunction with techniques that increase motivation to be abstinent and enhance medication compliance.

References:

NR546 Tuesday, May 22, 3:00 PM - 5:00 PM
Topiramate for the Treatment of Alcohol Dependence: Results of a Multi-Site Trial
Bankole A. Johnson, M.D., University of Virginia, Department of Psychiatry and Neurobehavioral Sciences, University of Virginia, 1670 Discovery Drive, Suite 110, Charlottesville, VA, 22911, 9000, Norman Rosenthal, M.D., Julie Capece, B.A., Frank Wiegand, M.D., Lian Mao, Amy McKay, Nassima Alt-Daoud, M.D.

Educational Objectives:
At the conclusion of this presentation, the attendees shall possess new knowledge on the neuropharmacology that underpins pharmacotherapeutic approaches to treating alcohol dependence. Additionally, participants shall be made aware of new data that further support the safety and potential of topiramate (a mixed GABA agonist and glutamate antagonist) as pharmacotherapy for alcohol dependence. Topiramate's anti-drinking potential shall be placed into context with other available promising or approved medications for treating alcohol dependence. Finally, attendees shall be informed on procedures and strategies for treating alcohol-dependent individuals who are still drinking heavily but who wish to stop consuming alcohol.

Summary:
Hypothetically, topiramate, a sulfamate-substituted fructosepyranose derivative, can reduce alcohol's reinforcing effects associated with its abuse liability through two principal pharmacological processes. These include the facilitation of central gamma-aminobutyric acid function and the inhibition of glutaminergic pathways at AMPA/kainate glutamate receptors in the cortex and hippocampus that are super-sensitized during alcohol withdrawal. Previously, in a proof-of-concept, single-site, 12-week, double-blind randomized controlled trial (RCT), it was shown that topiramate (up to a dose of 300 mg/day) was superior to placebo at improving the drinking outcomes of 150 alcohol-dependent men and women. In a recently completed 16-site, 14-week, double-blind RCT in which all subjects received weekly compliance enhancement therapy, we
sought to establish topiramate's efficacy as a treatment for alcohol dependence. In the present RCT (N = 364, intent-to-treat population) topiramate (up to 300 mg/day) was superior to placebo at reducing the percentage of heavy drinking days (from 82.1 ± 150% and 81.8 ± 1.47% to 22.9 ± 3.02% and 42.2% ± 2.72%, respectively; p < 0.001) as well as other drinking outcomes. Unique to pharmacotherapy studies of putative therapeutic agents for treating alcohol dependence, topiramate’s treatment effect was robust and consistent across both direct measures of drinking and indirect assessments of overall clinical outcome. Adverse events more likely to be associated with topiramate compared with placebo treatment included: paresthesia — 50.8% vs. 10.6%; taste perversion —23.0% vs. 4.8%; anorexia — 19.7% vs. 6.9%; and difficulty with concentration — 14.8% vs. 3.2%. We propose that these results provide further evidence that topiramate is a potential treatment for alcohol dependence. Additional studies were sought to support its efficacy — and to define the minimal effective dose and safety profile in this population — are warranted.

References:
2. Johnson BA: Recent advances in the development of treatments for alcohol and cocaine dependence: focus on topiramate and other modulators of GABA or glutamate function. CNS Drugs 2005; 19:873-896.

The Efficacy of Acamprosate in Enhancing Abstinence in Alcohol Dependence: A Meta-Analysis Evaluating Continuous and Controlled Abstinence
Philippe Lehert, Ph.D. FUCAM, Louvain Academy, Department of Statistics, Chaussée de Binche, 151, Mons, 7000, 4231, Eugene Schneider, M.D., Stavros Tourkodimitris, Ph.D., Frédéric Landron, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the clinically relevant effects of acamprosate in maintaining abstinence and reducing alcohol consumption during relapse in alcohol-dependent patients.

Summary:
Introduction: Acamprosate is an FDA-approved medication that enhances abstinence in alcohol-dependent patients. Clinical studies of acamprosate have measured continuous or total abstinence (TA) but not controlled abstinence (CA), a standard endpoint used in recent clinical trials in alcohol dependence. A meta-analysis was carried out to compare acamprosate with placebo on TA and CA.

Methods: A total of 21 randomized, placebo-controlled trials (RCTs) that fulfilled predetermined selection criteria were identified. Six studies were excluded because (1) they did not provide a comparable measure of abstinence; (2) they lacked a control group; or (3) data were not available at the time. Abstinence was documented at each study visit; common treatment intervals in all trials were Days 0-30, 30-90, 90-180, and 180-360. Primary outcome measures were percent days of TA (defined as zero drinks during the treatment interval) and CA (defined as <5 standard drinks/day during the treatment interval). Clinical relevance of the results was determined by estimating Relative Risk (RR). Differences in success rates and numbers needed to treat (NNT) were also calculated.

Results: Fifteen RCTs (N=3865) were included in the primary analyses. TA rates at study endpoint were significantly higher in the acamprosate-treated patients compared to placebo (29.1% vs. 19.9%; RR, 0.638; 95% CI, 0.538-0.757; P<.001) with an NNT=8.4. CA rates were also significantly higher with patients treated with acamprosate vs. placebo (40.5% vs. 27.2%; RR, 0.653; 95% CI, 0.569-0.749; P<.001) with an NNT=6.8.

Conclusion: In addition to helping alcohol-dependent patients maintain total abstinence, acamprosate can provide a significant benefit by reducing alcohol consumption during relapse.

References:

Touch Me Not! A Gesture of Detachment in Picasso’s La Vie Suggesting a Narcissistic Coping Mechanism in a Conflict Between Mother and Son
Peter M. Wehmeier, M.D. Lilly Deutschland GmbH, Medical Department, Clinical Research Physician, Saalburgstr. 153, Bad Homburg, 61350, 4280, Gereon Becht-Jordens, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should recognize that the gesture in the centre of Picasso’s painting La Vie from the Blue Period is a gesture of detachment, suggesting a narcissistic coping mechanism in dealing with a conflict between mother and son.

Summary:
The painting La Vie from 1903 is considered by many art historians to be the most important painting from the so-called Blue Period and one of the most important works by Picasso. The gesture in the centre of the painting should be seen in the iconographic tradition of the gesture “noli me tangere!” (touch me not!), as shown in the painting Noli me tangere by Correggio, which was on display in the Prado at the time Picasso was studying art in Madrid. The iconographic perspective allows an entirely new approach to the interpretation of La Vie, based on the combination of the iconographic analysis and an interpretation of the results by means of psychoanalytic concepts. This two-fold approach can lead out of the dilemma of entirely subjective and therefore arbitrary interpretation. The meaning of the gesture can be interpreted as signifying detachment. The time of closeness and wholeness is represented by the mother figure with the child in her arms, whilst the time of detachment and autonomy is represented by the young man, with the young woman leaning on his shoulder. Biographical change is suggested by confronting two successive modes of existence simultaneously in the same composition, separated by the gesture in the centre of the painting. Seen in this way, the masterwork deals with the dissociation of a formerly close relationship between mother and son and underlines the importance of detachment as a condition for the true autonomy of an adult individual. The painting also deals with the problem of separation and a narcissistic attempt at coping with loss. The painting can be understood as an answer to autobiographical experiences of the young Picasso.
NR549 Tuesday, May 22, 3:00 PM - 5:00 PM
Electronic Inpatient Treatment Plans: Optimizing the Process
Simon Kung, M.D. Mayo Clinic, Psychiatry, 200 First Street SW, Rochester, MN, 55905, 9000, Maria I. Lapid, M.D., Timothy W. Lineberry, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to: Recognize the utility of an electronic medical record in making inpatient treatment plans useful and meaningful.

Summary:
- Introduction: Inpatient treatment plans serve many purposes, including patient care and regulatory/accreditation requirements. With shorter length-of-stays and complex problems, documentation on paper impedes efficiency. We describe an in-house computerized treatment plan developed to improve the treatment planning process.
- Methods: We implemented a web-based computer application to replace the previously used paper treatment plans. After one year of use, we surveyed our staff regarding time savings, satisfaction, and benefits of the electronic treatment plan.
- Results: A total of 103 (37%) out of 282 physicians, nurses, and allied health staff members responded to the survey. In starting a new treatment plan, an average time savings of 4.8 minutes (12.6 for paper, 7.8 for computer) was seen. In updating an existing treatment plan, an average time savings of 3.0 minutes (7.1 for paper, 4.1 minutes for computer) was seen. Overall staff satisfaction increased by 44%, from 38% to 82%. Benefits of an electronic treatment plan include time and productivity savings, ease of accessibility and sharing, improved compliance of use, and more integrated multidisciplinary interactions.
- Conclusion: A user-friendly computerized treatment plan can make the inpatient treatment plan a useful document for patient care and improve provider satisfaction, in addition to meeting regulatory/accreditation requirements.

References:

NR551 Tuesday, May 22, 3:00 PM - 5:00 PM
Comparison of Female and Male Sex Offenders on the South Carolina Sex Offender Registry
Michelle E. Whitcomb, B.A. Beth Israel Medical Center, Psychiatry, First Avenue at 16th Street, Suite 6K42, New York, NY, 10003, 9000, Sophia Haeri, M.A., Frederick Weigel, M.D., Steven Frenda, B.A., Igor I. Galynker, M.D., Lisa J. Cohen, Ph.D.

Educational Objectives:
- At the conclusion of this presentation the participant should have become familiar with the differences between male and female sex offenders.

Summary:
- Background: Research regarding female sex offenders has traditionally been extremely limited and a sufficient understanding of this issue is presently lacking. Previous research on male sex offenders indicates that males who offend against minors may differ robustly from other male sex offenders on certain demographic and offense characteristics. The current research sought to compare male and female sex offenders on demographics and offense characteristics to discover if similar patterns emerged in the two populations.
Method: The South Carolina Sex Offender Registry was chosen because of its greater quantity of female sex offenders compared to other states’ registries and its relatively detailed information regarding demographics and offense characteristics. Data was collected and analyzed on 136 female sex offenders and a comparison group of 270 males.

Results: Female sex offenders were less likely than male sex offenders to be convicted for assault/sexual battery and use of violence; and more likely to be convicted for pornography/child exploitation, kidnapping, and miscellaneous offenses. There was no difference between males and females in convictions for offenses against minors.

Conclusion: Female sex offenders show distinct differences from male sex offenders, with fewer invasive and violent offenses and more instrumental offenses than males. Future research on this topic is needed to replicate and expand upon these findings.

References:

NR552 Tuesday, May 22, 3:00 PM - 5:00 PM
Monitoring Gender Equity In Mental Health In Lower, Middle and High Income Countries: A Feasibility Study

Natalia Diaz-Granados University Health Network, Women’s Health Program, 200 Elizabeth Street, EN 7-234, Toronto, ON, L4G 6H2, 1220, Sarah McDermott, Linda M. Dorado, Marie DesMeules, Jose Posada, Javier Saavedra, Donna E. Stewart

Educational Objectives:
At the conclusion of this presentation, the participant should be able to demonstrate which mental health indicators show the greatest gender inequities under different national economic conditions.

At the conclusion of this presentation, the participant should be able to identify those patient populations most vulnerable to gender inequities.

At the conclusion of this presentation, the participant should be able to use the gender-sensitive indicators to monitor and reduce gender inequities in mental health programs.

Summary:
Since indicators are vital to public policy development and program management, we set out to test the feasibility of measuring and comparing 19 mental health indicators in Peru, Colombia and Canada using gender/sex based analysis. The indicators were selected at a meeting in Colombia by a group of key experts using a mental health information framework proposed by WHO (Tier I: Health Status; Tier II: Determinants of Health; Tier III: Health Systems). Indicators were measured at a national level and the primary databases used included: Canada - CCHS v1.2 - Mental Health and Well-Being Survey; Colombia - National Study of Mental Health (WMH CIDI); Peru - 3 population-based studies (Lima, Sierra, Selva). Since Colombia and Canada’s surveys had similar questions (based on WMH-CIDI), 5 indicators were comparable with few modifications. Out of the first 9 indicators assessed (12 month prevalence of: depression, psychological distress; GAD, suicide attempts, alcohol dependence/abuse, social support, use of mental health services, psychological impairment, psychological well-being (self-esteem, sense of mastery and sense of vitality/energy)), all were feasible except for the measurement of self-esteem in Peru and GAD in Canada. The indicators that show greatest gender inequities are: depression, GAD, suicide attempts, use of mental health services and alcohol dependence/abuse. These female to male ratios ranged from 1.5 - 2.2. Significant gender-related trends were found when the indicators were considered by age, education, marital status and socio-economic status (income, employment). Data for special subgroups (immigrants/refugees, single-parent families and indigenous groups) were limited, with virtually none available in two countries. These indicators can be used to identify those patient populations most vulnerable to gender inequities in mental health. The results from this study will provide vital information to program planners who aim to implement, improve and monitor national mental health strategies that reduce gender inequities in different national economic conditions.

References:

NR553 Tuesday, May 22, 3:00 PM - 5:00 PM
Gender Differences and Somatic Symptoms in Depressive Psychiatric Patients

Jeronimo Saiz-Ruiz, M.D. Hospital Ramon y Cajal - Alcala University, Psychiatry, Ctra. Colmenar Viejo KM 9, 100, Madrid, 28034, 4700, Rita Prieto, M.D., M. Dolores Saiz Gonzalez, M.D., Carmen Garcia Calvo, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the importance of the gender differences in the prevalence of somatic symptoms in depressive patients in psychiatry and its potential impact on patient’s quality of life.

Summary:
Introduction: Epidemiological study to determine gender differences in the prevalence of somatic symptoms in depressive patients in psychiatry and its potential impact on patient’s quality of life.

Methods: Cross sectional, epidemiological study performed in Psychiatry in Spain in 2006. A sample of 1,164 patients over 18 years old, with clinical diagnosis of depressive syndrome (DSM-IV) and a score ≥ 17 on the Hamilton Depression Rating Scale (HAM-D17), was analyzed. A total of 428 psychiatrists participated in the study. The PHQ-15 (Patient Health Questionnaire) scores were determined to analyze gender differences in the prevalence of somatic symptoms.

Results: Statistically significant differences between genders have been observed on several HAM-D17 items. Men had higher scores on feelings of guilt (<0.05), suicide (<0.05) work and activities (<0.001), agitation (<0.05) and genital symptoms (<0.05). Women scored significantly higher on somatic anxiety (<0.01) and somatic symptoms general (<0.01).

The total mean score on the PHQ-15 is significantly higher (<0.001) in women (13.38 points) than in men (11.95 points).

In the PHQ-15, women scored significantly higher in abdominal pain (<0.05), backache (<0.01), joint or limb pain (<0.05), headache (<0.001), dizziness (<0.05), breathing trouble (<0.01), constipation, diarrhoea (<0.05) and nausea, gas or indigestion (<0.001). Men only showed significant differences in pain or trouble during sexual intercourse (<0.01).

A positive linear relationship of 0.392 has been observed between the HAM-D17 score and somatic symptoms (PHQ-15 total...
There were 256 patients seen by the team members. Baseline for primary care patients is feasible and well-received by most the Client Satisfaction Questionnaire. This demonstration project of patient rated their care as excellent or very good, scored by absence of a randomized controlled study, changes cannot be outcomes showed similar improvements in scores, however in the tional and mental health (p<0.05 for all t-tests). Other patient the team was completed showed significant improvements in SF-36 scores in the domains of physical functioning, physical role, general health perceptions, vitality, social functioning, role emotional and mental health (p<0.05 for all t-tests). Other patient outcomes showed similar improvements in scores, however in the absence of a randomized controlled study, changes cannot be ascribed to the mental health intervention alone. Eighty percent of patient rated their care as excellent or very good, scored by the Client Satisfaction Questionnaire. This demonstration project revealed that multidisciplinary collaborative mental health care for primary care patients is feasible and well-received by most patients.

References:

NR554
Collaborative Mental Health Care in a Primary Care Setting
John Robert Swenson The Ottawa Hospital, Psychiatry, Box 400, 501 Smyth Rd., Ottawa, ON, K1H 8L6, 1220, Katherine Gillis, M.D., Colleen MacPhee, M.H.A.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to appreciate processes and outcomes of providing mental health care to primary care patients in collaboration with their family physicians.

Summary:
This 15 month demonstration project evaluated the outcomes of a multidisciplinary mental health team composed of a psychiatrist, psychologist, nurse and social worker managing patients in a primary care setting in collaboration with their family physician. There were 256 patients seen by the team members. Baseline quality of life rated by the SF-12 questionnaire demonstrated a mean mental health component scale score of 32 (SD=12) which is considerably below the normative mean of 50. Diagnoses at baseline generated by the Patient Health Questionnaire revealed 34% of patients had somatic symptoms as part of their mental health problem, 36% met criteria for major depression, 25% reported a panic attack in the previous 4 weeks, and 21% had problems with alcohol abuse or dependence. Severity of illness at baseline evaluated by the Threshold Assessment Grid demonstrated approximately 40% of patients were rated as having moderate to severe psychological distress and 40% having social isolation or impaired relationships. Notably there were few patients rated at risk for self-harm or harm to others. Patient care provided by the team included assessment and diagnostic clarification, medication management, and short-term supportive or cognitive-behavioral therapy. Outcome measurement after treatment from the team was completed showed significant improvements in SF-12 scores in the domains of physical functioning, physical role, general health perceptions, vitality, social functioning, role emotional and mental health (p<0.05 for all t-tests). Other patient outcomes showed similar improvements in scores, however in the absence of a randomized controlled study, changes cannot be ascribed to the mental health intervention alone. Eighty percent of patient rated their care as excellent or very good, scored by the Client Satisfaction Questionnaire. This demonstration project revealed that multidisciplinary collaborative mental health care for primary care patients is feasible and well-received by most patients.

References:

NR555
Six Months Use of Outpatient Services and Past Year Use of Hospitalizations for Elderly: Results From a Community Survey
Sergio L. Blay, Ph.D. UNIFESP, Psychiatry, R Botucatu 740, Sao Paulo, 04023-900, 3510, Sergio B. Andreoli, Ph.D., Fabio L. Gastic, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the importance of medical services utilization as well as the medical/psychiatric and sociodemographic variables associated with service use.

Summary:
Objective: The main purpose of this study is to obtain data on patterns and predictors of 6-month outpatient and 12 month hospitalizations health service utilization in an elderly community population in Brazil
Method: Cross sectional population-based random sample of 7040 household residents aged 60 years and over, examined in a face-to-face interview. Six month outpatient consultations, 12 months hospitalizations, medical conditions and psychiatric assessment were assessed through a structured interview. The main outcome measure of the investigation is the proportions of subjects with different medical problems using health services. Logistic regression analysis was used in order to produce a model for the influence of psychosocial factors in predicting health service use.
Results: Within medical cases, 68.8 to 92.0 % received consultations in an outpatient setting and 20.7 to 55.6% were hospitali-ized. In logistic regression models, cancer, pneumonia, hypertension, chest pain, self rated health, diabetes, female, urinary infection head pain, age, among other variables emerged as predictors of 6-month out patient consultations. The odds of 6-month outpatient consultation are also affected by income, marital status. Female African descendents and female Asian descendents are less likely to seek out patient services. Considering 12-month hospitalizations, in logistic regression models, CVD, pneumonia cancer, urinary infection, self rated health, psychiatric morbidity, hypertension chest pain, emerged as predictors of hospitalizations. The odds of 12-months hospitalizations are also affected by low income, gender (female), age and the interactions Catholic/Caucasians and Evangelic / Caucasians.

Conclusion: The association of medical/psychiatric morbidity with service use (6-month outpatient services and 12 month-hospi-talizations) in late life is statistically strong in this surveyed population. Female African and Asian descendents constitute minorities at risk of not getting access to medical services.

References:
NR556  Tuesday, May 22, 3:00 PM - 5:00 PM

Probability of Increase in Healthcare Costs in Non-Stable Depressed Individuals Compared to Stable Patients

C. Daniel Mullins, Ph.D.  University of Maryland, Pharmaceutical Health Services Research, 220 Arch Street, 12th Floor, Room 01-200, Baltimore, MD, 21201, 9000, Brian Seal, R.Ph., Tony Yang, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant will comprehend the likelihood of increased direct medical costs associated with new treatment episodes of major depressive disorder (MDD); compare two anti-depressant use algorithms for categorizing patients as stable versus non-stable; and recognize how the likelihood of increases in direct medical costs differs for patients stabilized on therapy versus non-stable patients.

Summary:

Introduction/Hypothesis: Patients with major depressive disorder (MDD) respond to antidepressant treatment differently. Based on their antidepressants and other medical resources use, patients can be identified as stable or non-stable. Non-stable patients are patients who have undergone multiple changes in antidepressant treatment and/or had a depression-related event within one-year of treatment initiation. We hypothesize that more MDD patients in the non-stable versus stable category incur incremental cost increases following a new treatment episode.

Methods: A retrospective analysis of PHARMetrics data, a nationally representative claims dataset containing almost 1.9 million MDD patients, identified adults with new treatment episodes of MDD and stratified patients based upon two published treatment algorithms for defining non-stable and stable cohorts. A pre-post analysis covering the period January 2003 to June 2005 estimated the likelihood of higher annual medical costs for the 365 days following onset of new treatment versus the prior year. Differences in proportions were calculated using chi-square tests.

Results: Among the 11,169 MDD individuals meeting inclusion/exclusion criteria, the percentage with non-stable patients was 32% and 8% using the first and second algorithms. Increased total medical costs were statistically more likely among non-stable individuals with 79-84% and 72-73% of stable individuals incurring increased costs following a new treatment episode (p < 0.001). A post-hoc analysis documented that non-depression related costs were significantly more likely to increase (p < 0.001) in the non-stable cohort (67-73%) versus the stable cohort (59-61%). The results were insensitive to inclusion/exclusion of outlier values.

Conclusions/Discussion: An increase in direct medical costs is statistically more likely among non-stable versus stable MDD patients. Further research is needed to determine the magnitude of the incremental costs associated with non-stable depression and whether these additional costs can be reduced with enhanced clinical and pharmacologic management of depression.

References:


NR557  Tuesday, May 22, 3:00 PM - 5:00 PM

Racial Differences in Visit Duration of Outpatient Psychiatric Visits

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to (a) describe overall differences in the duration of psychiatric visits for black and white patients, (b) to describe patient, clinical, and psychiatrist/practice factors that influence racial differences in visit duration that are especially pronounced.

Summary:

Specific Purpose: The purpose of this presentation is to compare the duration of visits to office-based psychiatrists by black and white patients.

Methods: An analysis is presented of a nationally representative sample of visits to office-based psychiatrists that were provided between 2001 and 2004. Data were derived from the National Ambulatory Medical Care Survey. Visits are grouped by patient race as black (n=414) or white (n=5,649). The visits were compared with respect to the overall duration of face-to-face contact between the patient and psychiatrist, and stratified by patient, clinical, and psychiatrist/practice characteristics.

Results: Psychiatric visits by black patients (mean: 26.97 minutes) were five minutes shorter than visits by white patients (31.97 minutes) (p=0.011). In stratified analyses, patient factors associated with shorter visits for black patients included patient age 51-64 years (p<0.001), male gender (p=0.001), Medicare payment (p=0.07), returning patients (p=0.01), adjustment disorder (p=0.001), care provided solely by psychiatrists (p=0.005), medication prescription (p=0.018), and absence of psychotherapy (p<0.0001). In addition, racial differences in visit duration were most pronounced among visits provided by male psychiatrists (p<0.0001), psychiatrists older than 55 years of age (p=0.006), practices located in urban settings (p=0.004), and psychiatrists who provided fewer than 25 visits per week (p=0.0034). A difference in visit duration between black and white patients remained statistically significant after controlling for several potentially confounding variables.

Conclusions: As compared with psychiatric visits by white patients, visits by black patients are significantly shorter in duration. That this difference in visit duration exists across several patient, clinical, and psychiatrist/practice characteristics and raises the possibility that racial differences exist in the intensity of office-based psychiatric services provided to black and white patients.

References:


NR558  Tuesday, May 22, 3:00 PM - 5:00 PM

ECT Practice in Asia

Worrawat Chanpattana, M.D.  Srinakharinwirot University, Psychiatry, 508/35 Soi Ton Poo, Chaorenkrung 108, Bangkok, Bangkok, 10120, 5490, Barry Kramer, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the characteristics of ECT practice in Asia.
Objective: To examine the practice of electroconvulsive therapy (ECT) in Asia.

Method: Questionnaire was sent to 977 psychiatric facilities in 45 countries in Asia.

Results: Completed questionnaires were returned by 334 (34%) institutions in 29 countries. ECT was available in 257 (76.9%) of these institutions in 23 of the countries. During the year previous to the survey, 39,875 patients received 240,314 ECT treatments from 1,919 psychiatrists; 56.6% of these patients were treated in psychiatric hospitals. The male:female patient ratio was 1.6:1. Most patients (73.1%) were aged 18-44 years; few patients were aged <18 years or >64 years (6.0% and 4.4%, respectively). Patients received ECT for diagnoses of schizophrenia (41.8%), major depression (32.4%), mania (14.0%), catatonia (6.9%), drug abuse (1.8%), dysthymia (1.6%), and other indications. Brief-pulse ECT devices were used in only 103 (40.1%) of the institutions offering ECT. Routine EEG monitoring of the ECT seizure was conducted in only 59 (23.0%) institutions. Bilateral electrode placement was invariable in most institutions; the EEG is not commonly monitored during ECT; and no formal training in ECT is available. These findings may reflect real differences in standards of medical care in developing countries rather than a misuse of ECT.

Conclusions: The practice of ECT in Asia is largely suboptimal: schizophrenia, rather than depression, is the commonest indication; most institutions offer single wave ECT; unmodified ECT is administer more often than not; bilateral electrode placement is invariable in most institutions; the EEG is not commonly monitored during ECT; and no formal training in ECT is available. These findings may reflect real differences in standards of medical care in developing countries rather than a misuse of ECT.

References:

NR559
Tuesday, May 22, 3:00 PM - 5:00 PM
Understanding Mental Health Service Utilization of Veterans With Bipolar Disorder as Predicted By Psychotropic Medication Usage

Keiko Kurita, M.B.A. VA Palo Alto, Psychiatry Department, 3801 Miranda Avenue, Palo Alto, CA, 94304, 9000, Jennifer Hoblyn, M.D., John O. Brooks III, M.D.

Educational Objectives:
To increase our understanding of how psychotropic medication prescriptions and demographic variables may influence inpatient stays and outpatient visits in Veteran’s with bipolar disorder. This information may help improve patient care and the development of mental health delivery by highlighting those particularly at risk.

Summary:
Objective: We sought to examine how psychotropic medication usage and demographic factors predict the use of psychiatric hospitalization and outpatient visits in Veterans with bipolar disorder. Bipolar disorder is a significant cause of morbidity, mortality and costs society approximately $45 billion annually (1). Mood stabilizers, typical and atypical antipsychotics, and antidepressants are commonly used for treatment (2).

Method: This cross-sectional sample comprised 2,964 veterans with primary or secondary diagnoses of bipolar disorder in the VA Health Care System of the Veterans Integrated Service Network 21 during Fiscal Year 2004. Psychotropic prescriptions and demographic variables were used as predictors of longer psychiatric hospitalizations (>14 days) and regular attendance at outpatient clinics. A Receiver-Operating-Characteristic Program was used to generate the risk profiles.

Results: Of the sample, 86% were men, 81% had at least one mental health outpatient encounter and 20% had at least one hospitalization. Longer hospitalizations were associated with usage of typical antipsychotic prescriptions and no outpatient encounters (32% risk). Patients taking typical antipsychotics, with more clinic visits, had a lower risk (17%). Those not receiving typicals, with fewer clinic visits, and under 77 years had the lowest risk (3%).

Low numbers of outpatient visits (<7 annually) were associated with either a lack of psychiatric hospitalizations (67%) or long hospitalizations (34%). In addition, they were associated with those experiencing shorter hospitalizations, both with prescriptions for other antidepressants (46%) and those without them (51%).

Conclusion: Typical antipsychotic prescriptions and lack of outpatient follow-up are associated with a 38% risk of long psychiatric hospitalizations for veterans with bipolar disorder. However, patients on typical antipsychotics who attend clinic more frequently had a lower risk of long psychiatric hospitalization. Increased outpatient attendance may attenuate the risk of hospitalization in patients with bipolar disorder who are prescribed typical antipsychotics.

References:

NR560
Tuesday, May 22, 3:00 PM - 5:00 PM
Changes in Comorbidities, Medication Use and Treatment Costs after Diagnosis of Generalized Anxiety Disorder

Ralph W. Swindle Eli Lilly and Company, Outcomes Research, Lilly Corporate Center, DC4025, Indianapolis, IN, 46285, 9000, Zhongyun Zhao, Wenyu Ye, Baojin Zhu

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the impact of diagnosis of generalized anxiety disorder (GAD) on comorbidities, medication use and treatment costs.

Summary:
Purpose: To evaluate the impact of Generalized Anxiety Disorder (GAD) on diagnosed comorbidities, medication use and treatment costs.

Method: Claims were drawn from PharMetrics Integrated Outcomes Database for 12-month prior and post the first GAD (ICD9-CM: 30002) diagnosis between 1/2003 and 8/2004 (the diagnosis date as the index date). No GAD diagnosis 12-month prior the index date, 24-month continuous insurance eligibility and aged 18-64 were required. Changes in diagnoses of comorbidities, medication use patterns, and treatment costs between the year before and after the index date were examined. Comparison among subgroups of GAD patients with comorbid depression and pain was also investigated. Wilcoxon Signed Rank test and McNemar’s test were used to examine pre-post differences for continuous and categorical variables, respectively.
Results: A total of 240,041 patients were included in this study. The mean age was 41.7 years old and 67% were female. After diagnosis of GAD, a significantly higher percent of patients were diagnosed with depression (44.4% vs. 30.9%, p<.001), dyslipidemia (24.0% vs. 19.9%, p<.001), and diabetes (6.1% vs. 5.3%, p<.001) than before GAD diagnosis. The use of antidepressants increased from 42.3% to 56.8% (p<.001). Compared to the year prior to GAD diagnosis, total annual costs increased by $2,034 (p<.001) driven mainly by increases of inpatient and outpatient costs ($285 and $773, p<.001), GAD only and increased merely $306 for GAD patients with depression while GAD patients with pain and those with both pain and depression increased by $2,253 and $4,665 (both p<.001), respectively.

Conclusions: Diagnosis of GAD had significant impact on comorbidities, medication use and treatment costs. Furthermore, comorbid pain and depression had substantial extra burden on GAD patients as compared with those had GAD only. Recognizing these comorbidities is important in the treatment of patients with GAD.

References:

NR561 Tuesday, May 22, 3:00 PM - 5:00 PM
Predictors of Atypical Antipsychotic Prescriptions in 2,964 Veterans With Bipolar Disorder
Jennifer C. Hoblyn VA Palo Alto/Stanford University, Psychiatry Department, 3801 Miranda Avenue, Palo Alto, CA, 94315, 9000, Keiko Kurita, M.B.A., Deborah Rovine, M.D., Jacob S. Bailon, M.D., John O. Brooks III, M.D.

Educational Objectives:
To understand more clearly prescribing patterns of atypical antipsychotic agents in Veterans with bipolar disorder.

Summary:
Objective: We sought to evaluate potential predictors of atypical antipsychotic prescriptions for Veterans with bipolar disorder. Atypical antipsychotics variously are approved for use in bipolar disorder in the United States for the management of acute mania, maintenance as mood stabilizers, and recently the treatment of depression in bipolar disorder (1). Other psychopharmacologic agents include antidepressants, mood stabilizers, typical antipsychotics, and benzodiazepines.

Method: This retrospective study included 2,964 veterans with primary or secondary diagnoses of bipolar disorder in the VA Health Care System of the Veterans Integrated Service Network 21 during the 2004 fiscal year. Predictors included age, sex, mental health service usage, substance use, and psychotropic prescriptions. A Receiver-Operating-Characteristic Program was used to identify the best predictors of atypical antipsychotic prescriptions.

Results: Prescriptions for an atypical antipsychotic (olanzapine, risperidone, ziprasidone, or aripiprazole) were associated with prescriptions for benzodiazepines and age < 55 years (79%). Veterans > 55 years, on benzodiazepines had a lower risk of receiving atypicals (66%), but those who also were prescribed a typical psychotic were at a higher risk (88%). The highest risk was in those with a prescription of a typical antipsychotic, a selective serotonin reuptake inhibitor (SSRI), but not benzodiazepines (92%). There was a lower probability of an atypical antipsychotic prescription if the veteran did not have prescriptions for benzodiazepines, SSRIs, or mood stabilizers (28%).

Conclusion: Use of typical antipsychotics and SSRIs in the absence of benzodiazepines appear to be the strongest predictors of use of atypical antipsychotics in veterans with bipolar disorder. This may reflect atypical antipsychotic being added to medication regimens in an attempt to counteract affective flattening associated with typical antipsychotics or perhaps with excess affective up regulation resulting from SSRI usage. Overall, rates of all antipsychotic use were higher than previously reported in veterans with bipolar disorder (2).

References:

NR563 Tuesday, May 22, 3:00 PM - 5:00 PM
A Review of Prescribing Trends in Antidepressants Use

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand how antidepressant prescribing practices were affected by regulatory action

Summary:
Introduction: As detailed in our forthcoming paper[1], between October 2003 and September 2004, review of clinical trial data by regulators prompted a re-evaluation of risk for increased suicidality associated with antidepressant use in children and adolescents. The FDA issued a Public Health Advisory and required antidepressant manufacturers to include a Black Box warning covering the risk of suicidality. Although the FDA is currently analyzing suicidality data for adults, there has been little negative press regarding antidepressant use in the last two years.

To understand potential trends in the use of antidepressants in response to increased regulatory action, we examined Verispan retail pharmacy prescription data from January 2000 through July 2006.

Methods: The Verispan database captures more than 1.4 billion prescriptions per year, which is nearly half of all prescription activity in the U.S. Antidepressant prescriptions were gathered and combined to obtain rolling quarterly figures, and we calculated an annual growth rate for each rolling quarter.

Results: At the time of the FDA Advisory Panel in October 2003, the antidepressant market was growing at a rate of approximately five percent compared to the previous year. By January 2005, this market stopped growing and exhibited contraction. In January 2006, antidepressant prescribing again began to grow, and by July 2006, the market was approximately three percent larger than July 2005.

Conclusion: Coinciding with reports of increased risk for suicidality, a Public Health Advisory and stricter labeling requirements, the U.S. antidepressant market stopped growing and experienced contraction from October 2003 through January 2005. During 2006, antidepressant use appears to have recovered with a return to growth.
NR564  Tuesday, May 22, 3:00 PM - 5:00 PM

Service and Cost Implications of Extending FDA
Recommendations for Close Monitoring To Adult
Patients Starting Antidepressants or Changing Doses

Marcia T. Valenstein, M.D. Veterans Affairs/University of
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Ausin, M.P.H., Kara Bambauer, Ph.D., Frederick C. Blow, Ph.D.

Educational Objectives:
At the end of this presentation, participants will be familiar with
the FDA recommendations for close monitoring for youth following
antidepressant starts and dose changes.
Participants will appreciate the high rates of suicide among
patients receiving treatment for depression in VA settings, rates
that are higher following antidepressant starts and dose changes.
Finally, participants will understand the services and cost impli-
cations of extending the FDA recommendations for monitoring of
youth to this vulnerable adult population.

Summary:

Background: Because of risks of suicidality, the US Food and
Drug Administration (FDA) recommends “close monitoring” of all
patients starting antidepressants or changing doses. The FDA
specifies that monitoring for youth should generally include 7 pro-
vider contacts in the 12 weeks following these events. We exam-
going the implications of extending monitoring recommendations
for youth to adults receiving depression treatment in VA settings.

Methods: We randomly selected 100,000 patients receiving de-
pression treatment between 4/1/1999 and 9/30/2004 in Depart-
ment of Veterans Affairs facilities. We identified patient antidepres-
sant starts, dose changes, and suicides occurring during the study
period. We calculated the frequency of monitoring visits in the
12 weeks following antidepressant starts or dose changes and estimated the costs of incrementing visits to meet the FDA’s close
monitoring recommendations for youth.

Results: Patients experienced 197,443 antidepressant starts or
dose changes and completed an average of 2.4 monitoring visits
in the 12 weeks following these events. The suicide rate was 81.7/
100,000 person-years during the entire observation period and
181.6/100,000 person-years during the 12 weeks periods follow-
ing antidepressant starts or dose changes. Depending upon
whether incremental visits were brief telephone and in-person
visits or reflected current visit practices, meeting FDA close moni-
toring recommendations would increase average costs by $269-
$464 per patient in this population. For all VA patients (N=887,859)
treated for depression between 4/1/1999 and 9/30/2004, depres-
sion care costs would have increased by $239-412 million.

Conclusions: VA patients in depression treatment have high
suicide rates. They have frequent antidepressant starts and dose
changes, and their risks of suicide are higher following these
events. Extending the FDA recommendations for close monitoring
to this vulnerable population would require substantial increases
in visits and expenditures. Research is urgently needed to assess
the effectiveness of increased monitoring in preventing suicide.

References:
1. Nemeroff CB, Kalali A, Keller MB. Impact of publicity concern-
ing suicidality data on physician practice in the United States.
Arch Gen Psychiatry 2006; in press.
Drug Administration’s Deliberations on Antidepressant Use in

NR565  Tuesday, May 22, 3:00 PM - 5:00 PM

Hospitalizations and Medical Costs Associated with
Newer Versus Older Antidepressant Agents

David V. Sheehan, M.D. University of South Florida, Psychiatric
Research, College of Medicine, 3515 East Fletcher Avenue,
Tampa, FL, 33613-4706, 9000, Michael Eaddy, Ph.D., John E.
Kraus, M.D., Ph.D., David J. Carpenter, M.S., Stan Krulewicz,
M.A.

Educational Objectives:
Participants will review results of a retrospective database anal-
ysis conducted on claims data from the PharMetrics Patient-Cen-
tric Database (Watertown, MA) representing managed care pa-
tients initiating antidepressant therapy for the treatment of
depression and/or anxiety between January 1, 2002 and Septem-

At the conclusion of this presentation, participants should be
able to describe differences in hospitalization rates and medical
costs among antidepressants launched on or after January 1,
2002 and those launched prior to this date.

Summary:

Introduction: Data suggest that newer antidepressants may offer
improved adherence when compared to older agents, which could
result in lower hospitalization rates and medical costs. The pur-
pose of this study was to compare hospitalization rates and medi-
care consumption among patients receiving older versus
newer antidepressants for the treatment of depression and/or
anxiety.

Methods: Using claims data from the PharMetrics Patient-Cen-
tric Database, a retrospective database analysis was conducted
on managed care patients initiating antidepressant therapy be-
tween January 1, 2002 and September 30, 2004. Adults diagnosed
with depression and/or anxiety disorder within a 6-month period
preceding or within 30 days after the initial prescription were
included. Patients were followed for the 6-month period after initia-
ting therapy to evaluate rates of hospitalizations and total
healthcare charges. Antidepressants were categorized as newer
agents (NA) if launched on or after January 1, 2002 and as older
agents (OA) if launched prior.

Results: A total of 266,665 unique patients were included for
analysis: 167,255 (63%) had a depressive diagnosis, 82,477
(31%) had an anxiety diagnosis, and 16,933 had both (6%). Of
patients on OAs 16% were hospitalized at least once within 6
months of therapy initiation compared to 13% of patients on NAs
(OR = 1.10; 95% CI: 1.05 to 1.14; P < 0.0001). Six-month total
medical costs were $4297 per patient on an OA compared to
$3769 per patient receiving a NA (parameter estimate = 0.155;
standard error = 0.009; P < 0.0001). Among newer agents, hospi-
talization rates ranged from 12.7% to 11%, and medical costs
ranged from $4977 to $3273 per patient.

Conclusion: Patients receiving newer antidepressants experi-
enced fewer hospitalizations and lower total medical costs than
patients who received older agents. Small differences in the rates
of hospitalization may result in important savings in medical costs.
Supported by a Collaborative Research Grant from Glaxo-
SmithKline

References:
1. American Psychiatric Association. Practice guideline for the
assessment and treatment of patients with suicidal behaviors.
2. U.S. Food and Drug Administration. FDA Public Health Advi-
sory: Suicidality in Adults Being Treated with Antidepressant
Medication [Web Page]. 2005 Jun 30; Available at http://
(Accessed 2006 Sep 10).
NR566 Tuesday, May 22, 3:00 PM - 5:00 PM
A Comparison of Medication Use, Hospitalizations, and Costs Among Newer and Older Antidepressants For Treatment of Depression and Anxiety in Bipolar Disorder

David V. Sheehan, M.D. University of South Florida, Psychiatric Research, College of Medicine, 3515 East Fletcher Avenue, Tampa, FL, 33613-4706, Michael Eaddy, Ph.D., John E. Kraus, M.D., Ph.D., David J. Carpenter, M.S., Stan Krulewicz, M.A.

Educational Objectives:
Participants will review results of a retrospective database analysis conducted on claims data from the PharMetrics Patient-Centric Database (Watertown, MA) representing managed care patients initiating antidepressant therapy for the treatment of bipolar disorder and depression and/or anxiety. At the conclusion of this presentation, participants should be able to describe how rates of therapy adherence, therapy change, hospitalizations, and total medical charges compared in patients with bipolar disorder receiving antidepressants launched on or after January 1, 2002 versus those launched prior to this date.

Summary:
Objective: Bipolar disorder (BPD) is associated with medication non-adherence, high hospitalization rates, and significant healthcare consumption. The purpose of this study was to compare rates of therapy adherence, therapy change, hospitalizations, and total medical charges in patients receiving early or late generation antidepressant agents in the treatment of BPD and depression/anxiety.

Methods: A retrospective database analysis was conducted on patients newly initiating antidepressant therapy between January 1, 2002 and September 30, 2004. Adults diagnosed with BPD and depression/anxiety within the 6-month period preceding or within 30 days of the initial prescription were included. Antidepressants were categorized as newer agents (NA) if launched on or after January 1, 2002 and as older agents (OA) if launched prior. Patients were defined as adherent if they filled 144 days of therapy over the first 180 days of follow-up (80% medication possession ratio) without a 30-day gap in therapy. Differences in adherence, hospitalization rates, and hospitalization charges were assessed using multivariate analysis.

Results: A total of 579 patients were included: 393 received OAs, and 186 received NAs. Over 6 months, 22% of patients (19% OA vs 26% NA) were adherent to therapy. Overall, 37.5% of patients (42% OA vs 28% NA) had a therapy change within 6 months. Hospitalization rates were similar between the two groups, with 44% of patients experiencing at least one hospitalization. However, OA patients incurred 30% higher total medical costs than did NA patients: $7652 vs $5372.

Conclusion: Therapy adherence, change rates, and hospitalization rates were statistically similar between newer and older agents. However, patients receiving newer agents incurred less total medical charges.

Funding Support: Supported through a collaborative research grant provided by GlaxoSmithKline

References:
NR568  Tuesday, May 22, 3:00 PM - 5:00 PM

A Social Worker Managed Depression Treatment Program Leveraging Electronic Health Records in Primary Care: Geisinger Health System

Etta Lindenfeld, M.D., Geisinger Health System, Psychiatry, 100 North Academy Avenue, Division of Psychiatry, Danville, PA, 17822, 9000

Educational Objectives:

At the conclusion of this presentation, the participant should be able to 1. Discuss the advantages of a standardized questionnaire for depression screening in primary care 2. Describe the elements of an integrated automated screening and treatment program for depression 3. Explain the utility of the electronic medical record system in coordinating care between a social worker and a primary care physician in a primary care setting

Summary:

Background: Depression identification and treatment is a challenge in primary care (PC) settings. Economic and time disincentives pose barriers in even the most well-intentioned of health care settings. The Patient Health Questionnaire (PHQ) is a self-administered instrument with good sensitivity and specificity for depression screening.

Methods: The electronic health record (EHR) can be used to identify patients at increased risk for depression who are scheduled for a PC appointment. We are implementing a system to invite these patients to complete an optical character recognition (OCR) version of the PHQ in the waiting room prior to their PC visit. These self-administered forms are scanned and automatically scored. PHQ scores generate automated responses. All patients receive a result letter. Patients with positive scores are phoned and scheduled for an appointment with a SW at the patients' PC clinic. Physicians are notified of positive scores and if the patient scheduled or refused an appointment. PHQ scores and their meanings are displayed as a lab result in the EHR. The SW-patient visits conform to the highly structured IMPACT model for primary care, which has shown improved outcomes over usual depression care at 6, 12 and 24 month follow up. That program addresses patient defined life problems with practical plans. The intra-visit components for that model, including a full depression evaluation at the first visit, are recorded in the EHR. Visit components and repeat PHQ scores can analyzed and visualized in combined graphic and text presentations. SW-patient EHR visit records are forwarded to the patient’s PC physician, and may include an antidepressant prescription request.

Conclusions: This system streamlines care for depressed patients identified in PC and enables a clinical SW to perform duties generally assigned to a higher credentialed provider. Depression outcomes can be assessed in the context of the complete medical record.

References:


Christopher N. Sciamanna, M.D., Mark Salzer, Ph.D., David Oslin, Barry W. Rovner, M.D.

NR569  Tuesday, May 22, 3:00 PM - 5:00 PM

Internet Access and Use in Patients Being Treated With Antidepressant Medications


NR570  Tuesday, May 22, 3:00 PM - 5:00 PM

The Economic Implications of New Episodes of MDD for Non-stable Versus Stable Depression

C. Daniel Mullins, Ph.D. University of Maryland, Pharmaceutical Health Services Research, 220 Arch Street, 12th Floor, Room 01-200, Baltimore, MD, 21201, 9000, Vijay N. Joish, Ph.D., Tony Yang, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant will comprehend the economic impact of new treatment episodes of major
depressive disorder (MDD); recognize the major cost drivers of increased direct medical expenditures associated with these treatment episodes; and compare the magnitude of cost increases among patients categorized as stable versus non-stable based upon two published anti-depressant use algorithms.

Summary:

Introduction/Hypothesis: Major depressive disorder (MDD) costs are significant and rise substantially during new treatment episodes. Based on their antidepressants and other medical resources use, MDD patients can be identified as stable or non-stable. Non-stable patients are patients who have undergone multiple changes in antidepressant treatment and/or had a depression-related event within one-year of treatment initiation. We hypothesize that the magnitude of increase in direct medical costs in the year following a new treatment episode will be substantially greater for individuals with non-stable depression vs. those defined as stable.

Methods: A retrospective cost analysis used the PHARMetrics database, a nationally representative claims dataset 1.9 million MDD patients during the study time period of January 2003 to June 2005. Adults with new MDD treatment episodes were stratified based upon two published anti-depressant use algorithms. A pre-post comparison of annual medical cost increases following new treatment episodes was performed and differences in mean cost increases for the non-stable vs. stable cohort were calculated using t-tests.

Results: The percentage of non-stable subjects was 32% or 8%, depending on the algorithm utilized. The mean increase in total direct medical costs using the less restrictive (more restrictive) algorithm was $4,801 ($8,047) for the non-stable cohort versus $1,722 ($2,249) for the stable cohort, representing increases from baseline of 104% (181%) for non-stable individuals and 44% (55%) for stable individuals. The major components of these cost increases were outpatient cost increases of $2,199 ($3,952) vs. $934 ($1,115); inpatient cost increases of $1,317 ($2,106) vs. $239 ($423); and increases in antidepressant costs of $657 ($992) vs. $315 ($376) for non-stable and stable cohorts, respectively. All differences were statistically significant at p < 0.001.

Conclusions/Discussion: The increased costs of MDD are substantial following the onset of a new treatment episode and significantly higher among non-stable than stable depressed patients.

References:

NR571 Tuesday, May 22, 3:00 PM - 5:00 PM
The Status Quo of Private Health Insurances Including Psychiatric Illnesses And Not in Korea
Geon-Ho Bahn, M.D. Kyung Univ Hospital School of Medicine, Psychiatry, 1 Hoegi-Dong Dongdaemun-Gu, Seoul, 130-702, 5800, Ahrang Cho, M.D., YoungJong Kim, M.D.

Educational Objectives:
Educational objective: General population in Korea is covered by national medical insurance since 1989. However, national fund is not enough to pay all medical practices. Private health insurances increase steeply for last 10 years. More than 800 goods are sold, but most of them exclude psychiatric disorders from their contracts. Why do they discard psychopaths from their markets?

Summary:

Introduction: Korean psychiatrists noticed that private health insurance does not pay for most psychiatric disorders. Probands and family members complained about that. Even, probands cannot join the insurance because of their psychiatric histories. Authors investigated and reviewed contracts of private insurance goods to find clues why psychiatric disorders are expelled from insurance companies.

Methods: Authors reviewed about 800 insurance goods, 51 companies.

Results: Among goods, some psychiatric diagnoses such as dementia and organic mental disorders can have insurance. Less than 10 goods guarantee insurance for psychiatric illnesses. Most insurance companies have contracts what prohibit F-codes. There was not enough reasonable comments on agreement.

Conclusions: Psychiatric illnesses do have small rooms in national medical insurance system and almost no rooms in private health insurance system. It is very urgent issue to find the space in insurance for psychiatrists and also patients with psychiatric illnesses.

References:

NR572 Tuesday, May 22, 3:00 PM - 5:00 PM
Improved Medication Adherence in the Developmentally Delayed Population with An Extended Release Dosage Form of Divalproex and the Effect of Residence on Medication Compliance: A 30 Month Longitudinal Review
Lawrence Plon, Pharm.D. University of California Irvine, Psychiatry/Pharmacy, 101 The City Drive South, Neuropsychiatric Center, room 209, Orange, CA, 92868, 9000

Educational Objectives:
At the conclusion of the poster presentation, the participant will be able to determine which of the listed factors influence medication adherence in the developmentally delayed population.

Summary:

Introduction: We sought to determine if residence, age, poly pharmacy, sex, or valproic acid dosage forms effect medication adherence.

Method: Records for 2,229,970 prescriptions filled from 1/2000 to 6/2002 for the Medicaid patient population of Orange County, California, were cross- referenced to isolate the medication utilization of the Developmentally Delayed clients of Regional Center. 1765 clients were identified representing 84,176 psychoactive drug prescriptions. Based on prescriber instructions and number of doses dispensed, calculations were performed to determine if the prescriptions were filled on schedule. Adherence was defined as maintaining a refill rate (ratio=number of days of drug supply/number of days from first fill to last fill) between 0.75 and 1.10 over the study period. Client's living arrangements were divided into private home (living with parent/guardian, independently, or in a supported living arrangement) or in a community care facility (CCF). Intermediate and skilled nursing facilities were not included. It was not possible to determine if the medication was utilized for seizure control or mood stabilization.

Results: Age, sex or poly pharmacy had no statistically significant effect on adherence rate. Considering all valproic acid drug forms together, residence has a significant effect on adherence
rate (p<0.00005). Non-compliance was 6.19 times more likely in private homes than in CCFs. There was statistically significant lower adherence when maintained on divalproex enteric coated (74.4%) compared to the once daily dosage form (85.3%), (p<0.0001). Patients on extended release divalproex formulation are 2.01 times more likely to adhere than on the divalproex enteric formulation.

Conclusions: For this population, the type of residence influenced medication adherence. Once-a-day formulation of divalproex had statistically improved compliance.

References:

NR573 Tuesday, May 22, 3:00 PM - 5:00 PM
Personality Features Associated With Daily Cigarette Smoking in a Community Sample of Bucaramanga, Colombia

Educational Objectives:
At the conclusion of this presentation, the participants should recognize the personality features may be associated with daily cigarette smoking.

Summary:
Background: Various researchers report the association between personality features and cigarette smoking. However, this relationship has not been studied among Colombian people.
Objective: To determine the association between personality features and daily cigarette smoking among urban adults in Bucaramanga, Colombia.
Method: A population-based cross-sectional study was carried-out. A probabilistic sample of 18- to 65-year adults was surveyed. Personality features were established with the self-reporting questionnaire of the Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II); abusive alcohol consumption with CAGE questionnaire; and common mental disorders with General Health Questionnaire (GHQ-12). Current daily smokers were who consumed cigarette everyday within the last month. Logistic regression analysis controlled confounding factors.
Results: A group of 2496 adults participated in this survey. The mean age was 38.0 years (SD=13.5), the mean scholarship was 9.2 years (SD=4.1), 69.7% were women, 58.1% were married, 49.1% had an employ, and 67.8% lived middle social status. Bor-
derline

NR575 Tuesday, May 22, 3:00 PM - 5:00 PM
Evaluation of the First Module of a Relapse Prevention Program for Alcoholic Patients According to Four Psychological Variables.
Géraldine Martet University of Clermont, Department of Psychology, LAPSCO UMR CNRS 6024, 34 av Carnot,

References:
Clermont-Ferrand Cedex, 63037, 4279, François Planche, M.D., Pierre-Michel Llorca, M.D., Nadia Chakroun, Ph.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to discuss the importance of a relapse prevention program with the purpose of extending the abstinence of people who have been weaned off alcohol.

Summary:

Objectives: The purpose of the relapse prevention program is to create an incentive for the patient to deeply change his behavior and to adopt a healthier life style, in order to maximize the abstinence period. The efficiency of the therapy has been proved on several occasions, particularly in the long run. Monti adapted this theory in three therapeutic modules. The first one is entitled "How to avoid the risks of relapse". Patients concentrate on self-observation, preventive awareness of risky situations, on changing their cognitions and adopting new coping skills that are effective and appropriate.

Method: Fifteen patients, (two women and thirteen men, aged 46 years on average), volunteers and hospitalized in rehab centres, followed the first module. They filled in four questionnaires, related to self-assertion, quality of life, the kind of coping skill used (either focused on the problem, emotion, or social support) and a feeling of self-efficiency, on their admission and when discharged, one mouth later.

Results: Globally, the results showed a significant increase in self-assertion (<0.001) and quality of life (p<0.001). The problem-centred coping skill score had the greater increased compared to the other two coping skills (p<0.001). Cognitive escapism into alcohol or non-constructive emotional distress comes second (p<0.05), finally, the coping focused on emotion significantly decreased (p<0.05). All our analysis were realized with the test of Student.

Discussion: The results are promising. We measured the changes in behavior and cognition at the end of the first module. In addition, we pinpointed which variables change most in the group to explain its efficiency and understand it. Within the next six months, that efficiency will be re-assessed as well as the percentage of people who relapse, and the measure of the four variables.

References:


NR576 Tuesday, May 22, 3:00 PM - 5:00 PM

Frequent Users of Acute Psychiatric Care Services: Analysis by Cost and Diagnosis.

Shilpa Srinivasan, M.D. University of South Carolina School of Medicine, Neuropsychiatry and Behavioral Science, 3555 Harden Ext., Suite 301, Columbia, SC, 29203, 9000, Ronald E. Prier, M.D., Kimberly B. Rudd, M.D., Meera Narasimhan, M.D., Richard K. Harding, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be able to identify high users of acute psychiatric services, including emergency room and in-patient hospitalization by diagnosis and payer source. The participant should recognize the connection between lengths of hospitalization and payer source and diagnoses, as well as the impact of shorter hospitalization length on rates of recidivism.

Summary:

Objective: To compare characteristics of high users of emergency services and inpatient hospitalizations within South Carolina's Department of Mental Health (DMH) vs. non-DMH users, by payer source and diagnosis.

Methods: High users of South Carolina psychiatric emergency services were identified as adults with two or more ER visits and/or inpatient hospitalizations for primary behavioral health diagnoses (by ICD-9 codes) from 2003-2004. Data was obtained from the South Carolina State Budget Control Board. Comparisons were made to ensure unduplicated counts. Specialty hospitals were excluded.

Results: Health services utilization by diagnosis:

- Among DMH clients, 40% of financial charges were for psychotic disorders and 33% for mood disorders. For non-DMH clients, mood disorders contributed to 32% of financial charges, followed by alcohol and drug dependence at 28%.

Health services utilization by payer source:

- DMH clients comprised 57% of all adult frequent users of acute psychiatric visits (totaling $82,143,978) with the majority covered by Medicare and Medicaid; compared to non-DMH clients (43% at $62,615,804) who were covered mainly by Medicare and private insurance.

Direct cost (in-patients):

- Large differences in inpatient lengths of stay were found by diagnosis and payer source.

- Indigent/self-pay users had lower lengths of stay across all diagnoses among DMH (6.6 days) and non-DMH (5.3 days) users. ER lengths of stay were not influenced. (Figures 1, 2).

- Among those insured by Medicaid and Medicare, lengths of stay were highest for mood and psychotic disorders (9.2 vs. 10.6 days respectively) (Figures 3, 4).

Conclusions: Results from this study are very reflective of national trends. It emphasizes higher recidivism rates for indigent/self-pay users, due to shorter lengths of hospitalization. Further research is necessary to analyze whether intensive case-management services may impact hospital course length and potentially decrease recidivism rates.

References:

were followed for 12 months. Out of 200 patients, 176 patients (age=53.99±13.28 years) were recommended either psychotherapy (TX) or pharmacotherapy (RX) or both. These patients were followed for acceptance or rejection of recommended treatment, and adherence to it. There were 85.72% of patients (age=54.01±12.91 years) who accepted RX, in contrast to only 41.67% of patients (age=55.05±13.16 years) who accepted TX (p<0.005). Those patients accepting treatment showed greater adherence (p<0.05) to RX (276.17±129.86 days) in comparison to TX (181.90±150.18 days). In each group, those who accepted treatment were older in age, the difference being non-significant. These data show that patients themselves have certain desires and expectations for their treatment need. MH evaluation, treatment recommendations and resource allocation should consider these patient perspectives. 

References:

NR578
Tuesday, May 22, 3:00 PM - 5:00 PM
The Impact of Aripiprazole Augmentation on Metabolic Parameters for Patients with Schizophrenia

Educational Objectives:
- Describe the importance of routine access to psychiatric and medical care for patients with serious mental illness.
- Understand the role of augmentation strategies in the treatment of schizophrenia.

Objective:
Antipsychotic treatment is associated with metabolic abnormalities which increase the risk of cardiovascular disease. Routine medical monitoring for metabolic changes is essential to reduce risk. A longitudinal evaluation of adjunctive aripiprazole treatment on weight, lipids and glucose metabolism and symptom control was conducted. Data was collected from patients diagnosed with schizophrenia.

Method:
Included a chart review of all inpatients and outpatients receiving adjunctive aripiprazole treatment (N=65). All subjects had a medical history, physical exam, BPRS and screening blood tests before and during treatment.

Results:
Subject characteristics: Age (yrs) - 51.4 ±15.8 (23-87), Female=19, Hispanic=7, African American=15, Native American=1. Patients had been stabilized on clozapine (N=17), olanzapine (N=19), risperidone (N=13), quetiapine (N=10) and haloperidol (N=5) prior to adjunctive treatment with aripiprazole. There was no significant difference between these groups for weight, fasting blood glucose (FBG), and lipids (P=.43). After 381.6 ±231.4 (110-970) days of adjunctive aripiprazole treatment there was significant reduction in FBG (113.6mg/dl to 92.5mg/dl, P=.008, t=2.519) and total cholesterol (TC) (185mg/dl to 156mg/dl, P=.004, t=2.768) in the clozapine group. In the olanzapine group there was significant reduction in weight (89.8kg to 78.8kg, P=.039, t=1.79), FBG (114.7mg/dl to 91.1mg/dl, P=.0017, t=3.12), TC (172.7mg/dl to 153.7mg/dl, P=.003, t=2.87), HDL (44.7mg/dl to 104.2mg/dl, P=.0001, t=8.56), LDL (109mg/dl to 54.7mg/dl, P=.0001, t=8.31) and triglycerides (113.9mg/dl to 104.2mg/dl, P=.039, t=1.809). There was no significant change in weight, lipids and glucose for the risperidone, haloperidol, and quetiapine groups. There was no significant change in symptoms (BPRS: 44.1±9.3 to 41.6±10.9, P=.09, t=1.30).

Conclusion: Augmentation with aripiprazole may be useful in clozapine and olanzapine induced metabolic abnormalities. Access to novel treatments is essential to optimize positive outcomes while minimizing antipsychotic induced morbidity. These preliminary results warrant large randomized placebo-controlled trials to more thoroughly determine efficacy and safety with this combination.

References:

NR579
Tuesday, May 22, 3:00 PM - 5:00 PM
Smoking Cessation and Decreased Behavioral Restraints in Inpatient Psychiatry
Stephanie A. Woodard, M.S. PAVAHCS & Stanford University, Psychiatry & Behavioral Sciences, 3801 Miranda Avenue, Ward 281, Palo Alto, CA, 94304, 9000, Robert A. Zeiss, Ph.D., Robinetta Wheeler, Ph.D., Robert Brown, R.N., Jennifer C. Hoblyn, M.D., Ph.D., Anil Sharma, M.D., John O. Brooks

Educational Objectives:
At the conclusion of this presentation, the participant should be able to identify key components of a successful smoking cessation program for inpatient psychiatry and know effects on behavioral restraints.

Summary:
Introduction: The incidence of tobacco smoking remains twice as high in psychiatric populations as in the general public (Lasser et al., 2000), yet smoking is typically not addressed during psychiatric hospitalizations (Ziedonis et al., 2003). Many inpatient units allow psychiatric patients to smoke due to continued apprehension about the enforcement of smoking bans and concerns of increased disruptions to the therapeutic environment. Our experience demonstrates the feasibility of implementing a supportive smoking cessation policy on an acute psychiatric inpatient unit that decreased the number of violent incidence and restraints.

Method: On an acute inpatient psychiatric unit, a complete smoking ban was instituted. All patients were offered support in smoking cessation including counseling groups and nicotine patches. To evaluate the associated changes in violent behaviors and restraints after banning smoking, we considered all instances of behavioral restraints for 6 months before through 6 months after the intervention.

Results: The number of admissions to the unit remained constant over the entire 6-month period after the ban was instituted. There was a marked decrease in the incidence of behavioral restraints after the smoking ban was implemented, as the number of restraint episodes plummeted from an average of 21.81 per month to an average of 8.8 per month after the intervention. For the following year, restraints occurred at the mean rate of 6.75 per month.

Conclusion/Discussion: Effective non-smoking policies can be enacted without major disruptions to the milieu on an inpatient unit. In fact, a smoking ban was associated with decreased rates of patient restraint. The positive influence of decreased restraints
on therapeutic milieu and health benefits from smoking cessation argue in favor of eliminating smoking for inpatient psychiatric patients.

References:

NR580 Tuesday, May 22, 3:00 PM - 5:00 PM
The Compliance With Antipsychotic Medication From the Patients' Perspective. A Qualitative Research Based on Focus Groups and the Grounded Theory
Maria Barbera, Psy.D. Hospital La Fe, Psychiatry, Psychiatry Department. Hospital La Fe, Avda. Campanar, 21, Valencia, 46009, 4700, Julio Sanjuan, Candelaria Santiago, Mikel Munarriz, Enrique Novella

Educational Objectives:
At the conclusion of this presentation, the participant should be familiarized with the qualitative research methodology in psychiatry and acquainted with the dynamic subjective processes that lead patients to continue or discontinue their antipsychotic medication.

Summary:
Purpose: To assess the perceived reasons of patients with schizophrenia for taking or not their antipsychotic medications.
Method: A qualitative research based on focus groups was performed. Verbal interactions were recorded and transcribed. Transcripts were paraphrased and incorporated according to the grounded theory. Major categories were identified to fit all the information recorded. Subcategories, themes and notions were also generated. Last, an inductive exercise was performed to create hypotheses that may aid in increasing patients' proactivity in their treatment.

Results: Patients were able to provide very useful and dense information. It was classified into two classes regarding: a) perceived effects of medication, and b) patients' attitudes, beliefs and prospects around their disease, treatment, health care staff and social environment. Both types of subjective processes emerge influenced by the result of initial dysphoria associated to personal insight, the perception of the efficacy of medication that was distinct for typical with respect to atypical as well as among atypical antipsychotics, the degree of insight, long-term side-effects and social and cultural contexts. At last, patients are pursuant of social and occupational functionality for which achievement they see medication as necessary; but only a few succeeded and thus assured compliance. These were generally those with whom a sound therapeutic alliance could be established in the absence of upsetting side-effects. Usually, these succeeding patients were treated with atypicals, engaged in psychotherapy and/or rehabilitation, and retained a reasonable sense of self-control of their management.

Conclusion: Qualitative research appears as a valuable inductive tool to support and complement quantitative deductive research. We have shown that compliance with antipsychotics is determined by both the long-term complex subjective processes elaborated on perceived effects and the achievement of personal prospects related to functional recovery. Elucidations of these processes were rather complex and hardly describable exclusively through the items of subjective scales.

References:

NR581 Tuesday, May 22, 3:00 PM - 5:00 PM
Residency Training Clinic Patient No-Show Rate: Understanding the Reasons and Planning the Changes
Ludmila De Faria, M.D. University of Miami, Psychiatry, 1400 NW 10 Ave, suite 304A, Miami, FL, 33186, 9000, Patricia Junquera-Herrera, M.D.

Educational Objectives:
At the conclusion of presentation, the participant should be able to identify reasons why patients in an adult outpatient psychiatric setting fail to keep their appointment and the impact of no-show rates on patient care, continuity of care, clinic productivity as well as learning experience.

Summary:
Patients no-show rates have a negative impact in clinic productivity, continuity and quality of care, and learning experience for the residents. It directly increase time mismanagement and frustration in general. The literature has shown that making and keeping appointments is a multifactorial function rather than the result of a single decision by any given patient. Yet, most measures used to compensate for no-shows, such as overbooking, charging, etc., may reinforce the behavior, since patients perceive the experience of coming to their appointments as punitive and unrewarding. Studies available have used interview questions as well as exit interviews with patients coming to their appointments in an attempt to identify and improve patient compliance with care. These studies left out the actual no-show population and failed to answer the original question. Our study aims to identify reasons that patients give for not keeping their appointments and implement interventions that may ameliorate them. We developed a structured questionnaire that can be easily administered by phone and facilitates gathering data from absent patients. Patients enrolled at the clinic and who signed General Consent for Treatment were contacted by one of the co-investigators personally (if they are attending their scheduled appointment) or by phone (if they have missed it). All patients were given a brief introduction explaining the nature of the research and the purposes of collecting the data and were asked to participate. They were given a self-reporting structured questionnaire developed by the researchers. Questionnaires do not include any identifiers. Subject participation is limited to agreeing to answer the questionnaire. No follow up is necessary. Preliminary results indicate that most of the reasons for no-show can be improved by making minor changes in clinic structure, however full data analysis in process. Understanding patient's needs and limitations is fundamental to improve compliance to care.

References:
Educational Objectives:

At the conclusion of this presentation, the participant should be able to get informed in respect the prevalence of self reported sleep disturbances within the elderly community population and the medical/psychiatric and sociodemographic variables associated with service use.

Summary:

Objective: Investigate the prevalence of disturbed sleep and its association with medical conditions and service use in older adults.

Method: A cross sectional study of 6,961 household residents aged 60 years old and over, recruited from a population-based random sample, examined in a face to face interview.

Results: The overall prevalence of disturbed sleep is 33.7% (95% CI: 32.5 - 34.8); this condition is higher in women 37.2% (95% CI: 35.8 - 38.6), than in men 27.4% (95% CI: 25.4 - 29.3). The overall rate of medical consultations is 78% (95% CI: 76.0 - 79.9) and hospitalizations 20.2% (95% CI:18.88-21.52). In logistic regression models, sociodemographic variables and health problems emerged as independent predictors of disturbed sleep especially: female, Caucasian, rural origin, depression and anxiety, self-rated health, pneumonia, urinary infection, among others. Age has a negative effect on disturbed sleep. There is no association between 6-month outpatient consultation and 12-month hospitalization and sleep disturbance.

Conclusion: Sleep disturbance is a frequent problem in the study population and is associated with health conditions. Age has a negative effect and there is no association between sleep problems and use of medical services in the surveyed population.

References:


NR583 Tuesday, May 22, 3:00 PM - 5:00 PM
Sleep Disorders, Depression and Drug Abuse By Students: Mirtazapine is a Treatment Option
Andrei Ilankovic, M.D. Institute of Psychiatry, Neuropsychiatry, Pasterova 2, Belgrade, YU-11000, 4799, Tanja Lakovic, M.D., Nemanja Lakovic, Jelena Laçmanovic, Nikola N. Ilankovic, M.D.

Educational Objectives:

At the conclusion of this session, the participants should understand the correlations between sleep disorders, depression, and drug addiction by students.

Summary:

Objective: Our investigation is an prospective analysis of groups of students in their sleep and wake behavior, depression, and tendency to drug abuse.

Methods: In the group were 70 students from high school (16-17 years old) with and without data of drug abuses. For assessment we used: (1) the scale for assessment of sleep-wake behavior, (2) the Hamilton Depressive Scale (HAM-D), and (3) the Zung scale for self-measurement of depression. The statistical analysis was made with Mc Pearson test of linear correlation, with Student t-test and with linear regression. Results: (1) The linear correlation (Mc Pearson) is very high and statistically very significant (p<0.0001) between delay of sleeping time (after midnight), depression score (HAM-D and Zung), and tendency to drug abuse. (2) The predictive models (made with linear regression) as risk factors for addictive behavior point out: smoking, night life, different pains, abuses of analgetics drugs, delay of time going to sleep (to the morning!), and very high score of depressivity.

Conclusions: 1. The disorders of sleep (especially disorders of circadian sleep and wake cycles) by students is a big risk to developing depression and tendency to drug abuse. 2. The therapy with mirtazapine was successful in 63% of students.

References:


NR584 Tuesday, May 22, 3:00 PM - 5:00 PM
Exposure-Response Modeling of the GABAA Receptor Partial Agonist NG2-73: An Approach for Determining Target Onset and Duration of Sleep Efficacy While Minimizing Next Morning Effects
Matthew M. Riggs, Ph.D. Metrum Research Group LLC, Quantitative Pharmacology, 2 Tunxis Road, Suite 112, Tariffville, CT, 06081, 9000, Marc R. Gastonguay, Ph.D., Leonid Gibiansky, Ph.D., Gary Zammit, Ph.D., Ken Sprenger, M.D., Lynn Anello

Educational Objectives:

Recognize the importance of quantitative descriptive relationships between pharmacokinetic exposure and pharmacological response of NG2-73 for determining target onset and duration of sleep efficacy while minimizing next morning effects.

Compare exposure-response properties of NG2-73 with zolpidem to inform the therapeutic development of NG2-73 for the treatment of insomnia.

Understand how these pharaco-statistical models of drug efficacy and safety offer an important approach to improving drug development knowledge management and development decision making, as suggested in the March 2004 US Food and Drug Administration Critical Path Initiative.

Summary:

Introduction: NG2-73, a GABAA partial agonist with preference for a3 subunit receptors, represents a potential insomnia treatment with comparable efficacy and fewer safety concerns relative to existing therapeutics. As with all therapeutics, determination of appropriate dose(s) and dosage formulation(s) is imperative to an efficient development program. To assist informed decision making, NG2-73 clinical development is being supported through extensive Exposure-Response (ER) modeling, in order to identify an optimal pharmacokinetic (PK) profile for sleep onset and maintenance while minimizing next morning effects.

Methods / Results: Study 1, a Phase 1 crossover study where 19 subjects received single oral doses (1, 3, 5, 10 mg NG2-73, zolpidem 10 mg (Z10), and placebo), compared ER between NG2-73 doses and zolpidem. Plasma concentrations associated with half-maximal visual analog scale effects were approximately 13-fold greater for zolpidem vs. NG2-73. Maximal concentration (Cmax) for NG2-73 10 mg was approximately 6-fold less than Z10. Altogether, ER indicated an approximately 4-5 mg oral NG2-73 dose would provide similar maximal response relative to Z10, which supported Study 2 dose selection. From digit symbol substitution test (DSST) modeling, next morning NG2-73 concentrations of < 2 ng/mL were targeted to minimize residual effects.

Study 2, a Phase 2A parallel study (placebo, 1, 3, 10 and 20 mg NG2-73 ) in healthy adults (N=369, PK in 133 subjects), evaluated NG2-73 sleep onset (latency to persistent sleep, LPS) relative to placebo. NG2-73 related to half-maximal LPS decrease was less than Cmax observed from NG2-73 1 mg. DSST ER modeling consistently supported the < 2 ng/mL target to minimize next morning effects.
NR585 Tuesday, May 22, 3:00 PM - 5:00 PM
No Evidence of Dependence With Zolpidem Extended-Release Taken as Needed 3-7 Nights/Week for 6 Months by Adult Patients With Chronic Primary Insomnia
Andrew Krystal, Duke University, Psychiatry, Box 3309, Duke University Medical Center, Durham, NC, 27710, 9000, Milton Erman, Gary Zammit, Christina Soubrane, Thomas Roth

Educational Objectives:
At the conclusion of the presentation, the participant should be able to understand that use of zolpidem extended-release treatment by patients with chronic primary insomnia for a duration of 6 months “as needed”, 3-7 nights per week, is not associated with development of dependence, based upon evaluation of patient-reported measures of sleep efficacy and medication strength, rebound insomnia, and analysis of tablet-taking behavior.

Summary:
Purpose: To assess the potential for dependence to zolpidem extended-release 12.5 mg, taken “as needed” 3-7 nights/week for 6 months by patients with chronic insomnia, by evaluation of efficacy variables (for evidence of tolerance), rebound insomnia, and tablet-taking behavior.

Methods: Double-blind, multicenter, randomized study in adults (18-64 years; n=1025; zolpidem extended-release [n=674]) with chronic primary insomnia. Zolpidem extended-release 12.5 mg or placebo was taken “as needed” 3-7 nights/week for 6 months. Efficacy was assessed every 4th week by patient global impression (PGI) evaluation of medication strength, and by monthly assessments of multiple sleep variables from daily morning questionnaires. Additional evaluations included rebound insomnia in zolpidem extended-release patients where their non-pill nights and the 3 nights post-discontinuation at study end were compared with baseline. We also examined tablet-taking behavior over time.

Results: 436/674 (64.7%) zolpidem extended-release- and 184/351 (52.4%) placebo-treated patients completed the 6-month treatment period. Discontinuation due to lack of efficacy was 23.4% (placebo) and 4.7% (zolpidem extended-release). There was no evidence of a loss of therapeutic effect of zolpidem extended-release over time in terms of ratings of medication strength (Table), wake time after sleep onset (WASO, Table) and total sleep time (TST, Table). Differences from placebo on all of these measures remained significant throughout the 6-months of treatment (P<0.0001). No worsening from baseline was found on non-pill nights for WASO (months 1-6) or TST (months 2-6), or on the 3 nights following discontinuation at the end. Mean weekly zolpidem extended-release tablet intake was stable (4.9-5.2 tablets/week; Figure).

Conclusions: There was no evidence of dependence to zolpidem extended-release 12.5 mg during 6 months of treatment: 1) tolerance did not occur; 2) there was no rebound insomnia; and 3) pill-taking did not increase over time. These findings support the feasibility of a long-term “as needed” pharmacotherapy strategy for chronic insomnia treatment.

References:

NR586 Tuesday, May 22, 3:00 PM - 5:00 PM
Sustained Efficacy and Improvements in Patient-Reported Next-Day Functioning Following Administration of Zolpidem Extended-Release 12.5 mg Taken “As Needed” 3-7 Nights Per Week for 6 Months
Andrew Krystal Duke University Medical Center, Psychiatry, Box 3309, Duke University Medical Center, Durham, NC, 27710, 9000, Milton Erman, Gary Zammit, Christina Soubrane, Thomas Roth

Educational Objectives:
At the conclusion of the presentation, the participant should be able to evaluate the long-term effects of zolpidem extended-release on subjective sleep measures and reported ability to function in the morning in patients with primary insomnia.

Summary:
Purpose: To measure the long-term (6-month) efficacy of zolpidem extended-release 12.5 mg at improving sleep onset and sleep maintenance symptoms and reported morning function in patients with chronic primary insomnia.

Methods: In this double-blind, randomized, placebo-controlled, multicenter study, adults (18-64 years; n=1025) with chronic primary insomnia were randomized to either zolpidem extended-release 12.5 mg or placebo treatment taken “as needed” 3-7 nights/week for 6 months. Efficacy was assessed every 4th treatment week by patient and clinician Global Impression scales of sleep continuity and treatment response, and by daily morning questionnaires assessing multiple sleep measures, including morning sleepiness and ability to concentrate upon awakening.

Results: Completers were comprised of 436/674 (64.7%) zolpidem extended-release- and 184/351 (52.4%) placebo-treated patients. Compared with placebo, zolpidem extended-release treatment resulted in significant, sustained improvements in the following measures: patients’ impression of treatment aid to sleep and time to sleep onset, clinician impression of improvements in insomnia severity (from baseline assessment) (Table), and total sleep time and wake time after sleep onset (derived from morning diary) throughout the 6-month study (P<0.0001, for each month, for each measure). Zolpidem extended-release-treated patients also reported sustained and significant improvement in morning ratings of ability to concentrate (Figure) and morning sleepiness (P<0.0001 versus placebo for each month). The most frequent adverse events were headache (zolpidem extended-release 10.5% vs placebo 9.5%), anxiety (6.3% vs 2.6%) and somnolence (5.7% vs 2.0%).

Conclusions: These findings provide the strongest support to date for the utility of long-term “as needed” insomnia pharmacotherapy. They also establish the efficacy of “as needed” 6-month dosing of zolpidem extended-release 12.5 mg, in terms of sustained and significant improvements in sleep onset and sleep maintenance symptoms, as well as improved next-day concentration and reduced morning sleepiness.
NR587  Tuesday, May 22, 3:00 PM - 5:00 PM
Effects of Eszopiclone/Fluoxetine Co-therapy on the Percentage of Patients Experiencing Coincident Resolution of Both Insomnia and Depression in Patients with Insomnia Co-existing with Major Depressive Disorder
Andrew Krystal, M.D. Duke University Medical Center, Department of Psychiatry and Behavioral Sciences, Trent Drive Box 3309, Durham, NC, 27710, 9000, Jack Edinger, Ph.D., Colleen Carney, Ph.D., David Amato, Ph.D., Kendyl Schaefer, M.S., Robert Rubens, M.D., Maurizio Fava, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to determine the effects of eszopiclone/fluoxetine co-therapy on coincident resolution of insomnia and depression relative to fluoxetine monotherapy.

Summary:
Introduction: In a study of insomnia co-existing with major depressive disorder (MDD), eszopiclone/fluoxetine co-therapy improved insomnia and depression compared with placebo/fluoxetine. This report we re-analyze data from that study to determine the effects of co-therapy on the likelihood of patients showing resolution of both insomnia and MDD symptoms.

Methods: Patients meeting DSM-IV criteria for both MDD and insomnia received fluoxetine and were randomized to nightly eszopiclone 3mg (ESZ+FLX; n=270) or placebo (PBO+FLX; n=275) for 8 weeks. Insomnia severity was assessed using the ISI; depression was assessed using the HAM-D. For both instruments, response was defined as at least a 50% reduction from baseline at Week 8 and remission was defined as a total score of ≤7 at Week 8.

Results: Eszopiclone co-therapy significantly increased the likelihood of meeting both insomnia and depression response and remission criteria relative to fluoxetine monotherapy. Few patients in either treatment group experienced response or remission of only ISI or only HAM-D (≤25%).

Conclusion: The results of this analysis demonstrate that eszopiclone/fluoxetine co-therapy improved measures of both insomnia (ISI) and MDD (HAM-D) relative to fluoxetine monotherapy and their joint improvement was related.

References:

NR588  Tuesday, May 22, 3:00 PM - 5:00 PM
Impact of Four Weeks’ Insomnia Treatment on Health-Related Quality of Life in Primary Insomnia and Insomnia Co-morbid with Major Depressive Disorder or Rheumatoid Arthritis
W. Vaughn McCaill, M.D. Wake Forest University, Department of Psychiatry and Behavioral Medicine, Medical Center

NR589  Tuesday, May 22, 3:00 PM - 5:00 PM
An Analysis of 3.5mg vs. 1.75mg Sublingual Zolpidem Tartrate: Optimal Efficacy and Safety with 3.5mg in Adults With Middle-Of-The-Night (MOTN) Insomnia
Bradley D. Vince, D.O. Vince and Associates Clinical Research, 6600 College Blvd #330, Overland Park, KS, 66221, 9000, Tom Roth, Ph.D., Martin Scharf, Ph.D., Steven Hull, M.D., Nikhil Singh, Ph.D., Yu Ping Maguire, Ph.D.

Educational Objectives:
At the end of this presentation, the participant should be aware that a new formulation of zolpidem shows promise for an under-treated patient population - insomnia patients experiencing prolonged middle-of-the-night awakenings.

Summary:
Introduction: There are no hypnotics currently approved for use on a prn basis to treat prolonged awakenings in the Middle-Of-The-Night (MOTN). This polysomnography (PSG) study evaluated the efficacy and safety of sublingual transmucosal (ST) zolpidem
1.75 and 3.5 mg in adults with MOTN insomnia utilizing a planned MOTN awakening.

Methods: Non-elderly adults (N=83) with a diagnosis of DSM-IV-TM primary insomnia and a history of prolonged MOTN awakenings were evaluated in this randomized, double-blind, placebo-controlled, 3-way crossover study of 2 consecutive nights of dosing with placebo or low dose ST zolpidem. Four hours after initial lights out patients were awakened for 30 minutes, and after dosing were allowed 4 additional hours in bed. Sleep parameters were measured by PSG and by patient report.

Results: ST zolpidem significantly reduced Latency to Persistent Sleep after the planned MOTN awakening (LPSMOTN) as measured by PSG and as indicated by subject report of Latency to Sleep Onset (LSOMOTN) (both ps<0.001). The LPSMOTN adjusted means were 9.6 and 16.8 minutes respectively with ST zolpidem 3.5 mg and 1.75mg, as compared to 28.1 minutes with placebo (p<0.001 for 3.5mg vs. 1.75mg). PSG measured Total Sleep Time (TSTMOTN) and Sleep Efficiency (SEMOTN), as well as subjective Total Sleep Time (sTSTMOTN) and Sleep Quality were all significantly improved with both active ST zolpidem doses (ps<0.001). Only 3.5mg ST zolpidem showed significantly increased TST and decreased wake time in the second hour post-dose, which was independent of LPS improvements. Adverse events were comparable to placebo for both dose strengths.

Conclusions: In adults with insomnia characterized by MOTN awakening, low-dose 3.5mg ST zolpidem was well tolerated and more effective than 1.75mg at reducing sleep onset and increasing sleep duration, and demonstrates an optimal benefit-risk profile in this population.

Funding: This study was fully funded and supported by TransOral Pharmaceuticals, Richmond, CA

References:

NR590 Tuesday, May 22, 3:00 PM - 5:00 PM
Efficacy and Tolerability of Gaboxadol in Adults with Primary Insomnia: a 3-month, Randomized, Double-blind, Placebo-controlled Trial

Thomas Roth, Ph.D. Henry Ford Hospital, Sleep Disorders Research Center, 2799 West Grand Boulevard, CFP3, Detroit, MI, 48202, 9000, Donald Anderson, M.D., Yan-Ping Zheng, M.D., Kristel Vandormael, Ph.D., Andrew Smith, M.S., Michael Li, B.S., Donna DiGravio, M.S.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand: a) the utility of a model of transient insomnia for assessing the hypnotic efficacy of new treatments; b) clinical data relating to the efficacy and tolerability of gaboxadol, the first in a new class of hypnotic agents, in a model of transient insomnia.

Summary:
Introduction: Gaboxadol is a selective extrasynaptic GABA\textsubscript{A} agonist (SEGA) with demonstrated improvements in sleep maintenance and onset measures in preliminary studies in insomnia patients. This study evaluated gaboxadol in a model of transient insomnia.

Methods: Healthy subjects (18-64y) completed a randomized, double-blind, parallel-group study in which the sleep period was advanced 4h from habitual sleep time. Polysomnographic (PSG) and self-reported sleep measures were used to compare gaboxadol 10mg (N=271) and 15mg (N=274) versus placebo (N=277). Results: In the placebo group, the phase-advance procedure resulted in disrupted sleep maintenance and onset measures in short-duration preliminary studies. This study evaluated the efficacy and tolerability of 2 doses of gaboxadol over 3 months of treatment in adults with primary insomnia.

Methods: Adults 18-64 years of age with DSM-IV primary insomnia entered a randomized, double-blind, parallel-group, patient report study in which they were randomized to receive gaboxadol 15mg (N=308), gaboxadol 10mg (N=310), or placebo (N=309) every night for 3 months. Efficacy measures were recorded daily by patients using electronic diaries. Tolerability was assessed by adverse event reports and other safety measures.

Results: Gaboxadol 15mg improved patient-reported total sleep time (sTST) and time to sleep onset (sTSO) versus placebo over 3 months. The estimated mean change from baseline improvement in sTST at month 3 was 87.6min for gaboxadol 15mg and 67.2min for placebo; the estimated difference between gaboxadol 15mg and placebo was approximately 20min (p<0.01). The estimated mean change from baseline reduction in sTSO at month 3 was 44.2min for gaboxadol 15mg and 34.4min for placebo; the estimated difference between gaboxadol 15mg and placebo was approximately 10min (p<0.01) Gaboxadol 10mg did not differ significantly from placebo on these measures at month 3. Gaboxadol was generally well-tolerated over 3 months.

Conclusion: Gaboxadol 15mg, but not 10mg, was effective at improving sleep maintenance and onset over 3 months in adults with primary insomnia. Both gaboxadol doses were generally well-tolerated.

Funding: Merck Research Laboratories

References:

NR591 Tuesday, May 22, 3:00 PM - 5:00 PM
Gaboxadol Improves Sleep Maintenance and Onset in a Model of Transient Insomnia: Results from a Randomized Clinical Trial

James Walsh, Ph.D. St. Johns and St. Lukes Hospitals, Sleep Medicine, Sleep Medicine and Research Center, 232 S. Woods Mill Road, Chesterfield, MO, 63017, 9000, David Mayleben, M.D., Christine Guico-Pabla, M.D., Kristel Vandormael, Ph.D., Rebecca Martinez, B.S., Steve Deacon, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand: a) the utility of a model of transient insomnia for assessing the hypnotic efficacy of new treatments; b) clinical data relating to the efficacy and tolerability of gaboxadol, the first in a new class of hypnotic agents, in a model of transient insomnia.

Summary:
Introduction: Gaboxadol is a selective extrasynaptic GABA\textsubscript{A} agonist (SEGA) with demonstrated improvements in sleep maintenance and onset measures in preliminary studies in insomnia patients. This study evaluated gaboxadol in a model of transient insomnia.

Methods: Healthy subjects (18-64y) completed a randomized, double-blind, parallel-group study in which the sleep period was advanced 4h from habitual sleep time. Polysomnographic (PSG) and self-reported sleep measures were used to compare gaboxadol 10mg (N=271) and 15mg (N=274) versus placebo (N=277). Results: In the placebo group, the phase-advance procedure resulted in disrupted sleep maintenance and onset measures in short-duration preliminary studies. This study evaluated the efficacy and tolerability of 2 doses of gaboxadol over 3 months of treatment in adults with primary insomnia.

Methods: Adults 18-64 years of age with DSM-IV primary insomnia entered a randomized, double-blind, parallel-group, patient report study in which they were randomized to receive gaboxadol 15mg (N=308), gaboxadol 10mg (N=310), or placebo (N=309) every night for 3 months. Efficacy measures were recorded daily by patients using electronic diaries. Tolerability was assessed by adverse event reports and other safety measures.

Results: Gaboxadol 15mg improved patient-reported total sleep time (sTST) and time to sleep onset (sTSO) versus placebo over 3 months. The estimated mean change from baseline improvement in sTST at month 3 was 87.6min for gaboxadol 15mg and 67.2min for placebo; the estimated difference between gaboxadol 15mg and placebo was approximately 20min (p<0.01). The estimated mean change from baseline reduction in sTSO at month 3 was 44.2min for gaboxadol 15mg and 34.4min for placebo; the estimated difference between gaboxadol 15mg and placebo was approximately 10min (p<0.01) Gaboxadol 10mg did not differ significantly from placebo on these measures at month 3. Gaboxadol was generally well-tolerated over 3 months.

Conclusion: Gaboxadol 15mg, but not 10mg, was effective at improving sleep maintenance and onset over 3 months in adults with primary insomnia. Both gaboxadol doses were generally well-tolerated.

Funding: Merck Research Laboratories

References:
Boxadol 15mg also reduced mean LPS compared to placebo (15.7min versus 19.4min, p<0.01) and both 10mg and 15mg reduced mean nTSO (19.0 and 17.0min versus 23.0min) compared to placebo (p<0.01). PSG and self-reported total sleep time as well as ratings of sleep quality were improved with both gaboxadol doses relative to placebo (all p<0.01). The amount of slow-wave sleep was greater with both doses of gaboxadol than with placebo (p<0.001). No group differences in the amount of rapid-eye-movement sleep were found. Most PSG and self-report measures suggested a possible dose-response. The percentage of subjects with ≥1 adverse event was low (<10% in any treatment group); events were mild/moderate, none were serious, and gaboxadol did not impact morning gait or coordination.

**Conclusion:** Gaboxadol 10mg and 15mg were efficacious in reducing the sleep maintenance and onset disruption produced by this model of transient insomnia, with beneficial effects generally being most pronounced for the 15mg dose.

**Funding:** Merck Research Laboratories

**References:**

**NR592**

**Tuesday, May 22, 3:00 PM - 5:00 PM**

**Polysomnography Outcomes Confirm An Optimal Pharmacokinetic and Pharmacodynamic Profile of Sublingual Zolpidem Tartrate for Treating Middle-Of-The-Night (MOTN) Insomnia**

Bradley D. Vince, D.O. VInce and Associates Clinical Research, -, 10103 Metcalf, Ste. 300, Overland Park, KS, 66212, 9000, Tom Roth, Ph.D., Martin B. Scharf, Ph.D., Steven Hull, M.D., Nikhilish Singh, Ph.D., Yu Ping Maguire, Ph.D.

**Educational Objectives:**
- At the end of this presentation, the participant should be aware that a new, low-dose formulation of zolpidem induces sleep more rapidly than the currently marketed version without producing next-day sedation following middle-of-the-night dosing

**Summary:**
**Introduction:** Individuals with insomnia characterized by middle-of-the-night (MOTN) awakenings and difficulty returning to sleep have no treatment option approved for dosing on a prn basis following a nighttime awakening. A low dose of sublingual transmucosal (ST) zolpidem was evaluated using performance assays after daytime administration and was compared to PSG defined assays with nocturnal administration.

**Methods:** Healthy adults (N=24) participated in a double-blind, placebo-controlled, crossover study of morning dosing with placebo, 1.75 and 3.5 mg ST zolpidem. PD endpoints and PK assessments were evaluated on Day 1 and 2 respectively.

A double-blind, placebo-controlled, 3-way crossover PSG study, assessed the same doses in adult insomniacs (N=83).

**Results:** ST zolpidem Cmax and AUC were dose-proportional, and Tmax was 37.9 minutes for both doses. Within 20 minutes post-dose, both 1.75mg and 3.5mg achieved plasma zolpidem levels greater than 20 to 25 ng/ml, the estimated levels for onset of sleep. Significant changes in Digit Symbol Substitution Test scores were evident from 20 minutes after dosing (3.5 mg: p=0.001, 1.75 mg: p=0.013), lasting 1.5 hours post-dose.

In the PSG study 75.0%, 56.1% and 28.4% of patients on 3.5mg, 1.75mg and placebo respectively had sleep onset (LPSMOTN) <20 minutes after lights-out (p<0.001 for both doses). No residual sedation was observed 4.5 hours post-dose.

**Conclusions:** ST zolpidem has a dose and Tmax of about one third of the approved dose of oral zolpidem in adults. Sedative effects peak at 20 minutes, and wane by 2 hours post-dose. When administered after nighttime awakening with more than 4 hours of sleep remaining, rapid sleep onset and duration without next-day somnolence was confirmed. This unique combination of rapid onset of action and lack of residual effects, suggests ST zolpidem is well suited for individuals with MOTN insomnia.

**Funding:** This study was fully funded and supported by TransOral Pharmaceuticals, Richmond, CA

**References:**

**NR593**

**Tuesday, May 22, 3:00 PM - 5:00 PM**

**Efficacy and Safety of Doxepin 3 and 6 mg in Adults with Primary Insomnia**

Alan Lankford, Ph.D. Sleep Disorders Center of Georgia, Sleep Research, 5505 Peachtree Dunwoody Road, Suite 380, Atlanta, GA, 30342, 9000, Steven Hull, M.D., Martin B. Scharf, Ph.D., Howard Schwartz, M.D., Philip Jochelson, M.D., Roberta Rogowski, B.S.N., Thomas Roth, Ph.D.

**Educational Objectives:**
- At the end of this presentation, the participant should be able to evaluate the safety and efficacy of 3 and 6 mg of doxepin on measures of sleep for the treatment of adults with chronic primary insomnia.

**Summary:**
**Introduction:** The efficacy and safety of doxepin (DXP) 3 and 6mg were evaluated in adults with primary insomnia.

**Methods:** This was a randomized, double-blind, placebo-controlled study of adults with insomnia. Subjects reported ≥3 months of DSM-IV-TR primary insomnia, with confirmation by polysomnography (PSG). Subjects were randomly assigned to nightly doses of placebo (POO; N=73), DXP 3mg (N=75) or DXP 6mg (N=73) for 35 days. Efficacy was evaluated objectively (PSG) and subjectively; data from the first and last PSG assessment points, nights 1 (N1) and 29 (N29), are reported. DXP endpoints included wake-after-sleep-onset (WASO), latency-to-persistent-sleep (LPS), and sleep efficiency (SE; overall and by third-of-the-night).

**Primary endpoint was N1 WASO.**

**Results:** Compared with PBO, DXP 3 and 6mg statistically significantly improved WASO at N1 (p<0.0001) and N29 (3mg p=0.0299; 6mg p=0.0012), LPS at N1 (3mg p=0.0110; 6mg p=0.0018), and overall SE at N1 (p<0.0001) and N29 (3mg p=0.0262; 6mg p=0.0003). The significant differences on N1 LPS were not observed on N29, primarily due to PBO improvement. DXP 3 and 6mg generally demonstrated statistically significant improvements in SE by third-of-the-night on N1 and N29. There were no significant group differences in next-day residual sedation, incidence of adverse events was similar between groups, and sleep architecture was generally preserved.

**Conclusions:** In adults with insomnia, DXP 3 and 6mg were well-tolerated and produced significant improvement on the primary endpoint WASO and on multiple secondary endpoints on N1; these improvements were maintained on N29 for sleep mainte-
nance and duration endpoints. On sleep onset, there was significant improvement in LPS at N1 with no loss of drug effect at N29, though statistical significance was not maintained. Additionally, the incidence of adverse events was comparable to PBO; there were no reports of amnesia, no reports of anti-cholinergic effects, and no significant hangover/next-day residual effects.

References:

NR594 Tuesday, May 22, 3:00 PM - 5:00 PM
Efficacy and Safety of Doxepin 6 mg in a Model of Transient Insomnia
Howard Schwartz, M.D. Miami Research Associates, Sleep Research, 7500 Southwest 87th Avenue, Suite 202, Miami, FL, 33173, 9000, Steven Hull, M.D., David Seiden, M.D., Roberta Rogowski, B.S.N., Philip Jochelson, M.D., Elizabeth Ludington, Ph.D., Thomas Roth, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to evaluate the safety and efficacy of 6mg of doxepin on measures of sleep for the treatment transient insomnia in healthy adults.

Summary:
Introduction: The efficacy of doxepin (DXP) 6mg tablets was evaluated in healthy adults using a model of transient insomnia.

Methods: This was a randomized, double-blind, parallel-group, placebo-controlled study in healthy adults using a model of transient insomnia. The insomnia model incorporated a phase advance in combination with the First Night Effect. Subjects received a single nighttime dose of placebo (PBO; N=282) or DXP 6mg (N=283) in a sleep lab. Efficacy was evaluated objectively (polysomnography; PSG) and subjectively (morning questionnaire). Primary endpoint was latency to persistent sleep (LPS); secondary PSG endpoints included wake-after-sleep-onset (WASO), total sleep time (TST), wake time after sleep (WTAS) and sleep efficiency (SE; overall, by third-of-the-night and hourly); secondary subjective endpoints included latency to sleep onset (LSO), subjective WASO (sWASO), subjective TST (sTST) and sleep quality. Results: DXP 6mg statistically significantly improved LPS (13 minute improvement versus PBO; p<0.0001), WASO (39 minute improvement versus PBO; p<0.0001), TST (51 minute improvement versus PBO; p<0.0001), WTAS (p<0.0001), overall SE (p<0.0001), SE in each third-of-the-night (p<0.0001) and SE in all eight hours (p<0.0003), all versus PBO. Additionally, DXP 6mg statistically significantly improved subjective variables including LSO (16 minute improvement versus PBO; p<0.0001), sWASO (p=0.0063), sTST (p<0.0001), and sleep quality (p=0.0004), all versus PBO. There were no clinically meaningful effects on measures of next-day residual sedation, and sleep architecture was generally preserved. Incidence of adverse events was comparable to placebo.

Conclusions: In this model of transient insomnia, DXP 6mg demonstrated significant improvements in sleep onset, sleep maintenance, sleep duration and sleep quality. These data suggest that doxepin 6mg may improve sleep impairment in adults with transient insomnia.

References:

NR595 Tuesday, May 22, 3:00 PM - 5:00 PM
Adults With Middle-Of-The-Night (MOTN) Insomnia Are Able To Accurately Self-Identify Their Condition
Bradley D. Vince, D.O. Vince and Associates Clinical Research, - , 10103 Meitcaif, Ste. 330, Overland Park, KS, 66212, 9000, Tom Roth, Ph.D., Martin B. Scharf, Ph.D., Steven Hull, M.D., Nikhilsh Singh, Ph.D., Yu Ping Maguire, Ph.D.

Educational Objectives:
At the end of this presentation, the participant should be aware that subjective patient reports of middle-of-the-night insomnia appear to be a valid diagnostic tool as they appear to be strongly correlated with objective PSG recordings.

Summary:
Introduction: Middle-of-the-night (MOTN) awakenings with difficulty returning to sleep is a well recognized manifestation of insomnia. However, insufficient attention has been paid to this form of insomnia, in part due to the absence of rapidly effective, prn therapies that can be taken during the night without next-day residual sedation. This study evaluated the reporting accuracy of subjects in self-identification and characterization of MOTN insomnia relative to PSG screening.

Methods: Adults (N=113) with a diagnosis of DSM IV primary insomnia and a history of prolonged MOTN awakenings. Subjects completed a 10-day sleep diary to confirm MOTN insomnia before undergoing 2 nights of polysomnography (PSG) screening. In order to pass the sleep diary screen, individuals had to indicate that they experienced at least 3 MOTN awakenings per week with Latency to Sleep Onset (LSO) of >30 minutes per awakening. PSG entry criteria required a mean of >20 minutes Latency to Persistent Sleep (LPS) for two successive nights. Using sleep diary data in conjunction with subsequent single-blind placebo PSG assessments of sleep, the relationship between subjective self-reporting and objective PSG assessments was explored.

Results: A total of 113 subjects identified themselves as having MOTN insomnia that met the study LSO entry criteria. This self-diagnosis was subsequently confirmed for 83 (73%) subjects who during 2-nights of PSG evaluation had mean LPS values of 54.6 minutes (SE 3.7).

Conclusions: MOTN insomnia can be diagnosed with a relatively high degree of accuracy using subject sleep diaries. This study indicates that individuals can correctly self-identify their MOTN insomnia, and sleep diaries can be reliable tools to assist clinicians with the diagnosis of MOTN insomnia.

Funding Source: This study was fully funded and supported by TransOral Pharmaceuticals, Richmond, CA.

References:
NR596  Tuesday, May 22, 3:00 PM - 5:00 PM
Patient and Physician-Reported Improvements with Ropinirole CR in RLS
June M. Fry, M.D. Center for Sleep Medicine, Center for Sleep Medicine, 443 Germantown Pike, Lafayette Hill, PA, 19444, 9000, Ronald B. Ziman, M.D., Nancy L. Earl, M.D.

**Educational Objectives:**
At the conclusion of this presentation, the participant should be able to understand the effect of treatment with a novel extended-release formulation - ropinirole CR - in patients with moderate-to-severe primary Restless Legs Syndrome (RLS), as assessed by patient- and physician-reported measures.

**Summary:**

**Introduction:** RLS is a neurological disorder characterized by an irresistible urge to move the legs, with a negative impact on patients' lives. Many patients with RLS experience symptoms that begin in the late afternoon/early evening and continue throughout the night, and may benefit from once-daily extended-duration treatment.

**Methods:** Patients with moderate-to-severe primary RLS experiencing symptoms in the evening and nighttime were randomized to ropinirole CR (n=189), 0.5-6 mg/day, or placebo (n=195), titrated as needed and tolerated, taken once daily (≥4pm) 1-2 hours before usual onset of RLS symptoms in a 12-week pivotal study (protocol 101468/205). Primary endpoint: mean change from baseline in IRLS total score at Week 12 LOCF. Additional endpoints included: proportion of responders (rated 'very much improved' or 'much improved') on the Clinical Global Impression - Improvement (CGI-I) scale at Week 12 LOCF and patient-rated assessment of change on the Patient Global Improvement (PGI) scale at Days 2-4. Patient satisfaction with treatment was also captured at Week 12 LOCF.

**Results:** At Week 12 LOCF, mean change in IRLS total score was significantly greater (improved) for ropinirole CR vs. placebo (adjusted mean treatment difference: -5.9; p<0.001). The proportion of CGI-I scale responders was significantly greater for ropinirole CR vs. placebo at Week 12 LOCF (79% vs. 50%; adjusted odds ratio: 4.6; p<0.001). Significantly greater proportions of PGI scale responders were observed for ropinirole CR vs. placebo on Days 2 (30% vs. 12%), 3 (35% vs. 18%), and 4 (42% vs. 24%); all p<0.001. At Week 12 LOCF, more patients receiving ropinirole CR vs. placebo reported being 'very satisfied' (56% vs. 34%) or 'satisfied' (23% vs. 17%) with treatment (not tested).

**Conclusions:** Ropinirole CR significantly improves RLS symptoms and is associated with patient- and clinician-reported improvements, as well as higher satisfaction with treatment, compared with placebo.

**STUDY SUPPORTED BY:** GlaxoSmithKline R&D.

**References:**

NR598  Tuesday, May 22, 3:00 PM - 5:00 PM
Ropinirole CR Significantly Improves Quality of Life in Patients with RLS
Ronald B. Ziman, M.D. Northridge Neurological Center, Northridge Neurological Center, 18433 Roscoe Blvd, Ste 210, Northridge, CA, 91325, 9000, Michael O. Calloway, Ph.D.

**Educational Objectives:**
At the conclusion of this presentation, the participant should be able to describe the efficacy and tolerability of ropinirole CR, a new extended-release formulation for the treatment of moderate-to-severe primary Restless Legs Syndrome (RLS). Efficacy was assessed by the International Restless Legs Scale (IRLS) and the Clinical Global Impression - Improvement (CGI-I) scale score in patients with RLS. Tolerability and safety were assessed by adverse event (AE) reporting, vital signs, and discontinuations.

**Summary:**

**Introduction:** RLS is a neurological disorder characterized by an urge to move the legs, with a prevalence of 5-10% in the general population. Many patients with RLS experience symptoms occurring in the late afternoon/early evening that continue through the night, and may benefit from once-daily extended-release treatment.

**Methods:** In a 12-week pivotal study (protocol 101468/205), patients with moderate-to-severe primary RLS experiencing symptoms in the evening and throughout the night were randomized to ropinirole CR (n=189), 0.5-6 mg/day, or placebo (n=195), titrated as needed and tolerated, taken once daily (≥4pm), 1-2 hours before usual onset of RLS symptoms. Primary endpoint: mean change from baseline in IRLS total score at Week 12 LOCF. Secondary endpoints included the proportion of responders (rated 'very much improved' or 'much improved') on the CGI-I scale at Week 12 LOCF. Safety and tolerability were assessed by AE reporting, vital signs, and discontinuations.

**Results:** At Week 12 LOCF, mean (SD) doses of ropinirole CR and placebo were 2.5 (1.9) and 3.8 (2.1) mg/day, respectively. Mean change from baseline in IRLS total score at Week 12 LOCF was significantly greater (improved) for ropinirole CR vs. placebo (adjusted mean treatment difference: -5.9; p<0.001). The proportion of CGI-I scale responders was significantly greater for ropinirole CR at Week 12 LOCF (adjusted odds ratio: 4.6; p<0.001). The three most frequent AEs were nausea (28% vs. 7%), headache (20% vs. 18%), and somnolence (9% vs. 6%) in the ropinirole CR vs. placebo groups, respectively. AEs leading to withdrawal were reported by 7/189 (4%) and 5/195 (3%) of ropinirole CR and placebo patients, respectively.

**Conclusions:** Ropinirole CR treatment significantly improves RLS symptoms and is generally well tolerated when given once-daily for late afternoon/early evening and nighttime treatment cov- erage in patients with moderate-to-severe primary RLS.

**Study Supported by:** GlaxoSmithKline R&D.

**References:**
release formulation treatment, on HRQoL and daily functioning, compared with placebo, in patients with moderate-to-severe primary RLS.

Summary:

Introduction: RLS can have a significant negative impact on patients' HRQoL, who report a disease burden similar to that of other chronic medical conditions such as type-2 diabetes and clinical depression. Although some patients experience symptoms only at night, many also experience RLS symptoms beginning in the late afternoon/early evening and continuing throughout the night. A once-daily, extended-duration formulation of ropinirole was developed to provide coverage of evening and nighttime symptoms in patients with RLS.

Methods: Patients with moderate-to-severe primary RLS experiencing symptoms in the late afternoon/early evening and throughout the night, were randomized to ropinirole CR (n=189), 0.5-6 mg/day, or placebo (n=185) titrated as needed and tolerated, taken once daily (≥4pm), 1-2 hours before onset of usual RLS symptoms in a 12-week pivotal study (protocol 101468/205). The primary endpoint was mean change from baseline in International Restless Legs Scale (IRLS) total score at Week 12 LOCF. Secondary endpoints included assessment of HRQoL using the patient-reported Overall Life Impact score on the disease-specific Restless Legs Syndrome Questionnaire (RLS-QoL) Questionnaire and the non-disease-specific Short-Form-36 (SF-36) Health Survey.

Results: Ropinirole CR significantly reduced (improved) mean IRLS total score at Week 12 LOCF compared with placebo (adjusted mean treatment difference [AMTD]: -5.9; p<0.001). A significantly greater improvement from baseline in mean RLSQoL score was seen for ropinirole CR, compared with placebo, at Week 12 LOCF (AMTD: 9.2; p<0.001). In addition, a greater improvement favoring ropinirole CR vs. placebo was also seen in all domains of the SF-36 health survey at Week 12 LOCF (not tested).

Conclusions: Ropinirole CR treatment reduces RLS symptoms compared with placebo and significantly improves HRQoL, as measured by disease- and non-disease-specific measures of well-being and daily functioning, in patients with moderate-to-severe primary RLS.

STUDY SUPPORTED BY: GlaxoSmithKline R&D.

References:

NR599 Tuesday, May 22, 3:00 PM - 5:00 PM
NG2-73, a Novel GABAA Partial Agonist, Rapidly Induced Sleep in a Transient Insomnia Study
Martin B. Scharf Tristate Sleep Disorders Center, Director, 1275 East Kemper Road, Cincinnati, OH, 45246, 9000

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand that NG2-73 is a new non-benzodiazepine GABA<sub>A</sub> agonist sedative hypnotic that has a different pharmacological profile compared to the other GABA<sub>A</sub> agonists and that this difference may differentiate it from other sleep agents. Participants will comprehend the nature of the transient insomnia model of sleep onset insomnia, together with its limitations. Furthermore, they will understand the reduction in latency to persistent sleep resulting from the administration of NG2-73 in this model, and the subjective experiences of subjects as recorded in a next morning questionnaire.

Summary:

Introduction: The symptoms of RLS are often associated with sleep impairment. Many patients with moderate-to-severe RLS experience symptoms that present in the late afternoon/early evening and continue throughout the night, and may benefit from a once-daily, extended-duration treatment.

Methods: In a 12-week pivotal study (protocol 101468/205), patients with moderate-to-severe primary RLS experiencing evening and nighttime symptoms were randomized to receive ropinirole CR extended release (n=189), 0.5-6 mg/day, or placebo (n=195), titrated as needed and tolerated, taken once daily (>4pm), 1-2 hours before usual RLS symptom onset. Efficacy endpoints included: mean change from baseline in International Restless Legs Scale (RLS-QoL) at Week 12 LOCF (not tested), in addition, the participant should understand the potential benefits of treatment with a novel extended-release formulation of ropinirole CR, on core RLS symptoms and associated sleep disturbance in patients with moderate-to-severe primary RLS.

References:

NR600 Tuesday, May 22, 3:00 PM - 5:00 PM
Ropinirole CR Reduces Sleep Disturbance in RLS: Extended-Release Treatment
Philip M. Becker, M.D. Sleep Medicine Associates of Texas, 5477 Glen Lakes Drive, Suite 100, Dallas, TX, 75231, 9000, June M. Fry, M.D., Mary Castiglia, Pharm.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to describe the impact of Restless Legs Syndrome (RLS) on aspects of patients' sleep, including sleep adequacy and quantity. In addition, the participant should understand the potential beneficial effects of treatment with a novel extended-release formulation, ropinirole CR, on core RLS symptoms and associated sleep disturbance in patients with moderate-to-severe primary RLS.

Summary:

Methods: This double-blind, placebo-controlled, randomized, multi-center study was designed to determine the effects of 1,3, 10 and 20mg of NG2-73 compared to placebo on sleep onset as measured by Latency to Persistent Sleep (LPS) in healthy adults. The study design incorporated a single-night, polysomnography (PSG) model of transient insomnia using both first night sleep laboratory adaptation and "phase-advance" effects. Subjects were dosed in the sleep laboratory 2.5 hours prior to median habitual bedtime. "Lights off" and PSG recording started 30 minutes later. Safety was monitored by adverse event recording, physical exams, vital signs, ECG and clinical laboratory tests. 369 healthy subjects aged 24-63 with no self-reported sleep disorders were enrolled.

Results: LPS was statistically significantly reduced, compared to placebo, at all doses of NG2-73, and demonstrated a dose-response relationship. The mean times for LPS were 30.8 minutes for the Placebo group, and 17.8, 10.6, 7.8, and 6.6 minutes for the 1, 3, 10, and 20 mg NG2-73 groups, respectively. NG2-73 also had a statistically significant effect on Total Sleep Time and Sleep Efficiency at doses of 3mg and above. All doses had a significant effect on how refreshing subjects rated their sleep. NG2-73 was generally well tolerated with adverse events (AEs) primarily reflecting an extension of the drug's sedative effects, including sedation, somnolence and dizziness. There were no deaths, or drug-related serious AEs or discontinuations, and no clinically important changes in safety labs, vital signs or ECGs.

Conclusions: In this study, NG2-73 was shown to be a potent, well-tolerated, sedative hypnotic that significantly reduced time to onset of persistent sleep versus placebo at all doses tested.

References:
Legs Scale (IRLS) total score (primary endpoint), change in each of the four domains assessed by the patient-completed Medical Outcomes Study (MOS) Sleep Scale, and the proportion of subjects rated 4, 5, or 6 (‘fairly clear-headed’, ‘alert’, or ‘very alert’) on the patient-completed subject morning alertness question from the St. Mary’s Hospital (SMH) sleep questionnaire (all at Week 12 LOCF).

Results: Mean (SD) doses for ropinirole CR and placebo at Week 12 LOCF were 2.5 (1.9) and 3.8 (2.1) mg/day, respectively. Mean change in IRLS total score at Week 12 LOCF was significantly greater (improved) for ropinirole CR vs. placebo treatment (adjusted mean treatment difference [AMTD]: -5.9; p<0.001). Significantly greater improvements were also seen with ropinirole CR vs. placebo for the MOS Sleep Scale domains of sleep disturbance, daytime somnolence, sleep adequacy (AMTDs: -13.0; -7.9; 12.0, respectively; all p<0.001), and sleep quantity (AMTD: 0.31; p<0.05) at Week 12 LOCF. At Week 12 LOCF, more subjects taking ropinirole CR vs. placebo were ‘fairly clear-headed’, ‘alert’, or ‘very alert’ according to the SMH sleep questionnaire (74% vs. 65%; not tested).

Conclusions: Ropinirole CR significantly improves core RLS symptoms and reduces associated sleep disturbance in patients with moderate-to-severe primary RLS.

Study Supported by: GlaxoSmithKline R&D.

References:

Quality of Sleep and Quality of Life in the Haemodialysis Patients

Kyuong-Kyu Lee, M.D. Dankook University Hospital, Psychiatry, 29 Anseodong, Cheonan, 330-714, 5800, Young-Hyon Park, M.D., Ki-Chung Paik, M.D., Woo-chul Lee, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to demonstrate lower quality of life is common in the haemodialysis patients with chronic renal failure and is associated with lower subjective quality of life.

Summary:
Objectives: Sleep problems are very common in hemodialysis patients with chronic renal failure (CRF). The objectives of this study were to examine the prevalence of low sleep quality and the relations between quality of sleep and quality of life in hemodialytic patients with CRF.

Method: We measured quality of sleep by the Pittsburgh Sleep Quality Index (PSQI), quality of life by the 36-item Short-form Healthy Survey (SF-36), anxiety by the Beck Anxiety Inventory (BAI), and depression by the Beck Depression Inventory (BDI) in 92 hemodialysis patients (52 male and 40 female).

Results: In the SF-36 subscales, physical functioning was negatively correlated with age, BDI, BAI, and PSQI total, sleep onset latency, sleep efficiency, sleep disturbance, use of sleep medication and daytime dysfunction. Bodily pain was positively correlated with BDI, BAI, PSQI total, subjective sleep quality, sleep onset latency, sleep disturbance, use of sleep medication, daytime dysfunction, and time on dialysis. But the other subscales of SF-36 were not correlated significantly with PSQI total score. Sixty two (69.66%) subjects were ‘poor sleepers’ (global PSQI>5). Subjects with ‘poor sleepers’ showed higher scores of anxiety and depression, and showed lower scores of physical functioning, role-physical, and bodily pain in quality of life than ‘good sleepers’ (global PSQI<5).

Conclusion: The results of presenting study suggest that lower quality of sleep is common in hemodialysis patients with CRF and is related to lower subjective quality of life. So, we could conclude that the correction of sleep disturbance may be helpful to the hemodialysis patients with CRF who have sleep disturbance.

References:
NR603 Tuesday, May 22, 3:00 PM - 5:00 PM
Efficacy and Tolerability of Gaboxadol in Elderly Patients with Chronic Primary Insomnia: A 4-Week, Double-Blind, Placebo-Controlled Outpatient Study

Jan Hedner Sahlgrenska University Hospital, The Sleep Laboratory, Pulmonary Medicine, Bruna Stråket 1, Göteborg, 413 45, 4010, Henrik Loft, Goeran Hajak, Jonas Lundahl, Kirsten Hedegaard, Henrik Knoth, Richard Torstenson

Educational Objectives:
- The participant will obtain knowledge on the efficacy and tolerability of Gaboxadol in elderly patients suffering from chronic insomnia.

Summary:
Objective: Gaboxadol, a selective extrasynaptic GABA_A agonist (SEGA), has demonstrated hypnotic efficacy in short-term studies in patients with primary insomnia. This study evaluated the efficacy and safety of gaboxadol during 4-weeks of treatment in elderly insomnia patients.

Methods: Patients aged 64-91y (N=539; 62% female) met DSM-IV criteria for primary insomnia, and reported subjective Time to Sleep Onset (sTSO) ≥45min as well as subjective Total Sleep Time (sTST) <6.0h for >4 nights/week. Following a 1-week, single-blind, placebo run-in period, patients were randomized to 4 weeks of double-blind treatment with gaboxadol 5mg, 10mg or placebo. Daily morning and evening diary data were analyzed as weekly means versus placebo using repeated-measures of observed cases (week 1 and 4 presented). Safety was assessed weekly and withdrawal symptoms were evaluated using the Tyrer scale.

Results: Both gaboxadol doses improved sTST (weeks 1 and 4, p<0.05), Wake After Sleep Onset (weeks 1 and 4, p<0.05, except week 1 for 5mg gaboxadol) and sTSO (weeks 1 and 4, p<0.05). Patients reported improved sleep quality (weeks 1 and 4, p<0.01) and felt more refreshed (weeks 1 and 4, p<0.01) in the morning and experienced more daytime energy (weeks 1 and 4, p<0.05). Gaboxadol was generally safe and well tolerated. The most frequently reported adverse events (>5%) following gaboxadol treatment were dizziness, headache and nausea with no apparent influence of dose level. The overall incidence of adverse events for both gaboxadol doses did not differ significantly from the placebo group. No withdrawal symptoms were detected after discontinuation of treatment.

Conclusion: In this 4-week study gaboxadol 5mg and 10mg improved patient reported sleep maintenance and induction. Patients felt more refreshed in the morning and reported improved energy during the day. Gaboxadol was generally safe, well tolerated and no withdrawal symptoms were detected in this elderly population of insomniacs.

References:
2. Lundahl J, Staner L, Staner C and Deacon S. Gaboxadol improves sleep maintenance and, in contrast to zolpidem, enhances slow wave sleep in adult patients with primary insomnia. Sleep 2006; 29: 720.

NR604 Tuesday, May 22, 3:00 PM - 5:00 PM
Placebo-Controlled, Double-Blind Trial Examining the Effects of Ramelteon vs Placebo with Zolpidem as a Reference on Balance in Older Adults After Middle-of-the-Night Awakening

Sherry Wang-Weligand, Ph.D. Takeda Global Research & Development Center, Clinical Research, One Takeda Parkway, Deerfield, IL, 60015, 9000, Gary Zammit, Ph.D., Xuejen Peng, Ph.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to describe middle-of-the-night performance on balance, mobility, and memory tasks in older adults with chronic insomnia following ramelteon or zolpidem treatment.

Summary:
Introduction: Drug treatments for insomnia that act at the GABA receptor can pose a significant risk for falls in older adults. This study compared the effects of ramelteon (a nonselective chronohypnotic selective for MT_1/MT_2 receptors) and placebo on balance, mobility, and memory in older adults awakened at night. Zolpidem was used as a positive control.

Methods: Thirty-three older adults (>65 years) with insomnia who reported symptoms at least 3 nights per week for >3 months received ramelteon 8 mg, zolpidem 10 mg, or placebo 5 minutes before bedtime for one night each in a double-blind, placebo-controlled, single-dose, 3-period crossover study. A 5-10 day washout period followed each drug administration. Subjects were awakened 2 hours after study drug administration to evaluate standing balance (NeuroCom EquiTest Sensory Organization Test [SOT]), turning speed and stability (NeuroCom EquiTest Step Quick Turn Test [SQT]), memory (immediate and delayed word recall tests), and adverse events. The primary endpoint was balance as assessed by SOT composite score at 2 hours post dose.

Results: Compared to placebo, a significant decrease in SOT composite scores was observed with zolpidem (P<0.001), but not with ramelteon (P=0.837). Significant increases in turn time and turn sway measured by SQT were also observed between zolpidem and placebo (P<0.001, both), but not between ramelteon and placebo (P=0.776 and P=0.982, respectively). Immediate memory recall declined significantly with zolpidem (P<0.002), but not ramelteon (P=0.683). Neither treatment significantly affected delayed recall. Adverse events were reported in 13 subjects during zolpidem treatment and 7 subjects each during placebo and ramelteon treatment. No serious adverse events were reported.

Conclusion: In older adults with primary insomnia, ramelteon did not impair middle-of-the-night balance, mobility, and memory performance relative to placebo, in contrast to zolpidem.

Funded by Takeda Pharmaceutical Company.

References:

NR605 Tuesday, May 22, 3:00 PM - 5:00 PM
Modafinil Improves the Ability to Engage in Everyday Situations in Patients With Excessive Sleepiness: An Analysis of the Individual Questions of the Ewport Sleepiness Scale

John Harsh, Ph.D. University of Southern Mississippi, Department of Psychology, Box 5025, Hattiesburg, MS, 3400-5025, 9000, Richard Bogan, M.D., Thomas Roth, Ph.D.
Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss which activities affected by excessive sleepiness experience the greatest and least response, as assessed by the Epworth Sleepiness Scale, following administration of modafinil in patients with obstructive sleep apnea or narcolepsy.

Summary:

Objective: Excessive sleepiness (ES) affects patients’ ability to engage in everyday situations. The effect of modafinil on patients’ functional status was evaluated by patient responses to questions of the Epworth Sleepiness Scale (ESS).

Methods: This analysis pooled data from 4 previously published studies of patients with ES associated with OSA (N=466) or narcolepsy (N=558). Patients were randomized to receive modafinil (200-400 mg/day) or placebo for up to 12 weeks. The ESS assesses the respondent’s likelihood of dozing in each of 8 situations using a 4-point scale (no, slight, moderate, or high chance). Response was defined as an improvement of ≥1 point from baseline.

Results: Response to modafinil versus placebo was significantly greater for all ESS questions in both populations, except for “sitting in a car while stopped in traffic” for OSA patients (32.3% responders for modafinil vs 26.1% for placebo; P<.001). For both populations, the percentage of responders to modafinil versus placebo was greatest for “sitting and reading” (OSA, 60.9% vs 35.6%; narcolepsy, 57.0% vs 31.1%; P<.0001 for both) and “watching television” (OSA, 59.8% vs 31.1%; narcolepsy, 55.6% vs 28.3%; P<.0001 for both). Compared with placebo, modafinil also showed a high percentage of responders for “sitting quietly after lunch without alcohol” (55.3% vs 31.7%; P<.0001) in patients with OSA and “sitting inactive in a public place” (58.7% vs 36.1%; P=.0001) in patients with narcolepsy. Significantly more narcolepsy patients receiving modafinil had reduced sleep propensity when “lying down to rest in the afternoon” (27.8% vs 8.9%; P<.0001) versus placebo.

Conclusion: In patients with ES associated with OSA or narcolepsy, modafinil significantly improved their ability to remain awake in everyday situations.

Funding Source: Cephalon, Inc.

References:


NR607 Tuesday, May 22, 3:00 PM - 5:00 PM

Modafinil Improves Functional Outcomes in Everyday Activities in Patients With Excessive Sleepiness

Russell Rosenberg, Ph.D. Northside Hospital Sleep Medicine Institute, None, 5780 Peachtree-Dunwoody Road, Suite 150, Atlanta, GA, 30342, 9000, Terri E. Weaver, Ph.D., Milton Erman, M.D., Wolfgang Schmidt-Nowara, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the life activities that are most affected by excessive sleepiness and those that receive the most benefit from clinical treatment with modafinil in patients with obstructive sleep apnea or shift work sleep disorder.

Summary:

Objective: Excessive sleepiness (ES) during the day can significantly affect patients’ ability to perform everyday activities. The effect of modafinil on patients’ functional outcomes was evaluated by determining patient responses on the Functional Outcomes Sleep Questionnaire (FOSQ).

Methods: This retrospective analysis pooled results from 4 studies (2 each) of patients with ES associated with obstructive sleep apnea (OSA; N=486) or shift work sleep disorder (SWSD; N=487). Patients were randomized to receive modafinil 200-400 mg/day for up to 12 weeks. For the 30-item FOSQ, total score, 5
domains of everyday living (general productivity, activity level, vigilance, social outcomes, and intimacy), and individual items were evaluated.

Results: Modafinil significantly improved mean total score and all 5 domain mean scores vs placebo (P<.05). In OSA, 45% of patients who received modafinil improved their total FOSQ score by ≥2 points vs 25% of placebo patients (P<.001); while in SWSD, corresponding percentages were 40% and 36% (P=.26). For both groups, there was a trend for a greater percentage of patients who received modafinil to improve by ≥1 point on each individual item of the FOSQ vs placebo. In OSA, the percent of patients who improved on modafinil was 52.9% vs 36.3% for placebo (P<.001) for being active in the evening; 49.6% vs 33.1% (P<.01) for participating in group activities; and 43.5% vs 27.4% (P<.001) for general ability to remember things. In SWSD, the percent of patients who improved on modafinil was 47.8% vs 38.3% for placebo (P<.05) for being active in the morning; 30.7% vs 13.8% (P<.001) for general level of activity; and 21.2% vs 13.3% (P<.05) for finishing a meal. Conclusion: Modafinil significantly improved the ability of patients with ES to function in everyday activities.

Funding Source: Cephalon, Inc.

References:

NR608 Tuesday, May 22, 3:00 PM - 5:00 PM
Objective Efficacy and Safety of Ramelteon 8 mg in Female Subjects with Chronic Insomnia: Analysis from Multiple Controlled Clinical Trials
Louis J. Mini, M.D. Takeda Pharmaceuticals North America, Inc., Neuroscience, One Takeda Parkway, Deerfield, IL, 60015, Teresa Osborn, Sherry Wang-Weigand, Jeff Zhang
Educational Objectives:
At the conclusion of this presentation, the participant should be able to discuss the efficacy and safety of ramelteon treatment in adult women with chronic insomnia.

Summary:
Introduction: Ramelteon is a potent, selective melatonin MT 1/MT 2 receptor agonist, FDA-approved for the treatment of insomnia.
Methods: Objective sleep latency data from adult female subjects (ages 18-64 years) with chronic insomnia were analyzed from two separate double-blind placebo-controlled trials; a short-term (2-night) crossover study and a longer-term (5-week) parallel study. In both trials, efficacy of ramelteon 8 mg was compared to placebo with a primary endpoint of latency to persistent sleep (LPS) as measured by polysomnography. Data on adverse events in female subjects of all ages were compiled from 18 clinical trials of various duration and design, comparing ramelteon 8 mg and placebo.
Results: A statistically significant mean reduction in LPS versus placebo (-15.5 min, P<0.001) was observed for adult female subjects taking ramelteon 8 mg in the 2-night study (n=67). In the 5-week study, adult female subjects taking ramelteon 8 mg nightly (n=82) had significantly reduced LPS compared to placebo (n=101) at all time points (-15.5 min at Week 1; P<0.001, -12.0 min at Week 3; P<0.05, and -8.8 min at Week 5, P<0.05). Across 18 clinical trials, headache was the only adverse event that occurred in >5% of all female subjects (8.1% ramelteon, 8.1% placebo).

Conclusions: Ramelteon is an effective and well-tolerated treatment for women with chronic insomnia. Statistically significant reductions in LPS occurred in both short-term and longer-term studies. The overall adverse event profile of ramelteon 8 mg across multiple clinical trials was comparable to placebo in all female subjects.

Funded by Takeda Pharmaceutical Company.

References:

NR609 Tuesday, May 22, 3:00 PM - 5:00 PM
Modafinil (Provigil®) Improves Engagement in Daily Activities and Does Not Interfere With Intended Sleep After the Night Shift in Patients With Chronic Shift Work Sleep Disorder (SWSD)
John K. Walsh, Ph.D. St. John’s/St. Luke’s Hospital, Sleep Medicine and Research Center, 232 South Woods Mill Road, Chesterfield, MO, 63017, 9000, Thomas Roth, Ph.D., David F. Dinges, Ph.D., Jonathan R. L. Schwartz, M.D., Sanjay Arora, Ph.D., Charles A. Czeisler, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to discuss the effect modafinil has on patients’ ability to engage in daily activities and on intended sleep in patients with excessive sleepiness associated with chronic shift work sleep disorder.

Summary:
Objective: Modafinil significantly improves the ability to sustain wakefulness during the night shift in patients with chronic SWSD, although patients may still have evidence of excessive sleepiness during the night shift. This analysis evaluated the effects of modafinil on the ability to engage in daily activities and fall asleep when intended after the night shift in patients with chronic SWSD.
Methods: This was a pooled analysis of 2 double-blind placebo-controlled studies of night-shift workers with nighttime excessive sleepiness. The most common occupational category included health care and social assistance (37%). Patients with SWSD were randomized to receive 200 or 300 mg of modafinil or placebo 1 hour before each night shift for 3 months. Assessments included Functional Outcomes of Sleep Questionnaire (FOSQ), to evaluate ability to engage in daily activities, and patient-completed electronic diaries, to record daytime sleep parameters after a night shift.
Results: Total and subscale FOSQ scores improved from baseline with modafinil compared with placebo: total score change (P<.002) and subscale score change, in Activity (P<.0002), Intimacy (P=.25), Productivity (P=.003), Social Outcome (P<.05), and Vigilance (P<.004). There was no significant difference between the modafinil and placebo groups in total sleep time, sleep efficiency, or percent of time in stages 1 through 4 or rapid eye movement sleep following the night shift (P>.05). Common adverse events reported by patients for modafinil vs placebo, respectively, were headache (23% vs 19%), nausea (11% vs 4%), nervousness (7% vs 2%), and insomnia (7% vs 1%).
Conclusions: In patients with chronic SWSD, modafinil improved daily activities as measured by the FOSQ, did not interfere with patients’ attainment or quality of intended sleep, and was well tolerated.

Funding Source: Cephalon, Inc.

References:

NR610 Tuesday, May 22, 3:00 PM - 5:00 PM
Sleep-Promoting Effects of Ramelteon: A Subanalysis of Adults with Severe Sleep-Initiation Difficulty
Louis J. Mini, M.D. Takeda Pharmaceuticals North America, Inc., Neuroscience, One Takeda Parkway, Deerfield, IL, 60015, 9000, Sherry Wang-Weigand, Jeff Zhang

Educational Objectives:
1. At the conclusion of this presentation, the participant should be able to describe the efficacy of ramelteon treatment in adults with chronic insomnia characterized by severe sleep-initiation difficulty.
2. At the conclusion of this presentation, the participant should be able to explain possible rebound insomnia. Next-morning residual effects were evaluated in a subset of adults with chronic insomnia exhibiting severe sleep-initiation difficulty.

Methods: A phase III, randomized, double-blind, placebo-controlled trial evaluated the efficacy and safety of 5 weeks of nightly ramelteon 8 mg administration in 405 adults who had chronic insomnia (DSM-IV-TR™) lasting at least 3 months. This post-hoc analysis examined a subset of 127 subjects who had baseline latency to persistent sleep (LPS) ≥60 minutes and who received ramelteon 8mg (n=65) or placebo (n=62). LPS was assessed with polysomnography (PSG) at Week 1 (Nights 1-2), Week 3 (Nights 15-16), and Week 5 (Nights 29-30). A 2-day placebo run-out period evaluated possible rebound insomnia. Next-morning residual effects were assessed using a Visual Analog Scale (VAS) of mood and feelings, Digit Symbol Substitution Test (DSST), Immediate and delayed recall tests, and measures of subjective levels of alertness and ability to concentrate.

Results: Ramelteon resulted in statistically significant reductions in LPS compared to placebo at Week 1 (change from baseline: -53.0 vs -35.2min, P=0.01), Week 3 (-55.8 vs -32.3min, P=0.002), and Week 5 (-58.7 vs -40.0min, P=0.01). No rebound insomnia was observed during the run-out period. No statistically significant differences between treatment groups were observed on DSST, memory tests, or level of alertness and ability to concentrate. Incidences of adverse events were similar between the rameleto and placebo groups. Only 4 adverse events (headache, somnolence, fatigue, and nasopharyngitis) were reported by >5% of subjects in either group.

Conclusions: In this subset of adults with chronic insomnia who had severe baseline sleep-initiation difficulties, statistically significant reductions in LPS were observed with ramelteon compared to placebo over 5 weeks of treatment with no evidence of next-morning pharmacologic effects or rebound insomnia.

Funded by Takeda Pharmaceutical Company.

References:

NR611 Tuesday, May 22, 3:00 PM - 5:00 PM
Effect of Ramelteon and Zopiclone on Body Sway at Peak Plasma Levels in Chronic Insomnia
Goran Hajak University of Regensburg, Dept of Psychiatry, Universitaetsstrasse 14, Regensburg, 93053, 4280, Inshaad Ebrahim, Mark Hibberd, Shoonah Vincent

Educational Objectives:
1. Use of traditional hypnotic agents in chronic insomnia is common, and may be associated with nocturnal falls leading to an increased risk of hip fracture, particularly amongst older people. Postural sway is an indicator of instability and is thought to be a predictor of falls; less postural sway implies a lower risk of falling. Ramelteon is a selective melatonin receptor agonist developed for treatment of insomnia. The primary objective of this study was to evaluate the effect on body sway, measured on a balance platform, at around maximum plasma concentrations of ramelteon 8mg once daily compared to placebo, with zopiclone 7.5mg as a reference treatment, in adult subjects with chronic primary insomnia. The primary variable was calculated area of centre of pressure (COP) recorded on the balance platform. 275 adults subjects underwent a 14-night, single-blind, placebo run-in, followed by 28 days double-blind treatment with placebo (n=94), ramelteon (n=88), or zopiclone (n=93). On Night 14 of treatment, subjects were admitted to the sleep laboratory. At 1.5 to 2 hours post dose, around peak plasma levels for ramelteon and zopiclone, subjects were awakened from sleep and the balance platform task performed. 260 subjects completed the Night 14 balance platform tests (ramelteon, n=95; zopiclone, n=94; placebo, n=91). One subject on zopiclone was unable to stand on the platform for the post-dose measurement. The mean log of COP post dose for placebo was 1.617 cm² and for ramelteon was 1.497 cm², P=0.293. For zopiclone the mean log of COP post dose was 3.593 cm², P=0.001 compared to placebo. In this study, ramelteon's effects on body sway at peak plasma levels were no different than placebo, while zopiclone significantly adversely affected postural sway compared to placebo.

Funded by Takeda Pharmaceutical Company.

References:
Modafinil Improves Behavioral Alertness in Patients With Shift Work Sleep Disorder (SWSD)

Kenneth P. Wright, Ph.D. The Sleep and Chronobiology Laboratory, Department of Integrative Physiology, University of Colorado at Boulder, 1725 Pleasant Street, Boulder, CO, 80302-0354, 9000, David F. Dinges, Ph.D., Thomas Roth, Ph.D., James K. Walsh, Ph.D., Sanjay Arora, Ph.D., Jonathan R. L. Schwartz, M.D., Charles A. Czeisler, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the benefit of modafinil in improving behavioral alertness, including sustained attention and speed of reaction times, in patients with excessive sleepiness associated with chronic shift work sleep disorder.

Summary:

Objective: Modafinil has been shown to significantly improve wakefulness in patients with SWSD, although evidence of excessive sleepiness may still be present during the night shift. This analysis assessed whether modafinil improved behavioral alertness in this patient population using multiple assessments of the Psychomotor Vigilance Test (PVT).

Methods: In this 3-month, double-blind, placebo-controlled study, night shift workers with nighttime excessive sleepiness and daytime insomnia for ≥3 months due to SWSD were randomized to receive modafinil 200 mg or placebo. To assess behavioral alertness, patients were administered the PVT, which assessed the ability to sustain attention without lapses, speed of reaction times (RT), wake state instability, and number of response errors as an index of impulsivity. Adverse events were monitored.

Results: Modafinil significantly improved patients' ability to avoid lapses of attention (difference from baseline in mean number of lapses for modafinil vs placebo was -3.8 vs +7.2, respectively; P<.01). Median RT at final visit increased by 0.3 msec for the modafinil group and 60.2 msec for the placebo group (P<.05). Wake state instability was improved by modafinil, with a significant difference in mean standard deviation of correct RTs for modafinil vs placebo (173.4 msec vs 441.8 msec, respectively; P<.05). There was no difference between modafinil and placebo in percentage of incorrect RTs. The most common adverse events reported by patients in the modafinil group were headache (modafinil, 26%; placebo, 19%) and nausea (modafinil, 9%; placebo, 3%).

Conclusion: Modafinil improved behavioral alertness compared with placebo in patients with excessive sleepiness due to SWSD by improving the ability to sustain attention and wake state instability and was well tolerated.

Funding Source: Cephalon, Inc.

References:


Evaluation of the Hamilton Depression Scale Following Eszopiclone Treatment for Insomnia in Patients with Insomnia Comorbid with Major Depressive Disorder or Generalized Anxiety Disorder

Maurizio Fava, M.D. Massachusetts General Hospital, Depression Clinical and Research Program, 15 Parkman Street, WACC-812, Boston, MA, 02114, 9000, Mark Pollack, M.D., Robert Rubens, M.D., David Amato, Ph.D., Andrew Krystal, M.D., Roza Hayduk, M.D., W. Vaughn McCall, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize the effect of insomnia treatment with eszopiclone on the Hamilton Depression Scale in patients with insomnia comorbid with Major Depressive Disorder or Generalized Anxiety Disorder.

Summary:

Introduction: Major Depressive Disorder (MDD) and generalized anxiety disorder (GAD) can coexist and patients with either or both often have insomnia marked by difficulty falling and/or staying asleep and potentially reduced quality of life (QoL) and functional abilities. Eszopiclone has been shown to improve sleep in patients with insomnia comorbid with MDD or GAD. The objective of this analysis is to examine the effects of eszopiclone co-therapy on the Hamilton Depression Scale (HAM-D17) over time in these two patient populations.

Methods: Patients with insomnia comorbid with MDD and baseline HAM-D17≥14 (excluding insomnia items; n=545) received morning fluoxetine and were randomized to receive nightly eszopiclone 3mg or placebo for 8 weeks. Patients with insomnia comorbid with GAD and baseline MADRS20 (n=593) received daily escitalopram oxalate and were randomized to receive nightly eszopiclone 3mg or placebo for 8 weeks. Clinician-administered HAM-D17 was evaluated at baseline and Weeks 4 and 8 in both studies.

Results: There were significantly greater reductions in HAM-D17 with eszopiclone co-therapy relative to monotherapy in both patient populations.

Conclusion: Targeted treatment of insomnia with eszopiclone was associated with significant improvements in HAM-D17 scores relative to fluoxetine or escitalopram monotherapy in patients with insomnia comorbid with MDD or GAD, respectively, even after removal of insomnia items from the scale.

References:


Modafinil is Well Tolerated During Long-Term Treatment in Patients With Excessive Sleepiness

Max Hirshkowitz, Ph.D. Michael E. DeBakey VAMC Sleep Center, Baylor College of Medicine, VAMC Sleep Center 1111, 2002 Holcombe Blvd., Room 6C344, Houston, TX, 77030, 9000, Russell Rosenberg, Ph.D., Ralph W. Richter, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that long-term administration of modafinil is well tolerated in patients with excessive sleepiness associated with shift work sleep disorder, obstructive sleep apnea, or narcolepsy.

Summary:

Objective: In double-blind, placebo-controlled studies, modafinil improved wakefulness and was well tolerated in patients with excessive sleepiness (ES) associated with shift work sleep disorder (SWSD), obstructive sleep apnea (OSA), and narcolepsy. The
long-term safety and tolerability of modafinil was evaluated in these patient populations.

Methods: Patients who previously completed double-blind placebo-controlled studies received oral modafinil for (a) 52 weeks at 200 or 300 mg/day in 2 SWSD studies, (b) 12 or 52 weeks at 200-400 mg/day in 2 OSA studies, and (c) 40 weeks at 200-400 mg/day in 2 narcolepsy studies. All patients were required to have a stable nasal continuous positive airway pressure regimen. Safety and tolerability were assessed by monitoring vital signs, clinical laboratory tests, electrocardiography (for OSA and narcolepsy studies only), physical examination, and treatment-related adverse events (AEs).

Results: A total of 1152 patients were evaluable for safety and tolerability (SWSD, 283; OSA, 391; narcolepsy, 478). Overall, there was no evidence of clinically meaningful abnormal trends in vital signs (heart rate, blood pressure, and weight), clinical laboratory tests, electrocardiography results, or physical examination findings. The tolerability profile for modafinil was similar to that seen in double-blind studies. Common treatment-related AEs in the SWSD studies were headache (7%-9%), insomnia (4%-7%), dry mouth (5%), abnormal liver function tests (3%), and nausea (3%). Common treatment-related AEs in the OSA studies were headache (21%), nervousness (8%), nausea (8%), rhinitis (8%), and anxiety (5%). In the narcolepsy studies, common treatment-related AEs were headache (13%-18%), nervousness (8%-10%), nausea (6%), and somnolence (6%). Most AEs were mild to moderate.

Conclusions: Modafinil appeared safe and well tolerated with long-term (up to 12 months) administration in patients with ES associated with SWSD, OSA, or narcolepsy.

Funding Source: Cephalon, Inc.

References:

NR615 Tuesday, May 22, 3:00 PM - 5:00 PM
Evaluation of Eszopiclone and Escitalopram Oxalate Co-therapy in Patients with Insomnia and Comorbid Generalized Anxiety Disorder
Mark H. Pollack, M.D. Massachusetts General Hospital, Center for Anxiety and Traumatic Stress Disorders, 185 Cambridge Street, Boston, MA, 02114-3117, 9000; Gustavo D. Kinrys, M.D., Andrew Krystal, M.D., W. Vaughn McCall, M.D., Thomas Roth, Ph.D., Holly Huang, M.S., Ranga R. Krishnan, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the effects of coadministration of eszopiclone and escitalopram oxalate in patients with insomnia and comorbid generalized anxiety disorder.

Summary:
Introduction: Generalized Anxiety Disorder (GAD) may occur with comorbid insomnia. We evaluated the efficacy of eszopiclone (ESZ) and concurrent escitalopram oxalate (EO) in patients with insomnia and comorbid GAD.

Methods: Patients meeting DSM-IV-TR criteria for GAD and insomnia received 10 weeks of EO 10mg and were randomized to co-therapy with either ESZ 3mg (n=294) or placebo (PBO) (n=301) for 8 weeks. For the following 2 weeks, ESZ was replaced with single-blind PBO to evaluate discontinuation effects. Sleep, daytime functioning and anxiety measures along with adverse events (AEs) were captured during the study.

Results: Compared with PBO+EO, ESZ+EO improved sleep and daytime functioning at each week and the average of the double-blind period (p<0.05). At Week 8, significantly more ESZ+EO patients had no clinically meaningful insomnia based on ISIs≤7. Significant improvements with ESZ+EO (relative to PBO+EO) were observed in HAM-A total scores each week, and at Weeks 4-10 excluding the insomnia item. CGI-I was improved with ESZ+EO at every timepoint (p<0.02), while CGI-S was not different between treatments after Week 1. Median time to anxiolytic response was reduced with ESZ+EO (relative to PBO+EO) based on HAM-A and CGI-I. HAM-A response and remission rates at Week 8 were higher with ESZ+EO, and HAM-D17 scores were improved at all time points (p<0.004). After eszopiclone discontinuation (Week 10), there was no evidence of rebound insomnia, and there were no treatment differences in sleep or daytime function measures. Significant treatment differences in anxiety and mood were maintained at Week 10. Overall AE rates were similar in the two treatment groups (78% for ESZ+EO vs 68% for PBO+EO).

Conclusion: In this study, ESZ+EO was well tolerated and associated with improved sleep and daytime function without evidence of tolerance. Improvements in anxiety and mood were observed with ESZ+EO compared to PBO+EO in patients with GAD and insomnia.

References:

NR616 Tuesday, May 22, 3:00 PM - 5:00 PM
Next-Day Driving Ability, Cognition and Psychomotor Function Following Nighttime Administration of Eszopiclone in Primary Insomniacs
Julia Boyle, Ph.D. University of Surrey, School of Biomedical and Molecular Sciences, University of Surrey, Guildford, GU2 7XP, 4120, Robert Rubens, M.D., James Roach, M.D., Kendyl Schaefer, M.S., Sigurd Johnsen, Ph.D., Leanne Trick, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the impact of eszopiclone therapy on next-day driving ability, cognition and psychomotor function in primary insomniacs.

Summary:
Introduction: This study evaluated next-day on-the-road driving ability and cognitive function following nighttime administration of eszopiclone 3mg in primary insomniacs.

Methods: This randomized, double-blind, placebo controlled, crossover study was performed in patients with primary insomnia (n=31). Eszopiclone 3mg was administered 30 minutes prior to lights out. On the road driving ability was assessed 9.5 to 10.25 hours after ingestion and additional objective cognitive and psychomotor testing was performed 9.75 to 10.5 hours after ingestion. Sleep and residual effects were also assessed subjectively in the morning.

Results: There were no significant differences in brake-reaction time (BRT) following nighttime administration of eszopiclone compared with placebo (p=0.39), and no significant differences between treatments on objective cognitive tests of information pro-
cessing, divided attention, psychomotor tasks and working memory as assessed by Critical Flicker Fusion, Choice Reaction Time, Continuous Tracking Task, Sternberg Short Term Memory Scanning Task, Rapid Visual Information Processing and Digit Symbol Substitution Test. Neither was there any significant effect on subjective next day ratings of morning sedation, co-ordination or mood as assessed by the Leeds Analog Rating Scale (LARS). There was significant improvement compared with placebo (p<0.0001) in subjectively rated ease of getting to sleep and quality of sleep the morning following dosing, and no perceived impairment of behavior following awakening or early morning awakenings as assessed by the Leeds Sleep Evaluation Questionnaire (LSEQ). PSG demonstrated significant increases in total sleep time and sleep efficiency, and significant reductions in time awake, wake after sleep onset, sleep onset latency (latency to sleep Stage 1) and latency to persistent sleep (p-values <0.005).

**Conclusion:** In this study, nighttime administration of eszopiclone 3mg improved objective and subjective sleep measures in primary insomniacs and did not impair next-day driving ability or other measures of cognition and psychomotor function.

**References:**

**NR617 Tuesday, May 22, 3:00 PM - 5:00 PM**

**Effects of Eszopiclone/Escitalopram Co-therapy on the Percentage of Patients Experiencing Coincident Resolution of Both Insomnia and Anxiety in Patients With Insomnia Co-existing With Generalized Anxiety Disorder**

Mark H. Pollack, M.D. Massachusetts General Hospital, Center for Anxiety and Traumatic Stress Disorders, Wang ACC-815, 15 Parkman Street, Boston, MA, 02114-3117, 9000, David Amato, Ph.D., Kendyl Schaefer, M.S., Robert Rubens, M.D., James Roach, M.D., Andrew D. Krystal, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to recognize the effects of eszopiclone/escitalopram co-therapy on the percentage of patients experiencing coincident resolution of both insomnia and anxiety in patients with insomnia co-existing with Generalized Anxiety Disorder.

**Summary:**

**Introduction:** In a study of insomnia co-existing with generalized anxiety disorder (GAD), eszopiclone/escitalopram co-therapy improved insomnia and measures of anxiety response vs placebo/escitalopram. In this report we re-analyze data from that study to determine the effect of co-therapy on the coincident resolution of both insomnia and GAD.

**Methods:** Patients meeting DSM-IV-TR criteria for both GAD and insomnia received eszopiclone or placebo and were randomized to nightly eszopiclone 3mg (ESZ+EO; n=294) or placebo (PBO+EO; n=301) for 8 weeks. Insomnia severity was assessed using the ISI; anxiety was assessed using the HAM-A. For both instruments, response was defined as ≥50% reduction from baseline at Week 8 and remission was defined as a total score of ≤ 7 at Week 8.

**Results:** Eszopiclone co-therapy with escitalopram significantly increased the rate of meeting both insomnia and anxiety response and remission criteria relative to escitalopram monotherapy.

**Conclusion:** The results of this analysis demonstrate that eszopiclone/escitalopram co-therapy improved measures of both insomnia (ISI) and anxiety (HAM-A) relative to escitalopram monotherapy and these improvements were related.

**References:**

**NR618 Tuesday, May 22, 3:00 PM - 5:00 PM**

**Improvement of Sleep Among Patients Receiving Double-Blind Pramipexole for Restless Legs Syndrome (RLS)**

Eric Lainey, M.D. Boehringer Ingelheim Pharmaceuticals, Inc., Clinical and Scientific Affairs-Neurology, 900 Ridgebury Road, Ridgefield, CT, 06877, 9000, John W. Winkelman, M.D., Stefan Albrecht, M.D., Juergen Koester, Ph.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to demonstrate an understanding of the impact of restless legs syndrome on sleep and daytime somnolence as well as the potential for improvement in sleep quality with pramipexole treatment, as measured by two scales.

**Summary:**

**Background and Aims:** Need for sleep improvement is the foremost reason patients with RLS seek medical attention and must be considered a test of RLS therapy.

**Methods:** In three-, six-, and 12-week double-blind trials, patients meeting diagnostic criteria of the International RLS Study Group received pramipexole (0.125-0.75 mg/d) or placebo. To evaluate sleep, patients were asked Question 4 of the International RLS Study Group Rating Scale (IRLS): “Overall, how severe is your sleep disturbance from your RLS symptoms?” on a scale of 0 (“none”) to 4 (“very severe”). To evaluate daytime sleepiness, patients rated the likelihood of falling asleep (from 0 to 3) in eight situations with the Epworth Sleepiness Scale (ESS). A score of 10 is considered abnormal. Change in ESS score from baseline to study end was analyzed by ANCOVA using baseline score and age as covariates.

**Results:** At baseline, the mean answer to IRLS Question 4 was 2.6 among 784 patients. At endpoint, the mean score was lower by 1.7 to 2.0 for pramipexole vs 0.8 to 1.2 for placebo. In each trial, the mean reduction was greater for pramipexole, by 0.47-1.14 (p<0.0037). At baseline, mean ESS scores were 6.0 to 8.2 in all trials and treatment groups among 782 patients. At endpoint, the scores were slightly reduced, by a mean 0.2 to 1.7. In the subgroup of patients with a baseline ESS score ≥10 (n=242), pramipexole reduced the adjusted ESS by 1.5 points more than placebo (p=0.0157). In the subgroup of patients with a baseline ESS score <10, no treatment difference was observed.

**Conclusions:** Across three double-blind pramipexole trials, RLS patients’ sleep improved from a mean rating between moderate and severe to a mean of none to mild. In the same trials, pramipexole reduced daytime somnolence among patients with elevated ESS scores at baseline.

**References:**
1. Allen RP, et al, for the International Restless Legs Syndrome Study Group: Restless legs syndrome: diagnostic criteria, spe-

legs syndrome (RLS) in a primary care population: the REST
(RLS epidemiology, symptoms, and treatment) primary care

NR619 Tuesday, May 22, 3:00 PM - 5:00 PM
The Effect of Total Sleep Deprivation on the
Physiological and Cognitive Function
Jong-Hyun Jeong, M.D., Ph.D. St. Vincent's Hospital, The
Catholic University of Korea, Neuropsychiatry, 93-6, Ji-dong,
Paldal-gu, Suwon, South Korea, Suwon, 442-723, 5800, Yoon-
Kyung Shin, M.D., Seung-Choil Hong, M.D., Ph.D., Jin-Hee
Han, M.D., Ph.D., Sung-Pil Lee, M.D., Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be
able to recognize physiological and cognitive effect after total
sleep deprivation.

Summary:

Objective: The purpose of this study was to investigate the
physiological and neurocognitive effects of total sleep deprivation
by using the laboratory blood test and the Vienna test system
(reaction test, vigilance test) in healthy subjects.

Methods: Sixteen healthy volunteers participated in this study.
Subjects were recommended to remain awake for 48 hours under
continuous surveillance. Cortisol, prolactin, thyroid hormone,
growth hormone, immunoglobulin (Ig G, Ig A, Ig M, Ig D, Ig E),
CBC, BC and the Vienna test system (reaction test, vigilance
test) were performed before and after 48 hours of total sleep
depression.

Results of the physiological and neurocognitive measures after
48 hours of sleep deprivation were as follows :
1. Concentration of T3 and T4 significantly increased after de-

2. In the reaction test, distribution reaction time significantly
increased, and correct reaction significantly decreased. In
the vigilance test, amount of correct reaction significantly
decreased, and the mean value of reaction time correct was significantly
delayed.
3. Level of fasting blood sugar, total protein, albumin, alkaline
phosphatase and potassium significantly increased, respectively.
But, total bilirubin level decreased.
4. After total sleep deprivation, WBC counts significantly in-
creased.
5. In immunoglobulin levels, manifested decreased Ig G, Ig A
and Ig M concentrations. But these differences were not statisti-
cally significant.

Conclusions: The effect of total sleep deprivation on the physio-
logical function was significant in thyroid hormone, and there were
partly consistent results in the immune system, prolacin level and
growth hormone. In blood chemistry, the components related with
hepato-biliary system altered, it suggested that sleep deprivation
may influence the metabolism of hepato-biliary system. And the
cognitive impairment resulting from total sleep deprivation were
markedly detected in the reactive and vigilant functions.

References:
1. Dement WC. Sleep extension: getting as much extra sleep as
2. Schuld A, Haack M, Hinze-Selch D, Mullington J, Pollmacher
T. Experimental studies on the interaction between sleep and
the immune system in humans. Psychother Psychosom Med

NR620 Tuesday, May 22, 3:00 PM - 5:00 PM
Clinical Burnout is Not Related With Hypothalamus-
Pituitary-Adrenal Axis Functioning: Comparison of
Basal Cortisol Level and Dexamethasone
Suppression Test in Burnout With Healthy Controls
Ozen Onen Sertoz, M.D. Ege University, School of Medicine,
Department of Psychiatry, Ege Universitesi Tip Fakultesi,
Psikiyatri Anabilim Dalı Bornova, Izmir, 35100, 4890, Ibrahim T.
Bincay, M.D., Hayriye Elbi Mete, M.D., Aysin Noyan, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be
able to investigate the possible underlying pathophysiological
pathways of a stress-related disorder, recognize the evaluation
of the hypothalamus-pituitary-adrenal (HPA) axis in burnout, the
comorbidity of psychiatric disorders in burnout, and the psychopa-
thological states of clinically diagnosed burnout subjects.

Summary:

Introduction: Burnout is presumed to be the result of chronic
stress, and chronic stress is known to affect the hypothalamus-
pituitary-adrenal (HPA) axis. To date, a few studies on HPA-axis
functioning in burnout have been carried out and have revealed
inconsistent results.

Method: Subjects who were clinically diagnosed as burnout (n=
37) according to ICD-10 work-related neurasthenia criteria
and healthy controls (n=35) were recruited. We assessed burnout
(Maslach Burnout Inventory), self-report psychological well-being
(Beck Depression Inventory, Beck Anxiety Inventory and Sym-
ptom Check List - SCL 90) and psychiatric status (The Structured
Clinical Interview for DSM-IV-TR). Blood cortisol level was sam-
ped to assess the basal cortisol levels. Also dexamethasone
suppression test (DST) was applied to determine the feedback
sensitivity of HPA-axis. In statistical analysis, descriptive statistics,
chi-square and t-test were performed.

Results: The burnout and healthy control groups did not differ
in age, gender and educational level. When compared with the
control group, the burnout group reported significantly higher lev-
els of emotional exhaustion and depersonalization (p<0.001,
p<0.001 respectively) on the burnout questionnaire, higher scores
both on Beck depression and Beck anxiety inventories (p<0.001,
p<0.001 respectively). The burnout group also scored significa-
tively higher on the global symptom index of SCL-90 (p<0.001).
There was no difference between the burnout and control group
in terms of basal cortisol level (F=0.042, p=0.6). Also no difference
observed in cortisol level after 1 mg DST between the burnout and
group (F=0.067, p=0.9). Exclusion of subjects with possible
influencing medications and comorbidity of psychiatric disorders
did not change the results.

Conclusion: Although the burnout group in present study re-
ported severe emotional exhaustion, there was no dysregulation in
the HPA-axis. We concluded that HPA-axis functioning of clinically
diagnosed burnout subjects seems to be normal.

References:
1. Mommersteeg PMC, Heijnen CJ, Verbraak MJPM, van Door-
en LJP: Clinical burnout is not reflected in the cortisol awaken-
ing response, the day-curve or the response to a low-dose
dexamethasone suppression test. Psychoneuroendocrinology
2006;31:216'22.
2. Eriksson PS, Wallin L: Functional consequences of stress-
related suppression of adult hippocampal neurogenesis ' a
novel hypothesis on the neurobiology of burnout. Acta Neurol
NR621  Tuesday, May 22, 3:00 PM - 5:00 PM
Risk Factors For Chronic Posttraumatic Stress Disorder Among War Veterans In Former Yugoslavia
Zeljko Spilic, A.A.S. Military Medical Academy, Psychiatry, Cmnotravska 17, Belgrade, 11000, 4799, Radomir Samardzic, Gordana Mandic-Gajic, Miroslav Radovanovic

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize risk factors for developing the chronic posttraumatic stress disorder (PTSD) in veterans from ex-Yugoslavia wars.

Summary:
Objective: The aim of this study was to assess the contribution of war stressors, personality features, presence of comorbid psychopathology and lack of postwar social support as risk factors for developing the chronic posttraumatic stress disorder (PTSD) in war veterans in former Yugoslavia.

Method: The study subjects were 190 war veterans (aged 19-56 years). 136 (71.6%) of them had current PTSD and 54 (28.4%) had lifetime PTSD. Self-report of severity of war stressors and postwar social support was assessed by the questionnaires designed for this study. Severity and frequency of PTSD symptoms were assessed by the PTSD Interview, DSM-III-R version. Comorbid psychopathology was assessed with the Symptom Check List (SCL-90) and Eysenck Personality Questionnaire (EPQ-90) was used for assessing personality. In the cross-sectional study canonical discriminant analysis was done to assess the difference between groups.

Results: The most important predictors for chronic PTSD were neuroticism, lack of social support in postwar period and comorbid depressive and anxiety disorders. Severity and frequency of war stressors as risk factors for developing the chronic PTSD were insignificant.

Conclusion: Personality features in veterans from ex-Yugoslavia wars have much stronger impact in prediction of PTSD chronicity than war stressors.

References:

NR622  Wednesday, May 23, 12:00 PM - 2:00 PM
The Spectrum of Worry in 2,146 Community-Dwelling Elderly Persons
Jeannette Golden, M.B. St. James’s Hospital, Department of Old Age Psychiatry, Department of Old Age Psychiatry, St James’s Hospital, Dublin, 8, 4190, Ronán M. Conroy, D.Sc, Brian A. Lawlor

Educational Objectives:
At the conclusion of this presentation, the participant should be able to distinguish severity points on the spectrum of worry, from simple worry to generalized anxiety disorder. They should be aware of the decline in worry with age in the elderly, and its association with gender. They also should be able to specify the graded association that worry shows with quality of life, independence of its association with depression.

Summary:
Aims: The study examines the prevalence and content of worry at levels of severity ranging from mild worry to Generalised Anxiety Disorder (GAD), and its association with quality of life and depression in a large sample of community dwelling elderly.

Methods: 2,146 elderly persons were interviewed using the AGECAT diagnostic interview system. Worry was classified on a 5-point scale comprising none, nonsevere worry, severe worry, intrusive severe worry and GAD.

Results: Worry of all types was more common in women. Between age 70 and 90, severe worry declined from 46% to 29% in women and 25% to 14% in men, and GAD declined from 7% to 3% in women and 5% to 2% in men.

There were sharp declines in self-rated quality of life and happiness across levels of worry. The proportion of people rating themselves ‘very happy’ declined from 53% in those non-worriers to 11% of those with GAD. The proportion with good self-rated quality of life declined similarly from 76% in non-worriers to 29% in those with GAD. All associations remained unchanged when depression was controlled for. Compared with non-worriers, age- and sex-adjusted risk of depression was elevated in severe worriers (odds ratio 7.2), intrusive worriers (OR 13.9) and GAD (OR 59.0, all P<0.001) but not elevated in nonsevere worry (OR 1.7, P=0.197).

Conclusions: Worry is common in the elderly and declines with age. There is a graded negative association with quality of life, suggesting that the concept of ‘healthy worry’ is unhelpful.

References:

NR623  Wednesday, May 23, 12:00 PM - 2:00 PM
Early Screening for Posttraumatic Stress Disorder in Injured Soldiers Using the PTSD Checklist
Thomas A. Grieger, M.D. Uniformed Services University, Psychiatry, USUHS, PSY, B3074, 4301 Jones Bridge Road, Bethesda, MD, 20814, 9000. David M. Benedek, M.D., Robert J. Ursano, M.D., Stephen J. Cozza, M.D., Charles C. Engel, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to discuss the performance characteristics of the PTSD Checklist when used as an early screening instrument with battle injured soldiers.

Summary:
Introduction: Following the 1991 Gulf War, soldiers reporting higher levels of Posttraumatic Stress Disorder (PTSD) symptoms at homecoming reported increasing PTSD symptoms during the next two years.(1) PTSD Checklist (PCL-17) score > 50 has often been used to identify PTSD in veterans whose combat experiences occurred years earlier.(2) Little is known about the predictive utility of the PCL-17 for PTSD when the scale is administered soon after return from combat injury.

Methods: Seriously injured soldiers (N=613) were screened for PTSD 1 month after injury. Of these, 294 soldiers were re-evaluated 7 months following injury.(3) A range of 1-month PCL-17 threshold scores were examined with regard to their ability to predict PTSD at 7 months.

Results: PTSD was present in 4% of soldiers at 1 month and 12% of soldiers at 7 months. Soldiers who met criteria for PTSD...
at 7 months had higher initial PCL-17 scores (Mean=37.5, SD=14.1 versus Mean=25.8, SD=8.3 p<0.0005). A 1-month PCL-17 score > 50 identified only 19% of soldiers who met criteria for PTSD at 7 months (sensitivity=.19, specificity=.98). In comparison, a 1-month PCL-17 threshold of 27 to 30 better identified those at risk for PTSD at 7 months (sensitivity=.67-.75, specificity=.66-.75).

Conclusions/Discussion: While a PCL-17 score > 50 may identify PTSD in injured soldiers years after combat exposure, a lower threshold may be better in predicting future PTSD in recently injured soldiers. Injured soldiers scoring above these lower PCL-17 thresholds should be seriously reassessed to facilitate identification of evolving illness and increased access to early treatment. Though false positive rates are higher at these lower PCL-17 thresholds, the consequences of a false negative screen appear outweighed by the potential to treat war related PTSD when it first becomes evident, rather than after it has contributed to functional impairments.

References:

NR624 Wednesday, May 23, 12:00 PM - 2:00 PM
Early Treatment of Generalized Anxiety Disorder with Alprazolam Orally Disintegrating Tablets Combined with SSRI or SNRI Antidepressants: Results from a Randomized, Naturalistic Trial
Mark H. H. Rapaport, M.D. Cedars - Sinai Medical Center, Psychiatry and Behavioral Neurosciences, 8730 Alden Dr. Suite C301, Los Angeles, CA, 90046, 9000, David J. Katzelnick, M.D., Kay E. McCrary, Pharm.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to assess whether earlier global improvement associated with benzodiazepine augmentation of SSRI or SNRI therapy is clinically important in the treatment of GAD.

Summary:
Objective: SSRIs and SNRIs are first-line treatments for generalized anxiety disorder (GAD), despite slow onset of action and potential to exacerbate anxiety symptoms early during treatment. This naturalistic study evaluated time to response in subjects with GAD treated with alprazolam orally disintegrating tablets (ODT) in combination with an SSRI/SNRI compared with SSRI/SNRI alone.

Methods: Subjects >18 years old with a primary diagnosis of GAD were randomized to 8 weeks open-label treatment with alprazolam ODT (4 weeks followed by 3 to 4 week taper) combined with an SSRI or SNRI, or SSRI/SNRI alone. The primary efficacy variable was time to response, defined as ≥50% decrease in Hamilton Rating Scale for Anxiety (HAMA) total score. Pre-specified secondary variables included mean change in HAM-A total and sub-factor scores, and improvement on the Clinical Global Impression of Improvement (CGI-I) and Patient Global Impression (PGI) scales.

Results: The intent-to-treat population comprised 245 subjects. There was no statistical difference between groups in the primary outcome of time to response. Significant differences favoring combination treatment were observed at weeks 2 and 4 in the HAM-A total score (P<0.05), weeks 1 and 2 in the HAM-A insomnia item (P<0.05), weeks 2 and 4 on the CGI-I scale (P<0.05), and weeks 2 and 3 on the PGI scale (P<0.05). One subject in each group discontinued due to adverse events. Fatigue and headache were the only adverse events reported by >5% of subjects in either treatment group.

Conclusion: Treatment with alprazolam ODT combined with an SSRI/SNRI was generally well tolerated. Although not different from monotherapy on the primary outcome, combination treatment was associated with more rapid improvement in insomnia and global measures of well being.

References:

NR625 Wednesday, May 23, 12:00 PM - 2:00 PM
Time to Response in Panic Disorder in a Naturalistic Setting: Combination Therapy With Alprazolam Orally Disintegrating Tablets and Serotonin Reuptake Inhibitors Compared to Serotonin Reuptake Inhibitors Alone
David J. Katzelnick, M.D. Healthcare Technology Systems, Incorporated, None, 7617 Mineral Point Road, Suite 300, Madison, WI, 53717, 9000, Mark H. Rapaport, M.D., Kay E. McCrary, Pharm.D.

Educational Objectives:
Learning Objective: At the conclusion of this presentation, the participant should be able to evaluate the potential therapeutic benefit of initiating treatment of panic disorder with a benzodiazepine in combination with an SSRI or SNRI.

Summary:
Objective: Results from previous controlled studies suggest benzodiazepine augmentation of SSRI treatment accelerates response in panic disorder. We sought to replicate and extend these findings in a naturalistic setting.

Methods: Subjects >18 years old with panic disorder with or without agoraphobia were randomized to 8 weeks open-label treatment with alprazolam orally disintegrating tablets (4 weeks treatment followed by 3 to 4 week taper) combined with an SSRI or SNRI, or SSRI/SNRI alone. The primary outcome was time to response, defined as ≥50% decrease from baseline in Hamilton Rating Scale for Anxiety (HAMA) total score. Pre-specified secondary measures included change from baseline in HAMA scores, and the Clinical Global Impression of Improvement (CGI-I) and Patient Global Impression (PGI) scales.

Results: The intent-to-treat (ITT) population comprised 245 subjects. There was no difference between groups in time to response in the ITT population, however, an a priori per protocol analysis (N=210) showed earlier response with combination treatment (P<0.05). Secondary measures in the ITT population showed greater improvement with combination treatment in HAMA total scores at weeks 1 and 2 (P<0.05), HAMA-M score subscale score at week 1 (P<0.01), and CGI-I and PGI scores early during treatment (P<0.05). Discontinuation due to adverse events occurred in 5.1% of subjects receiving combination treatment and 1.4% of subjects receiving monotherapy. Somnolence and headache were the only adverse events occurring in >5% of subjects in either treatment group.

Conclusion: Although alprazolam orally disintegrating tablets combined with an SSRI/SNRI did not separate from monotherapy on the primary efficacy measure, combination treatment appeared
to be well tolerated and may be associated with more rapid improvement in anxiety symptoms compared with an SSRI/SNRI alone.

References:


NR626 Wednesday, May 23, 12:00 PM - 2:00 PM
Generalized Anxiety Disorder, Somatic Pain and Health Care Costs

Ralph Swindle, Ph.D. Eli Lilly & Company, Outcomes Research, USMD, Outcomes Research, USMD, Eli Lilly (DC 5024, Building 1701, Col C7), Indianapolis, IN, 46285, 9000, Marc J. Gameroff, Ph.D., Mark Olsson, M.D.

Educational Objectives:

Educational Objectives: At the conclusion of this presentation, the participant should be able to describe the health care costs of primary care patients with generalized anxiety disorder (GAD) and describe the extent to which somatic pain contributes to these costs.

Summary:

Purpose: The purpose of this presentation is to describe associations between GAD, somatic pain, and health care costs among adult primary care patients and to evaluate whether and to what extent somatic pain adds to health care costs.

Methods: A systematic sample of primary care patients (N=1,029) from an urban practice were assessed with the PRIME-MD PHQ, Sheehan Disability Scale, a medical illness checklist, and the SF-12, which includes a measure of pain interference with daily activities that was classified as high (extremely or quite a bit) or low (moderately, a little bit, or not at all). Medical charges were assessed for the 6 month periods preceding and following the index medical visit. Patients with and without GAD are compared with respect to clinical characteristics and median medical charges. Mean predicted medical care charges were compared among four patient groups: 1) no GAD/low pain interference, 2) no GAD/high pain interference, 3) GAD/low pain interference, and 4) GAD/high pain interference.

Specific Findings: Compared to patients without GAD (n=191), patients with GAD (n=110) have significantly higher median health care charges ($2,375 vs. $1,448, z = 2.8, p = .006) and reported a significantly higher level of pain interference in daily activities (z=7.4, p<.0001). After controlling for patient age and gender, mean predicted health care costs were highest for patients with GAD/high pain interference ($42,620) (n=198) followed by no GAD/high pain interference ($9,601) (n=59) and lowest for patients with GAD/low pain interference ($6,757) (n=709), GAD/low pain interference ($3,204) (n=50).

Inferences: GAD is associated with increased health care costs; patients with GAD and high pain interference have especially high health care costs.

Conclusion: A strong clinical and economic rationale exists for developing and testing cost-effective interventions to treat primary care patients with GAD and somatic pain.

References:


NR627 Wednesday, May 23, 12:00 PM - 2:00 PM
Onset of Activity and Time to Response on CAPS-SX17 Individual Items in Patients With Posttraumatic Stress Disorder Treated With Venlafaxine XR: A Pooled Analysis

Barbara O. Rothbaum, Ph.D. Emory University School of Medicine, Psychiatry, WWHC, 1841 Clifton Road, Atlanta, GA, 30329, 9000, Xiao Wei Tian, M.S., Dan J. Stein, M.D., David S. Baldwin, D.M., Saeed Ahmed, M.D., Jeff Musgnung, M.Th, Ron Pedersen, M.S.

Educational Objectives:

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

Understand methods used to assess onset of activity and time to response of posttraumatic stress disorder symptoms following initiation of acute treatment with the SNRI venlafaxine XR.

Evaluate onset of activity and response on individual scale items of the CAPS-SX17, a widely-used measure for monitoring changes in response to treatment for PTSD.

Discuss the implications of the sequence of response for treatment of PTSD.

Summary:

Objectives: To examine onset of activity and time to response of posttraumatic stress disorder (PTSD) symptoms following initiation of acute treatment with venlafaxine extended-release (XR).

Methods: Pooled analyses of 2 randomized, placebo-controlled trials evaluated onset of activity and time to response on the 17 Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (DSM-IV) PTSD symptoms measured by the 17-item Clinician-Administered PTSD scale (CAPS-SX17). Mean changes from baseline and response rates (frequency and intensity score=1 or 2) over 6 visits (12 weeks) were evaluated by ANCOVA and logistic regression, respectively, with baseline severity as covariate.

Results: The intent-to-treat population comprised 687 patients (n=347, placebo; n=340, venlafaxine XR). Venlafaxine XR showed significant (P≤0.05) separation from placebo on most CAPS-SX17 items, with earliest onset (weeks 2-4) of activity and response on items 1 (intrusive recollections), 4 (psychological distress at exposure to cues), 5 (physiological reactivity on exposure to cues), and 14 (irritability or anger outbursts). Onset of activity and response occurred later (generally, weeks 6-8) on items 9 (diminished interest/participation in activities); 10 (detachment or estrangement); 11 (restricted range of affect); 12 (sense of foreshortened future), associated with numbing; 15 (difficulty concentrating); 16 (hypervigilance); 17 (exaggerated startle response), associated with hyperarousal; and 6 (avoidance of thoughts/feelings or conversations). Only item 8 (inability to recall important aspect of trauma) failed to separate from placebo on either measure.

Conclusions: Symptoms of psychological distress, physiological reactivity, and irritability/anger outbursts showed early and robust improvement with venlafaxine XR treatment, while symptoms of numbing and hyperarousal took longer, providing possible insights into the sequence of response to pharmacologic treatment in PTSD.

References:

NR628 Wednesday, May 23, 12:00 PM - 2:00 PM
Panic attacks induced by caffeine in panic disorder and depression with panic attacks
Isabela Nascimento, M.D. Federal University of Rio de Janeiro, Laboratory of Panic and Respiration, R. Prof. Hermes de Lima, 364/103, Rio de Janeiro, 22765095, 3510, Antonio E. Nardi, M.D., Alexandre M. Valencas, M.D., Fabiana L. Lopes, M.D., Valfrido Leão de Melo Neto, M.D., Rafael C.R. Freire, M.D., Gastão L Soares Filho, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the anxiogenic effects of caffeine on panic and depressed patients.

Summary:
Our aim was to observe if panic disorder (PD) patients and major depression with panic attacks patients (MDP) - DSM-IV - respond in a similar way to the induction of panic attacks by an oral caffeine challenge test. We randomly selected 29 PD patients, 27 patients with MDP, 25 patients with major depression without panic attacks (MD) and 28 normal volunteers. The patients had no psychotropic drug for at least a four-week period. In a randomized double-blind experiment performed in two occasions of 7 days apart, 480mg caffeine and a caffeine-free (placebo) solution were administered in a coffee form and anxiety scales were applied before and after each test. A total of 58.6% (n=17) PD patients, 44.4% (n=12) of patients with MDP, 12.0% (n=3) patients with MD and 7.1% (n=2) of control subjects had a panic attack after the 480mg caffeine challenge test (χ² = 16.22, df= 3, p<0.001).

The PD patients and MDP patients were more sensitive to caffeine than MD patients and normal volunteers. No panic attack was observed after the caffeine-free solution intake. The MD patients had a lower heart rate response to the test than all the other groups (two-way ANOVA, group by time interaction with Greenhouse-Geisser correction: F= 2.85, df= 3, 782, p=0.026). Our data suggest that there is an association between panic attacks, no matter if associated with PD or MDP, and hyperreactivity to an oral caffeine challenge test.

References:

NR629 Wednesday, May 23, 12:00 PM - 2:00 PM
Treatment Costs of Comorbid Generalized Anxiety Disorder, Depression and Pain
Zhongyuan Zhao Eli Lilly and Company, Health Outcomes, Lilly Corporate Center, Indianapolis, IN, 46285, 9000, Baojin Zhu, Wenyu Ye, Ralph W. Swindle

Educational Objectives:
At the conclusion of this presentation, the participant should be able to gain better knowledge on health care costs of managed care patients with generalized anxiety disorder (GAD) and describe the extent to which comorbid depression and somatic pain contributes to these costs.

Summary:
Purpose: To assess the impact of comorbid depression and pain on treatment costs for individuals diagnosed with Generalized Anxiety Disorder (GAD). The purpose of this study was to assess the impact of comorbid depression and pain on treatment costs for individuals diagnosed with Generalized Anxiety Disorder (GAD) in a managed care setting.

Method: Using the PharMetrics Integrated Outcomes Database, individuals were included in the study if they were: diagnosed with GAD (ICD-9-CM: 300.41) at any time period, 18-64 years old, had both depression and pain during the year, and had a minimum of 12 months of continuous coverage. The primary outcome measure was the total annual treatment cost, which included inpatient and outpatient costs. We used multiple linear regression models to identify factors associated with increased treatment costs and used the Geisser correction to adjust for multiple comparisons.

Results: We found that individuals with both GAD and depression and pain had significantly higher treatment costs compared to those with only GAD. The average total annual treatment cost for individuals with both disorders was $8,377, compared to $5,900 for those with GAD only. The total treatment costs for those with both disorders were $3,429 higher for GAD patients with depression (p<0.001), $7,503 higher for those with both depression and pain (p<0.001), and $3,429 higher for those with only depression (p<0.001).

Conclusions: Our results suggest that individuals with both GAD and depression and pain have significantly higher treatment costs compared to those with only GAD. Our findings highlight the importance of considering the comorbid conditions in the evaluation of treatment costs in managed care settings.

References:
Posttraumatic stress disorder (PTSD) is an anxiety disorder that may occur following exposure to an extremely stressful event, characterized by three symptom clusters: 1) re-experiencing, 2) avoidance and numbing and 3) hyperarousal (DSM-IV; APA, 1994). Using factor analysis, studies examining the adequacy of the DSM-model have yielded mixed results. Investigations do provide strong support for a separate “effortful avoidance” dimension (distinct from numbing), findings congruent with some theory. The current study is one of the largest and most comprehensive assessments of PTSD symptom structure, using state-of-the-art statistical methods, and the first to examine structure in a population-based sample of combat veterans during wartime.

**Summary:**

**Background:** Posttraumatic stress disorder (PTSD) is an anxiety disorder that may occur following exposure to an extremely stressful event, characterized by three symptom clusters: 1) re-experiencing, 2) avoidance and numbing and 3) hyperarousal (DSM-IV; APA, 1994). Using factor analysis, studies examining the adequacy of the DSM-model have yielded mixed results. Investigations do provide strong support for a separate “effortful avoidance” dimension (distinct from numbing), findings congruent with some theory. The current study is one of the largest and most comprehensive assessments of PTSD symptom structure, using state-of-the-art statistical methods, and the first to examine structure in a population-based sample of combat veterans during wartime.

**Objectives:** To determine the “best-fitting” PTSD structural model through a comparison of seven different models using confirmatory factor analysis.
Method: The research was prospective case-control study over 5 weeks. The first week was drug free, followed by 4 weeks treatment with escitalopram. We included 13 patients diagnosed with PD according to DSM-IV-TR and 13 age and gender matched controls (age 18-65). All subjects wear an Actiwatch-TS (Cambridge Neurotechnology Ltd), a watch like device that is used to measure peripheral body temperature (PBT) and capable to store data for 6 continuous days. Clinical course of the PD was assessed weekly applying CGI-S, CGI-I, Panic & agoraphobic scale. Change of body temperature was analysed using linear (mean, maximum, minimum, spectral analysis) algorithms. In order to compare the dynamical properties of the PBT non-linear (correlation dimension, lyapunov exponent) algorithms were used. Data were analysed separately for day, night, and full 24 hours cycles.

Results: No statistically significant difference was noted in the comparison of PBT between PD and controls. No statistically significant difference was noted in the PBT level during the 4 weeks treatment with escitalopram.

Conclusion: PD patients and controls have equal circadian PBT patterns. Also, the clinical respond to the SSRI agent escitalopram didn't change the observed temperature patterns across the time of treatment.

References:

NR633 Wednesday, May 23, 12:00 PM - 2:00 PM
OCD Has State Dependant Archiocingulate, Insula, Suplemental Sensorimotor Cortex Beta3 Hyperactivity
Cary L. Hamlin Atlantic Health, 385-2B Route 24, Chester, NJ, 07930, 9000

Educational Objectives:
At the conclusion of this presentation the participant should be aware that there are electrical tomographic abnormalities in OCD that vary as a function of symptom level.

Summary:
The archiocingulates in OCD have Beta hyperactivities. New Research 2006#508 confirmed Sherlin's finding in two EEGs on a 62 yr old male, before and after paroxetine, and extended it to demonstrate cortical involvement in the bilateral dorsal insula and supplemental sensorimotor cortex. This present study reports about seven separate EEGs performed over a three year interval upon one 46 yr old male patient. Over that time and on various medication trials, his OCD symptoms varied from severe to mild. A self-report of his symptoms, the Hopkins Symptom Checklist, was repeatedly measured. A 32 lead extended International 10/20 montage EEG was digitalized at 512 samples sec^-1 using a BioSemi amplifier-A/D converter. LORETA processing of the EEG data produces a mapping of spectral analysis data upon cortical regions of an averaged Talairach MRI Atlas. The patient's electrical tomogram was remapped against an EEG database of task, handedness, age, and gender matched neurometric normal controls. When all EEGs were grouped together, the comparison to normal revealed positive independent "t" test scores 2.1 or greater over the whole of the Beta3 (19-25 Hz) and Fast Beta (25-30 Hz) ranges selectively in the previously mentioned bilateral insula, archiocingulate, and supplemental sensorimotor cortexes. Compared to a subgroup of three EEGs when he had moderate to severe OCD subscale scores, a subgroup of three EEGs when he had mild to moderate OCD scores had independent "t" test scores of negative 2.1 or greater in the same bilateral insula, archiocingulate, supplemental sensorimotor cortaxes, but this was only found for the Beta3 range. With improvement, significant increase in Beta 3 activity within the normal range occurred, for the bilateral ventral insula, parahippocampus, temporal pole, lateral orbitofrontal cortaxes. This new finding suggests that the finding of insula, archiocingulate, supplemental sensorimotor cortex Beta3 abnormality is state marker of OCD severity.

References:

NR634 Wednesday, May 23, 12:00 PM - 2:00 PM
Social Anxiety and Blood-Injury Phobias In Turkish Medical Students
Elif Onur, M.D. Dokuz Eylul University Medical School, Psychiatry, Dokuz Eylul Univer Medical School Dept Psychiatry, Balcova, Izmir, 35340, 4890, Beyazid Yemez, M.D., Ceyhun Can, M.D., Ozden Sar#&305, Ph.D., Zeliha Tunca

Educational Objectives:
The objective of this presentation is to look for the rate of medical manipulation fear and to increase the attentiveness of social anxiety existing among medical students in whose professional lives social interactions and interpersonal relationships have a pivotal role.

Summary:
Social anxiety disorder (SAD) is common in young people. Medical profession is characterized by intense social interactions. SAD and other phobias such as blood and injury phobias were not adequately investigated in medical students. We used Liebowitz Social Anxiety Scale (LSAS) self-rated version and Marks & Matthews Fear Questionnaire (MMFQ) in Medical School students. Vocational School of Health Services (VSHS) students were recruited as a comparison group. T-test and one way ANOVA were used for statistical analyses. Study group consisted of 335 students. Two hundred and seventeen third year medical school students (64.8 %) (Med-early), 46 clerkship/internship students (13.7 %) (Med-late), and 72 second year students of VSHS (21.5 %) were included. Mean ages were 26.7±1.64, 23.5±1.86 and 19.3±1.59 respectively. The rate of severe social anxiety (LSAS score ≤ 96 point ) was 40.6 % in the whole group. Severe social anxiety was less frequent in Med-late group (23.9 %) than Med-early (40.1 %) and VSHS (52.8 %) groups. The mean total score of LSAS was lower in Med-late (83.1±18.22) than Med-early (91.8±21.75) and VSHS (97.82±24.99) groups (p=0.045 and p=0.001, respectively). The mean total score of MMFQ was also lower in Med-late (17.3±9.16) than Med-early (26.8±14.29) and VSHS groups (31.9±17.73) (p=0.001, 0.001 and 0.044, respectively). The mean blood/ injury phobia score in MMFQ was lower in Med-late (5.8±4.08) than Med-early (9.9±6.79) and VSHS (12.16±8.11) groups as well (p=0.001 and =0.0001). The mean total scores of LSAS and MMFQ did not differ between genders. The rate of fears related to medical manipulations was 3.3 % in the whole group.

Our Results showed that although severe social anxiety is lower in the late years of medical education than early years, it still affects about 25 % of this population.
for paroxetine and placebo respectively. This difference also was
of patients withdrawing due to lack of efficacy was 9.2% and 9.3%

2. Grant BF, Hasin DS, Blanco C, et al: The epidemiology of
social anxiety disorder in the United States: Results from the
National Epidemiologic Survey on alcohol and related condi-

References:
1. Raboch J: Prevalence of social phobia among medical stu-
2. Grant BF, Hasin DS, Blanco C, et al: The epidemiology of
social anxiety disorder in the United States: Results from the
National Epidemiologic Survey on alcohol and related condi-

NR635 Wednesday, May 23, 12:00 PM - 2:00 PM
A 36-week Paroxetine Immediate Release PTSD Relapse Prevention Trial
Cornelius D. Pitts, Pharm.D. GlaxoSmithKline Pharmaceuticals,
Clinical Research and Development, 2301 Renaissance
Boulevard, King of Prussia, PA, 19406, 3000, Karen Hewett,
Ph.D., David A. Duff, Ph.D., John E. Kraus, M.D., David J.
Carpenter, Pharm.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be
able to demonstrate an understanding of the use of paroxetine in
the prevention of relapse of Posttraumatic Stress Disorder
symptoms.

Summary:
Objective: To evaluate the efficacy of paroxetine in preventing
PTSD relapse
Methods: Following the screen visit and a placebo run-in period,
eligible patients received paroxetine during a 12-week single blind
treatment phase (flexible dosage design of 20-50mg daily). Re-
sponders (CGI-S improvement of > 2 points) at the end of the
single-blind period, were randomized to paroxetine or placebo
during a 24-week double blind treatment phase. Primary efficacy
was measured by the proportion of patients experiencing relapse of
efficacy (CGI-S deterioration) or withdrawal due to lack of effi-
cacy (investigators’ clinical judgement). Time to relapse and other
secondary measures were added to confirm results of the primary
variable. Safety and tolerability were measured by adverse event
(AE) incidence and the proportion of AE withdrawals.
Results: Two hundred sixty-five patients entered the single-
blind paroxetine phase. One hundred seventy-three responders
(63%) were evaluated during the double-blind treatment phase
(paroxetine, n=87; placebo, n=86). Patients were mostly female
(66%) and Caucasian (97%) with a mean age of 43.8 years.

References:
1. Tucker P, Zaninelli R, Yehuda, R, Ruggiero L, Dillingham K,
Pitts C: Paroxetine in the Treatment of Chronic Posttraumatic
Stress Disorder: Results of a placebo-Controlled, Flexible-Dos-
2. Schoenfeld F, Marmar C, Neylan T: Current Concepts in Phar-
macotherapy for Posttraumatic Stress Disorder, Psychiatric

NR636 Wednesday, May 23, 12:00 PM - 2:00 PM
Gender Differences in Clinical Presentation of GEneralized Anxiety Disorder, and Response to
Treatment With Pregabalin
M. A. Rynn, M.D. Columbia University, New York State
Psychiatric Institute, NY Psychiatric Institute, 1051 Riverside
Drive, New York, NY, 10032, 9000, Francesca Baldinetti, M.D.,
Teresa Loon, M.D., Francine S. Mandel, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should
better be able to recognize the similarities and differences in the
clinical presentation of generalized anxiety disorder in women
compared to men, and how gender influences treatment response
Summary:
Objective: To evaluate gender differences in the clinical presen-
tation of generalized anxiety disorder (GAD) and response to
treatment with pregabalin (PGB).
Methods: Data were pooled from six double-blind, placebo-
controlled, 4-6 week trials of outpatients who met DSM-IV criteria
for GAD with a minimum Hamilton rating scale for anxiety (HAM-
A) total score >18. Treatment response was analyzed for three
fixed-dosage groups, 150 mg/d, 300-450 mg/d, and 600 mg/d.
Results: The baseline presentation of GAD was similar for
women versus men, respectively, in terms of mean (+ sd) age
(38.6 + 12.3 vs. 39.4 + 11.5 years) and severity of depressive
symptoms (HAM-D score, 13.7 + 4.4 vs. 13.4 + 4.3); but women
had a modest but significantly higher mean HAM-A somatic factor
score (11.5 + 3.2 vs. 10.8 + 3.1; P<0.01). For both women and
men, treatment with PGB resulted in significantly higher LOCF-
endpoint improvement in HAM-A total score: women: PGB-150
mg, -10.7 + 0.82; PGB-300/450 mg, -11.8 + 0.68; PGB-600 mg,
-12.4 + 0.59 vs. Placebo, -9.5 + 0.51; P<0.001 for all comparisons;
men: PGB-150 mg, -10.8 + 0.81; PGB-300/450 mg, -12.6 + 0.59;
PGB-600 mg, -11.6 + 0.51 vs. Placebo, -8.7 + 0.47; P<0.001
for all comparisons. There were no between-dose differences in
treatment response for either women or men in the recommended
dosing range of 300-600 mg/day. CGI-I responder rates were
significantly higher (P<0.001) on PGB vs. placebo for both women
(50% vs. 35%) and men (53% vs. 38%). There were no gender
differences in attrition due to adverse events, or in proportion of
severe adverse events.
Conclusion: Women and men with GAD showed similar clinical
presentations, with the exception that women reported somewhat
more somatic symptoms. Pregabalin was an effective and well
tolerated treatment for GAD in both women and men.

References:
support for gender differences in response to fluoxetine for
generalized anxiety disorder. Depress Anxiety 2006;23:373-
376.
2. Steiner M, Allgulander C, Ravindran A, et al: Gender differ-
ces in clinical presentation and response to sertraline treat-
ment of generalized anxiety disorder. Hum Psychopharmacol

NR637 Wednesday, May 23, 12:00 PM - 2:00 PM
Levetiracetam Augmentation for Refractory
Generalized Anxiety Disorder
Gustavo Kinrys, M.D. Cambridge Health Alliance - Harvard
Medical School, Psychiatry, 1493 Cambridge Street,
Platelet Monoamine Oxidase Activity in Obsessive-Compulsive Disorder

Enrique Baca-Garcia, M.D. Columbia University Medical Center, Department of Neurosciences, 1051 Riverside Drive. Suite 2917 / Unit 42, New York, NY, 10032, 9000, Manuel Arrojo, M.D., M. Mercedes Perez-Rodriguez, M.D., Helen Dolengevich-Segal, M.D., Mercedes Navio-Acosta, M.D., Beatriz Rodriguez-Salgado, M.D., Jeronimo Saiz-Ruiz, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to recognize the differences in platelet MAO activity between a sample of patients with obsessive-compulsive disorder and a sample of healthy controls.

Summary:
- Introduction: Response to selective serotonin reuptake inhibitors (SSRIs) suggests the implication of the serotonergic system in obsessive compulsive disorder (OCD). However, biological studies on serotonergic function in OCD have yielded contradictory results. Platelet monoamine oxidase (MAO) activity has been proposed as an index of cerebral serotonin activity. The aim of this study was to examine platelet MAO activity in OCD patients and healthy controls matched by age, sex and tobacco use.
- Methods: Platelet MAO activity was measured in 29 OCD patients and 29 healthy controls matched by age, sex and tobacco use.
- Results: There were no differences in platelet MAO activity between OCD patients and healthy controls. OCD patients with aggressive obsessions had significantly lower levels of platelet MAO activity than patients without aggressive obsessions.
- Conclusions: Our results suggest that low platelet MAO activity may be associated with aggressive obsessions in OCD patients rather than with the disorder itself.

References:

NR638 Wednesday, May 23, 12:00 PM - 2:00 PM Platelet Monoamine Oxidase Activity in Obsessive-Compulsive Disorder

NR639 Wednesday, May 23, 12:00 PM - 2:00 PM A Pilot Study of Rhodiola Rosea for Generalized Anxiety Disorder (GAD)
References:

NR640 Wednesday, May 23, 12:00 PM - 2:00 PM
Prevalence and Predictive Factors of Bipolar Disorder (BP) in Young Adults with Pediatric Attention Deficit Hyperactivity Disorder (ADHD)

James G. Waxmonsky, M.D. State University-NY Buffalo, Psychiatry, Millard Fillmore Gates Hospital 8th floor, 3 gates circle, Buffalo, NY, 14209, 9000, Elizabeth Gnagy, Briannon O'Connor, Laura Straub, Brooke Molina, Ph.D., Oscar G. Bukstein, M.D., William Pelham, Ph.D.

Educational Objectives:
After reviewing the poster presentation, attendees will be familiar with the controversy surrounding the diagnosis of Bipolar Disorder (BP) in adolescents and young adults with ADHD. The presentation will assess the prevalence of BP in this population as well as risk factors for its development in patients with ADHD, including the manicogenic risks of stimulants.

Summary:
Objective: to assess the prevalence of BP and potential moderators in 364 ADHD children followed prospectively into young adulthood.

Methods: Subjects were assessed 8 years after participation in a therapeutic summercamps for ADHD. Subjects and parents were interviewed annually for 5 additional waves (ages 17-23). Demographically similar non-ADHD controls (N = 225) were recruited at follow-up. BP was diagnosed by review of treatment records, requiring a diagnosis of BP plus documented treatment with anti-manic medications for 2+ waves. Subjects requiring anti-manic medication for ADHD + internalizing disorder + anger outbursts but not diagnosed as BP were labeled Bipolar NOS. MDD was similarly confirmed and required one year of antidepressant usage for depression. Psychiatric diagnosis was also assessed using the SCID (age 18).

Results: 24 (6.5%) ADHD subjects developed BP vs. two controls (1%). On the self-reported SCID, five ADHD subjects and two controls meet criteria for BP. No SCID identified cases had been formally diagnosed with BP and therefore were not counted as positive cases. None of the treated BP cases were identified as bipolar on the SCID.

ADHD subjects were more likely to develop MDD (χ²=14, p<.001, OR=3.1) BP (χ²=11.6, p<.001, OR=8.4). ADHD subjects with BP were more likely to have a family history of mood disorders than ADHD subjects without a mood disorder (Beta = 1.1, p<.05).

There was no association between SES, lifetime stimulant usage and maternal depression and development of MDD/BP. Family conflict was higher in mood subjects vs. non-mood ADHD subjects (t=2.1, p<.05). Elevated childhood scores on the four mood symptoms from the Conner's Abbreviated Parent Questionnaire was associated with the development of BP (t=2.8, p<.01) and MDD (t=2.7, p<.01).

Our estimated prevalence of BP is greater than rates from other longitudinal ADHD studies (0%-1%) but less than the 15-20% reported in child psychiatry clinics.

References:

NR641 Wednesday, May 23, 12:00 PM - 2:00 PM
Nicotine Consumption and Alcohol Dependence in Patients With Comorbid Attention-Deficit/Hyperactivity Disorder (ADHD)

Martin D. Ohlmeier, M.D. Medical School Hannover, Clinical Psychiatry and Psychotherapy, Ohlmeier Martin@MH-Hannover.de, Hannover, 30625, 4280, Andreas Kordon, M.D., Bert T. Te Wilt, M.D., Marc Ziegenbein, M.D., Udo Schneider, Ph.D., Hinderk M. Emrich, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to diagnose and treat adult patients with combined nicotine and alcohol dependence with comorbidity of Attention-deficit/hyperactivity disorder (ADHD).

Summary:
Introduction: Several studies have shown that attention-deficit/ hyperactivity disorder (ADHD) presents a definite risk factor for exacerbation of addiction. 35% of adult ADHD patients are known to be addicted to alcohol. Many ADHD patients also have increased nicotine consumption, which typically leads to an improvement of attention, concentration ability and control of impulses. There may be pathophysiological connections here.

Methods: 91 adult patients addicted to alcohol were examined for ADHD using the WURS, the DSM-IV criteria for ADHD, as well as the CAARS. Furthermore, the probands were divided into diagnostic subgroups (inattentive, hyperactive-impulsive, combined type). Nicotine consumption was investigated with the Fagerstrom Test of Nicotine Dependence (FTND). The patients were divided into groups representing “minimal”, “average” and “high” level of nicotine dependence.

Results: 20.9% (WURS) of the patients addicted to alcohol showed evidence of ADHD in childhood, 26.3% (CAARS) demonstrated persisting ADHD in adult age. The FTND showed a statistically significant difference in alcohol dependence between those patients with and without ADHD in childhood. 78% of patients with ADHD were found to have an “average to high” level of nicotine dependence, a markedly higher percent compared to the 50% shown by those patients not suffering from ADHD. However, the number of ADHD patients not addicted to nicotine (8%) was significantly lower than shown by patients without ADHD (30.4%).

Discussion: The results of this investigation reveal that a large number of ADHD patients were subjected to alcohol dependence and even more an significant number to extreme nicotine dependence. The outcome indicates that there are very likely pathophysiological connections to alcohol and nicotine dependence in ADHD patients. This substance abuse is probably a form of “self-medication”. The results underline clearly the great importance in early and adequate diagnosis and therapy of ADHD in order to prevent exacerbation of addictive illnesses.

References:
NR642 Wednesday, May 23, 12:00 PM - 2:00 PM

Adult ADHD Investigator Symptom Rating Scale (AISRS) Validation: Effects of Atomoxetine

Thomas J. Spencer, M.D. Mass General Hospital, Psychiatry, 15 Parkman Street, WACC 7251, Boston, MA, 02114, 9000, Lenard Adler, Keith Saylor, Thomas E. Brown, James Holdnack, Martin Paczkowski, Douglas K. Kelsey

Educational Objectives:
At the conclusion of this presentation, the participant should be able to describe a new scale, the Adult ADHD Investigator Symptom Rating Scale (AISRS), and how scores on this new scale correlate with those of a well-known, validated measure of adult ADHD symptoms, the Conners’ Adult ADHD Rating Scale—Investigator Rated: Screening Version (CAARS-INV:SV).

Summary:

Objective: The Adult ADHD Investigator Symptom Rating Scale (AISRS) is an 18-item scale that assesses the 18 DSM-IV ADHD symptoms, modified for adults. The scale, developed as a semi-structured interview, assesses 9 hyperactive/impulsive behaviors and 9 inattentive behaviors. The AISRS was used as the primary efficacy measure in a randomized, placebo-controlled clinical trial that measured the efficacy of atomoxetine in adults with ADHD. Correlations between the AISRS scores and scores from a well-known, validated measure of adult ADHD symptoms, the Conners’ Adult ADHD Rating Scale—Investigator Rated: Screening Version (CAARS-INV:SV), were calculated.

Methods: Patients received once-daily atomoxetine (25 mg/day to 100 mg/day) or placebo, in the mornings, for about 6 months. Pearson's correlation coefficients between the AISRS and the CAARS-INV:SV were calculated.

Results: The mean ages of the atomoxetine patients (n=250) and placebo patients (n=251) were 37.7 and 37.4 years, respectively. A strong correlation was observed between the baseline AISRS and the CAARS-INV:SV scores (0.78; p<.001). The correlations continued to increase after 10 weeks and 6 months of treatment (0.88 and 0.89, respectively; p<.001) and all 5 clusters of ADHD-related executive function impairments improved significantly more than placebo patients for the total score (-27.0 versus -19.0 for atomoxetine (n=188) and placebo (n=195), respectively; p<.001) and all 5 clusters of ADHD-related executive function impairments (-6.1 versus -5.3, p=.002 for Organizing and Activating to Work; -5.7 versus -5.0, p=.004 for Regulating Alertness and Effort; -3.7 versus -2.2, p<.001 for Modulating Emotions; and -4.3 versus -3.1, p=.001 for Utilizing Working Memory).

Conclusion: Once-daily, morning-dosed atomoxetine can improve ADHD-related executive function impairments assessed by the Brown ADD Scale for Adults.

References:

NR643 Wednesday, May 23, 12:00 PM - 2:00 PM

Atomoxetine Alleviates Executive Function Impairments in Adults with ADHD

Thomas E. Brown Yale University, School of Medicine, 1188 Whitney Avenue, P.O. Box 6694, Hamden, CT, 06517, 9000, James Holdnack, Keith Saylor, Lenard Adler, Thomas J. Spencer, Martin Paczkowski, Douglas K. Kelsey

Educational Objectives:
Understanding the characteristics of ADHD based on information processing style (sequential-simultaneous processing model) of K-ABC-K and for establishing treatment and education objectives.

Summary:
The purpose of this study is to establish treatment and education planning of the children with attention deficit hyperactivity disorder (ADHD) based on information processing style (sequential-simultaneous processing model) of K-ABC-K. This study examined
383 children with ADHD who had visited neuropsychiatric department of YUMC were diagnosed as having ADHD from August 1, 1998 to August 30, 2005 using K-ABC-K, K-PIC, ADDES-HV. The children with ADHD was divided into three groups (sequential processing ability dominant group: N=243 (63.4%), simultaneous processing ability dominant group: N=111 (29.0%), same information processing ability dominant group: N=29 (7.6%) according to information processing style of K-ABC-K, and we analyzed K-ABC-K subscale scores of three groups. So, the sequential processing ability dominant group showed significant higher scores in subscale of autism than the other groups. There were no significant differences in behavioral symptom checklist through ADDES-HV. Simultaneous processing ability dominant group showed suggesting typical ADHD performance pattern. Some limitations suggested in this study that we had no alternative proposal about same information processing ability group, no verification of treatment and education plan for the children with ADHD based on information processing style, and then further analyses were suggested, like factor analysis, and cluster analysis for characteristic K-ABC-K performance of children with ADHD.

References:

NR645 Wednesday, May 23, 12:00 PM - 2:00 PM
Triple-Bead Mixed Amphetamine Salts (SPD465) Improves Quality of Life in Adults With ADHD

Educational Objectives:
At the conclusion of this presentation, participants should be able to
- Discuss changes in ADHD-specific quality of life among adults with ADHD following treatment with triple-bead mixed amphetamine salts compared to those who received placebo.
- Better recognize the potential benefits of up to 16 hours of ADHD symptom control on quality of life in adult patients with ADHD.

Summary:
Introduction: Adults with attention-deficit/hyperactivity disorder (ADHD) exhibit quality-of-life (QOL) impairments that impact occupational, social, and personal realms. This study evaluated the subject's perception of changes in QOL with triple-bead mixed amphetamine salts (MAS), an enhanced extended-release amphetamine formulation, vs placebo in adults with ADHD.

Methods: In this phase III, 7-week, randomized, double-blind, multicenter, placebo-controlled, dose-optimization study, adults 18-55 years old with ADHD received triple-bead MAS (12.5 mg/75 mg/d) or placebo. The adult ADHD Impact Module (AIM-A) evaluated QOL at baseline and study endpoint; the scale includes 6 multi-item domains: Living with ADHD, General Well-being, Performance and Daily Functioning, Relationships and Communication, Botheromeness and Concern, and Daily Interference. Safety was evaluated by recording treatment-emergent adverse events (TEAEs), vital signs, electrocardiograms (ECGs), and laboratory data.

Results: The randomized safety population comprised 272 subjects (137 on triple-bead MAS and 135 on placebo) and included 50% men and 50% women (mean age=36.5 years). The 127 subjects in the intent-to-treat population (who had evaluable AIM-A data and received triple-bead MAS) exhibited statistically significant improvements vs placebo from baseline to endpoint on all 6 AIM-A domains. Improvements with triple-bead MAS (least-squares mean difference) occurred on the Performance and Functioning (18.8, P<.0001), Relationships and Communication (10.2, P<.0001), General Well-being (8.2, P<.0001), Daily Interference (8.0, P=.003), Botheromeness and Concern (6.7, P=.01), and Living with ADHD (6.3, P<.0001) domains. The incidence of TEAEs was greater with triple-bead MAS vs placebo; insomnia (29.2%), dry mouth (22.6%), decreased appetite (19.7%), headache (18.2%), and weight decreased (13.1%) were the most common TEAEs with triple-bead MAS. Small changes in BP and pulse were observed.

Conclusions: In adults with ADHD, triple-bead MAS 12.5 mg/75 mg/d was associated with significant improvements in ADHD-specific QOL as measured by the AIM-A. Triple-bead MAS was generally well tolerated, with TEAEs consistent with those seen with amphetamine use.

References:

NR646 Wednesday, May 23, 12:00 PM - 2:00 PM
Efficacy and Safety of Methylphenidate in Adults With ADHD: The Long-Acting Methylphenidate in Adult ADHD (Lamda) Trial
Rossella Medori Janssen-Pharmaceutica N.V., EMEA Medical Affairs, Turnhoutseweg 30, Beerse, 2340, J.J. Sandra Kooij, Josep Antoni Ramos-Quiroga, Jan Buitelaar, Emma Lee, Miguel Casas

Educational Objectives:
At the end of this presentation, the participant should have an understanding of the key elements of adults with attention deficit/hyperactivity disorder (ADHD) clinical trial methodology and that treatment with methylphenidate improves the associated inattention and hyperactivity/impulsivity symptoms in a dose-dependent fashion in this patient population.

Summary:
Objective: To evaluate the safety and efficacy of OROS® methylphenidate at three fixed doses versus placebo in adults with attention deficit/hyperactivity disorder (ADHD).

Methods: Adults aged 18-65 years with a diagnosis of ADHD made using Conners’ Adult ADHD Diagnostic Interview for DSM-IV and SCID-I, and a clinician-rated Conners’ Adult ADHD Rating Scale (CAARS) score of ≥24 at screening were randomized to receive either methylphenidate 18, 36, 72 mg/day or placebo in the double-blind dose-response LAMDA trial. The primary efficacy endpoint was the change in the sum of the CAARS inattention and hyperactivity/impulsivity subscores from the start of treatment to end of the 5-week double-blind phase. Safety assessments included adverse events (AEs), vital signs, and laboratory parameters.
Results: 401 subjects were randomized and treated during the double-blind phase, with 394 eligible for the intent-to-treat analysis. All three doses of OROS® methylphenidate demonstrated statistically significant improvements in CAARS scores compared with placebo (Dunnett's test, P<0.05). A dose-response effect was evident, with effect sizes of 0.38, 0.43 and 0.62 in the 18, 36, and 72 mg/day dose groups, respectively. CAARS assessment interrater agreement was high (kappa statistic, 0.978). Pulse rate was slightly, but statistically significantly, elevated in all three methylphenidate groups (P<0.05) and there was a small, but statistically significant, increase in diastolic and systolic blood pressure at week 1 in the 72-mg group. The most frequently reported AEs by patients on active treatment included decreased appetite (25% versus 7% on placebo), headache (22% versus 18%), insomnia (13% versus 7%), nausea (13% versus 4%) and dry mouth (12% versus 2%). 12 subjects discontinued treatment due to an AE.

Conclusions: This study demonstrates that OROS® methylphenidate is safe and effective in adults with ADHD and that improvements in inattention and hyperactivity/impulsivity symptoms are dose-dependent in a 18-72 mg/day dose range.

References:
ersomeness and Concern (15.2, P<.0001), Daily Interference (14.2, P<.0001), General Well-being (12.6, P<.0001), Living with ADHD (8.1, P<.0001), and Relationships and Communication (8.1, P=.002) domains. The incidence of TEAEs was greater with triple-bead MAS than with placebo, most commonly insomnia, decreased appetite, dry mouth, headache, and weight decreased. Small changes in BP and pulse were observed.

Conclusions: Triple-bead MAS 25-75 mg/d was associated with significant improvements in QOL in this study of adults with ADHD. Triple-bead MAS was generally well tolerated, with TEAEs consistent with amphetamine use.

References:

NR649  Wednesday, May 23, 12:00 PM - 2:00 PM
Atomoxetine Treatment of Adults with Attention-Deficit/Hyperactivity Disorder and Comorbid Alcohol Abuse
Timothy E. Wilens, M.D. Massachusetts General Hospital, Pediatric Psychopharmacology Research Unit, 55 Fruit Street, YAW 6900, Boston, MA, 02114, 9000, Lenard A. Adler, M.D., Margaret D. Weiss, M.D., Kathleen T. Brady, M.D., David Michelson, M.D., Didier Renard, Ph.D., Louise R. Levine, M.D.

Educational Objectives:
At the conclusion of this presentation, the attendees should be aware that, in patients with ADHD and comorbid alcohol abuse, there are significant improvements in ADHD symptoms during treatment with atomoxetine and also the limitations of these data. Attendees should also be aware of the data suggesting that atomoxetine may reduce heavy drinking events in this population.

Summary:
Objective: This study tested the hypothesis that atomoxetine is superior to placebo in the treatment of ADHD symptoms and prevention of relapse of alcohol abuse in adults with both ADHD and comorbid alcohol abuse disorder.

Methods: Participants were 147 adults who met full DSM-IV-TR criteria for both ADHD and alcohol abuse and were recently abstinent from alcohol (4-30 days). Participants were randomly assigned to receive atomoxetine (25-100 mg daily, n=72) or placebo (n=75) for approximately 12 weeks. ADHD symptoms were assessed using the ADHD Investigator Symptom Rating Scale (AISRS). Time to relapse of alcohol abuse (4 standard alcoholic drinks for males or 5 standard alcoholic drinks for females within 24 hours, or at least 3 standard alcoholic drinks/day for at least 1 week) was defined as the amount of time (in days) from first dose of study medication to first occurrence of relapse and was analyzed using a 2-sided log-rank test based on Kaplan-Meier estimates. Cumulative heavy drinking events over time was measured post hoc with a recurrent event analysis using a stratified Andersen-Gill recurrent-event Cox model.1,2

Results: Atomoxetine was superior to placebo in the reduction of ADHD symptoms (AISRS total score, mean [SD], atomoxetine: -13.63 [11.35]; placebo: -8.31 [11.34], P=.007). Although the analysis of time to relapse showed no significant differences between treatment arms (P=.934), atomoxetine clinically and statistically significantly reduced the cumulative heavy drinking rate by approximately 24% compared to placebo using analysis of recurrent events (hazard ratio=0.761, P=.038). There were no serious adverse events, and the adverse event profile was similar to what has been demonstrated in previous studies.

Conclusions: This study of adult ADHD patients with comorbid alcohol abuse demonstrates robust effects of atomoxetine for reducing ADHD symptoms and suggests a positive effect for reducing cumulative heavy drinking events over time.

References:

NR650  Wednesday, May 23, 12:00 PM - 2:00 PM
Long-Term Global Improvement Following Treatment With Mixed Amphetamine Salts Extended Release in Adolescents With ADHD
Richard H. Weisler, M.D. UNC/Duke University, Psychiatry, 700 Spring Forest Road, Suite 125, Durham, NC, 27609, 9000

Educational Objectives:
At the conclusion of this presentation, participants should be able to:
• Identify the need for evaluation of psychostimulant medications in adolescents with ADHD.
• Characterize the long-term efficacy, safety, and tolerability of mixed amphetamine salts extended release in adolescents with ADHD.

Summary:
Introduction: Nearly 80% of children with attention-deficit/hyperactivity disorder (ADHD) continue to exhibit symptoms into adolescence, yet research evaluating psychostimulant use in adolescents is limited. This study examined the long-term global improvement and safety of mixed amphetamine salts extended release (MAS XR) in adolescents with ADHD.

Methods: Adolescents (ages 13-18 years) with ADHD who completed a previous 4-week double-blind, placebo-controlled (Part A) and a 6-month open-label (Part B) phase continued to receive treatment with MAS XR for up to 24 months (ie, an additional 18 months) in this phase III, multicenter, open-label study. Subjects were divided into 3 rollover groups (Part A-Placebo, Part A-MAS XR, and Part B-MAS XR) depending on their previous study participation. Clinical Global Impressions (CGI)-Severity was assessed at baseline, and CGI-Improvement (CGI-I; dichotomized as “improved” [very much improved” or “much improved”] and “not improved”) was measured at each clinic visit in the intent-to-treat (ITT) population. Safety was evaluated by measuring treatment-emergent adverse events (TEAEs).

Results: Of 238 subjects enrolled in the study, 71.8% were male and 28.2% were female; mean age was 14.6 years. CGI-I results at study endpoint indicated that nearly half (49.4%) of all subjects in the ITT population (n=237) were improved (including 71.4% of subjects in Part A-Placebo [n=20/28], 58.4% of subjects in Part A-MAS XR [n=66/113], and 32.3% of subjects in Part B-MAS XR [n=31/96]). Overall, MAS XR was safe and well tolerated, with most TEAEs reported as mild or moderate; the most frequently reported TEAEs included respiratory disorder (22.3%), headache (20.6%), and pharyngitis (17.2%). Six reports of serious AEs were considered unrelated to the study drug and there were no deaths.
Conclusions: This study demonstrated the long-term global improvement and safety of MAS XR during up to 24 months of treatment in adolescents with ADHD.

References:

NR651 Wednesday, May 23, 12:00 PM - 2:00 PM
Survey Evaluation of the Abuse Potential of Prescription Stimulants Among Patients With ADHD

George M. Bright, M.D. Adolescent Health Center, Clinic, 13821 Village Mill Drive, Midlothian, VA, 23114, 9000, Bruce Delphia, M.A., Barbara Wildberger, A.A.S.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
- Review survey findings on prescription stimulant abuse by patients with ADHD.
- Recognize differences in the risk for abuse of short- and long-acting stimulant medications by patients with ADHD.

Summary:

Introduction: Research has suggested that the abuse potential of short-acting stimulants is greater than that of long-acting stimulants. In this survey, subjects receiving treatment for attention-deficit/hyperactivity disorder (ADHD) were asked to assess the abuse potential of commonly used short-acting and long-acting prescription stimulant medications.

Methods: This is an interim analysis of an ongoing survey intended to be distributed to approximately 550 participants enrolled in an ADHD treatment center. In addition to general information about illicit drug use and misuse of prescribed stimulant medications, respondents were polled about the type of stimulant medication most frequently misused/abused (short-acting or long-acting) and how the stimulant was prepared and administered (crushed and inhaled; crushed and injected; soaked overnight in water and injected or consumed orally; heated in a microwave to melt down and inject, drink, or snort).

Results: From a total of 510 surveys included in this interim analysis, 444 (87%) respondents had a diagnosis of ADHD. Results indicate that 19.4% (n=99) of subjects surveyed abused prescription stimulants. Among these subjects, 78.9% (n=79) abused short-acting agents, 17.2% (n=17) abused long-acting agents, and 2.0% (n=2) abused both short- and long-acting stimulants. The most frequently reported method of preparation was crushing and inhalation (n=71, 14.7%) followed by crushing and injection or melting and snorting (6.3%, n=6, each).

Conclusions: In this interim analysis of data from a survey on abuse potential, one-fifth of the respondents abused prescription stimulant medications. Short-acting prescription stimulants were more likely than long-acting agents to be misused/abused. This suggests a relative benefit of long-acting stimulants in ensuring appropriate stimulant use and decreased stimulant misuse/diversion. However, considering that there is still a potential for abuse with long-acting stimulants, additional research is warranted to identify ADHD compounds with even less potential for misuse/abuse/diversion.

References:

NR652 Wednesday, May 23, 12:00 PM - 2:00 PM
Long-Term Cardiovascular Safety of Mixed Amphetamine Salts Extended Release in Adolescents With ADHD

Richard H. Weisler, M.D. UNC/Duke University, Psychiatry, 700 Spring Forest Road, Suite 125, Durham, NC, 27609, 9000

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
- Demonstrate understanding of the long-term cardiovascular effects of mixed amphetamine salts extended release in adolescents with ADHD.
- Recognize the adverse events most likely to occur in adolescents with ADHD receiving mixed amphetamine salts extended release.

Summary:

Introduction: Mixed amphetamine salts extended-release (MAS XR) has demonstrated short- and long-term safety and efficacy in patients with attention-deficit/hyperactivity disorder (ADHD). This study analysis evaluated the long-term cardiovascular safety of MAS XR in adolescents with ADHD.

Methods: This phase III, multicenter, open-label study evaluated the long-term (up to 24 months) cardiovascular safety of MAS XR, including subjects who had completed a prior, 4-week, double-blind, placebo-controlled phase (Part A) and a 6-month open-label phase (Part B). Part A subjects were started on MAS XR 10 mg/day and dosing was optimized over the first month. Part B subjects continued their optimized MAS XR dose. Daily MAS XR dose was titrated to 60 mg/d or tapered to 10 mg/d based on investigator judgment during the additional 18 months of open-label exposure. Diastolic blood pressure [DBP], systolic blood pressure [SBP], and pulse were measured based on subjects' previous study participation (Part A-Placebo, Part A-MAS XR, and Part B-MAS XR). Overall safety was evaluated by measuring treatment-emergent adverse events (TEAEs).

Results: Long-term cardiovascular safety data were collected from all 238 enrolled subjects. From baseline to endpoint, changes in DBP values of 5.9, 0.0, and -0.8 mm Hg were observed among the Part A-Placebo, Part A-MAS XR, and Part B-MAS XR subjects, respectively. Similarly respective SBP values of 5.3, 2.8, and 1.4 mm Hg and pulse values of 4.5, 1.1, and -3.4 bpm were observed. Overall, MAS XR was safe and well-tolerated, with respiratory disorder (22.3%), headache (20.6%), and pharyngitis (17.2%) the most frequently reported TEAEs. Six reports of serious AEs were considered unrelated to the study drug. No deaths were reported.

Conclusions: Long-term MAS XR exposure was safe and well tolerated in these adolescent subjects. The slight variation in BP and pulse rate changes is not unexpected considering the subjects' degree of previous stimulant exposure.

References:
NR653 Wednesday, May 23, 12:00 PM - 2:00 PM
"Immediate-Release Methylphenidate for ADHD in Children with Comorbid Chronic Multiple Tic Disorder"

Kenneth D. Gadaw, Ph.D., State University of New York, Psychiatry, Putnam Hall, Stony Brook, NY, 11794-8790, 9000, Joyce Sprafkin, Ph.D., Jeffrey Sverd, M.D., Edith E. Nolan, Ph.D., Jayne Schneider, Ph.D.

Educational Objectives:
- At the conclusion of this session, participants should better understand the safety and efficacy of immediate-release methylphenidate for the treatment of attention-deficit/hyperactivity disorder in children with comorbid, chronic multiple tic disorder.

Summary:
Summary: Introduction: Historically, one of the more contentious issues in the clinical management of children with attention-deficit/hyperactivity disorder (ADHD) is whether the preferred agents for the treatment of ADHD (i.e., stimulants) exacerbate tics in children with comorbid chronic multiple tic disorder. The goal of this study was to examine the safety and efficacy of immediate-release methylphenidate (MPH-IR) for the treatment of ADHD in children with comorbid, chronic multiple tic disorder.

Method: Two cohorts of children (N=71, 57 boys and 14 girls) between 6 and 12 years old (M=8.9) received placebo and three doses of methylphenidate (0.1, 0.3, and 0.5 mg/kg) twice daily for 2 weeks each, under double-blind conditions as part of their involvement in a long-term observation study (1989-2004). Treatment effects were assessed with an extensive battery of parent-, teacher-, child- and physician-completed rating scales and laboratory tasks.

Results: MPH-IR decreased the severity of ADHD (inattention, motor movement, impulsivity) symptoms (confirmed with both rating scales and laboratory tasks), oppositional behavior, and interpersonal peer aggression and improved work output. There was no evidence that MPH-IR altered the overall severity of tic disorder or symptoms of obsessive-compulsive disorder. Teacher ratings indicated that MPH-IR therapy decreased tic frequency and severity.

Conclusion: MPH-IR appears to be a safe and effective short-term treatment for ADHD in the majority of children with comorbid, chronic multiple tic disorder; nevertheless, the possibility of tic exacerbation in susceptible individuals warrants careful monitoring of all patients.

References:

NR654 Wednesday, May 23, 12:00 PM - 2:00 PM
Long-Term Efficacy, Safety, and Tolerability of Mixed Amphetamine Salts Extended Release in the Treatment of Adolescents With ADHD

Andrew J. Cutler, M.D., University of Florida, Department of Psychiatry, 807 West Morse Boulevard, Suite 101, Winter Park, FL, 32789, 9000

Educational Objectives:
- At the conclusion of this presentation, participants should be able to:
  - Identify the need for effective and safe treatment of adolescents with attention-deficit/hyperactivity disorder.
  - Characterize the long-term efficacy, safety, and tolerability of mixed amphetamine salts extended-release in adolescents with ADHD

Summary:
Introduction: Attention-deficit/hyperactivity disorder (ADHD) is common in adolescents. Long-term efficacy, safety, and tolerability of mixed amphetamine salts extended-release (MAS XR) were evaluated in adolescent ADHD.

Methods: In this multicenter, open-label study of MAS XR, adolescents (ages 13-18 years) with ADHD previously enrolled in a 4-week double-blind, placebo-controlled, forced-dose-titration (Part A) and 6-month open-label, flexible-dose (Part B) study were rolled over to receive MAS XR (10-60 mg/d) for up to 24 months (ie, additional 18 months' MAS XR exposure). The primary efficacy measure was the ADHD Rating Scale-IV (ADHD-RS-IV) total score and hyperactivity/impulsivity and inattention subscale scores. Safety assessments included changes from baseline in vital signs and recording of treatment-emergent adverse events (TEAEs).

Results: In the entire study population (N=238, mean age=14.6 years), 71.8% of the subjects were male and 28.2% were female. ADHD-RS-IV total scores in the intent-to-treat population (n=237) improved significantly from baseline to endpoint in two of the three rollover groups: Part A-Placebo (-1.1, P<.001) and Part A-MAS XR (-3.9, P=.0001). Change from baseline to endpoint score in the Part B-MAS XR group was 0.3 (P=.NS). Similar results were observed on the hyperactivity/impulsivity and inattentiveness subscales. Mean changes in vital signs were modest, with differences in magnitude of change based on rollover category. Most TEAEs were mild to moderate and included respiratory disorder (22.3%), headache (20.6%), pharyngitis (17.2%), anorexia (16.4%), insomnia (15.5%), and weight loss (14.7%). Six serious AEs were reported; all were considered unrelated to study drug and there were no deaths.

Conclusions: This study demonstrated continued efficacy, safety, and tolerability for up to 24 months with MAS XR in adolescents with ADHD. As expected based on previous MAS XR exposure, only subjects previously on placebo and fixed doses of MAS XR (Part A) demonstrated significant improvement in ADHD-RS-IV total scores with long-term open-label MAS XR exposure.

References:

NR655 Wednesday, May 23, 12:00 PM - 2:00 PM
Efficacy and Safety of a Novel Enhanced Extended-Release Amphetamine Formulation (Triple-Bead Mixed Amphetamine Salts, SPD465) in Adults With ADHD

Thomas J. Spencer, M.D. Mass General Hospital, Pediatric Psychopharmacology Research Unit, 55 Fruit Street, Warren 705, Boston, MA, 02114, 9000, Richard H. Weisler, M.D., Sharon H. Youcha, M.D., Colleen S. Anderson, M.Ed., Arthur Silverberg, Ph.D.

Educational Objectives:
- At the conclusion of this presentation, participants should be able to:
  - Recognize that many adults with ADHD require symptom control beyond 12 hours.
- Describe the rationale for developing a stimulant formulation with an extended duration of action (up to 16 hours) to treat adults with ADHD.

- Discuss triple-bead mixed amphetamine salts as a safe and effective treatment of ADHD in adults.

**Summary:**

**Introduction:** Triple-bead mixed amphetamine salts (MAS) is a once-daily, 3-component, enhanced extended-release amphetamine formulation designed to provide a duration of action up to 16 hours. This study evaluated the efficacy and safety of triple-bead MAS vs placebo for adult ADHD.

**Methods:** Adults (18-55 years old) with ADHD were randomized to triple-bead MAS (25, 50, or 75 mg/d) or placebo in this phase III, 6-week, randomized, double-blind, multicenter, forced-dose titration, placebo-controlled trial. The primary efficacy measure was change from baseline to endpoint in the clinician-administered ADHD-Rating Scale-IV (ADHD-RS-IV) total scores. Safety assessments included treatment-emergent adverse events (TEAEs), vital signs, electrocardiograms (ECGs), and laboratory evaluations.

**Results:** In the intent-to-treat population (n=405), the least-squares mean of 411 subjects in the randomized safety population, 57% were men and 43% were women (mean age=37.1 years). In the intent-to-treat population (n=405), the least-squares mean differences in ADHD-RS-IV total scores between triple-bead MAS and placebo (baseline to endpoint) were -10.6 (total triple-bead MAS), -9.9 (25 mg), -10.6 (50 mg), and -11.2 (75 mg) (P<.0001); all triple-bead MAS treatment groups were also statistically significantly superior to placebo during weeks 1-6 (P<.0001). There were no statistically significant differences between the triple-bead MAS groups, but numeric improvement was observed with increasing dose. The TEAE incidence was higher with triple-bead MAS vs placebo, but similar across all doses [insomnia (41.7%), decreased appetite (30.6%), dry mouth (26.4%), headache (21.5%), and weight decreased (12.1%)]. Small mean increases in pulse (3.5 bpm) and systolic blood pressure (0.3 mm Hg), and decreases in diastolic blood pressure (0.1 mm Hg) at endpoint were observed with triple-bead MAS.

**Conclusions:** These results support the efficacy and safety of triple-bead MAS, designed to provide ADHD symptom control up to 16 hours in adult ADHD. Triple-bead MAS was generally well tolerated, with TEAEs and a safety profile consistent with that previously seen with amphetamine use.

**References:**


**NR656**

**Wednesday, May 23, 12:00 PM - 2:00 PM**

**Randomized, Double-Blind Study of Guanfacine Extended Release in Children Aged 6 to 17 Years With Attention-Deficit/Hyperactivity Disorder (ADHD)**

**Floyd R. Sallee, M.D. Cincinnati Children's Hospital Medical Center, Department of Psychiatry, 3333 Burnet Avenue, Cincinnati, OH, 45229-3039, 9000, Joseph Biederman, M.D., James J. McGough, M.D., Timothy Wigal, Ph.D., Jessica Donahue, M.P.H., Andrew Lyne, M.S.C., Joseph Biederman, M.D.**

**Educational Objectives:**

- Participants should be able to evaluate the efficacy and safety of guanfacine extended release compared with placebo in children and adolescents with attention-deficit/hyperactivity disorder.

**Summary:**

**Objectives:** Previous studies have shown that the immediate-release formulation of the selective α2A-adrenoceptor agonist guanfacine improves symptoms of attention-deficit/hyperactivity disorder (ADHD). This study compared the efficacy of 1, 2, 3, and 4mg doses of guanfacine extended release (GXR) with placebo in children aged 6 to 17 years with ADHD.

**Methods:** In this double-blind, parallel-group, dose-ranging, multicenter, phase 3 trial, children and adolescents aged 6 to 17 years with ADHD were randomized to receive once-daily oral GXR in 1, 2, 3, and 4mg doses or placebo. The primary efficacy endpoint was change in total ADHD Rating Scale (ADHD-RS-IV) score. Secondary endpoints included changes in hyperactive/impulsive and inattentive ADHD-RS-IV subscale scores, improvement in Clinical Global Impression (CGI) and Parent Global Assessment (PGA) scores, duration of clinical effect as measured by the Conners’ Parent Rating Scale (CPRS), and safety of each GXR dose compared with placebo.

**Results:** Statistically significant reductions were observed in mean ADHD-RS-IV at study endpoint at all dose levels of GXR. Clinically meaningful changes in hyperactive/impulsive and inattentive subscales were also significant for each GXR dose at endpoint. Small to modest changes in blood pressure, pulse rate, and ECG were observed with GXR but were not clinically meaningful. GXR had no effect on laboratory parameters. Adverse events occurring in ≥5% of all GXR-treated subjects included dizziness, fatigue, headache, irritability, nausea, sedation, somnolence, and upper abdominal pain.

**Conclusions:** GXR was effective in reducing symptoms of ADHD as measured by investigator and parent rating scales, and was generally well tolerated.

**References:**

(GXR, SPD503) for the treatment of children and adolescents aged 6 to 17 years with ADHD. Interim results are reported here.

Methods: In this multicenter, open-label extension study of two previous trials, patients received GXR starting at 1mg/d and were titrated weekly in 1mg increments until their optimal dose was achieved (to a maximum of 4mg/d). Optimal doses were maintained until month 23, when doses were tapered in weekly 1mg decrements. Safety was assessed by AEs, laboratory tests, electrocardiograms (ECGs), and physical examination. Primary efficacy was change in ADHD Rating Scale-IV (ADHD-IV) total score at endpoint.

Results: Thirteen of 259 patients (5%) experienced 17 serious AEs and all were brief and resolved. The most commonly reported AEs were somnolence, headache, upper respiratory tract infection, fatigue, and sedation. No clinically relevant trends in vital signs, ECGs, hematologic parameters, urinalysis, or physical examination were seen. Mean changes in ADHD-IV total score at interim endpoint were statistically significant and clinically meaningful for all GXR doses: -18.1 (P=0.003) for 1mg, -22.4 (P<0.001) for 2mg, -22.5 (P<0.001) for 3mg, and -20.5 (P=0.001) for 4mg.

Conclusion: GXR (up to 4mg/d) was well tolerated in children and adolescents with ADHD, and efficacy appeared to be maintained over their treatment for those subjects who remained in the study.

References:

NR659 Wednesday, May 23, 12:00 PM - 2:00 PM
A Randomized, Double-Blind, Placebo-Controlled Study of Guanfacine Extended Release in Children and Adolescents With Attention-Deficit/Hyperactivity Disorder

Joseph Biederman, M.D. Massachusetts General Hospital, Clinical and Research Program in Pediatric Psychopharmacology, 55 Fruit Street, Warren Building 705, Boston, MA, 02114, 9000, Raun Melmed, M.D., Anir Patel, M.D., Keith McBurnett, M.D., Jessica Donahue, M.P.H., Andrew Lyne, M.S.C.

Educational Objectives:
- Participants should be able to describe the long-term efficacy, safety, and tolerability of guanfacine extended release in children and adolescents with attention-deficit/hyperactivity disorder.

Summary:
Objective: Guanfacine is a noradrenergic agonist that is believed to improve symptoms of attention-deficit/hyperactivity disorder (ADHD) through selective actions of α2A-adrenoceptors in prefrontal cortex. In small studies, immediate-release guanfacine has demonstrated efficacy in ADHD. A recent double-blind, multicenter trial (SPD503-301) confirmed the efficacy and tolerability of guanfacine extended release (GXR) for pediatric ADHD. We report on an open-label extension of this trial, conducted to study safety and clinical effect for up to 2 years.

Methods: Two hundred and forty children aged 6 to 17 years with a diagnosis of ADHD previously enrolled in an acute randomized trial were eligible for this extension study. GXR was titrated as needed from 2 to 4mg once a day (in 1mg increments) to achieve optimal clinical response.

Results: The most common treatment-emergent adverse events were somnolence (30.4%), headache (26.3%), fatigue (14.2%), and sedation (13.3%). Sedative events (somnolence, sedation, and fatigue) typically occurred early in the study, and most resolved as treatment continued. Small reductions in mean blood pressure and mean pulse rate were evident at monthly visits; however, cardiovascular-related adverse events were uncommon. ADHD Rating Scale-IV total and subscale scores improved significantly from baseline to endpoint for all dose groups (P<0.001 for all comparisons, intent-to-treat population).

Conclusions: GXR was well tolerated for up to 24 months of treatment and efficacy appeared to be maintained over this period for those patients who remained in the study.

References:

NR659 Wednesday, May 23, 12:00 PM - 2:00 PM
A Randomized, Double-Blind, Placebo-Controlled Study of Guanfacine Extended Release in Children and Adolescents With Attention-Deficit/Hyperactivity Disorder

Joseph Biederman, M.D. Massachusetts General Hospital, Clinical and Research Program in Pediatric Psychopharmacology, 55 Fruit Street, Warren Building 705, Boston, MA, 02114, 9000, Raun Melmed, M.D., Anir Patel, M.D., Keith McBurnett, M.D., Jessica Donahue, M.P.H., Andrew Lyne, M.S.C.
Conclusions: All GXR-treated subjects showed significant improvements in CGI-I and PGA scores and significant reduction in the overall duration of therapy as measured by CPRS-R and CTRS-R scores compared with placebo-treated subjects. Additionally, the primary endpoint, change in ADHD-RS-IV score from baseline, was significant for all subjects. A secondary subgroup efficacy analysis conducted on children aged 6-12 was significant compared with placebo, but not for subjects of greater weight aged 13-17. Further dosing analysis in this group is necessary.

References:

NR660 Wednesday, May 23, 12:00 PM - 2:00 PM
Long-Term Effects of Methylphenidate Transdermal System Treatment of ADHD on Growth
Stephen V. Faraone, Ph.D. SUNY Upstate Medical University, Psychiatry, 750 East Adams St, Syracuse, NY, 13210, 9000, Joseph Kerkering, M.B.A.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
- Describe the clinical use of the methylphenidate transdermal system (MTS) in pediatric subjects.
- Demonstrate an understanding of the effects of MTS on growth, and their clinical significance, when used to treat children with ADHD.

Summary:
Objective: To examine the long-term effects of the methylphenidate transdermal system (MTS) on the growth of children being treated for attention-deficit/hyperactivity disorder (ADHD).

Methods: Height, weight, and body mass index were measured in 188 children, ages 6 to 12 years, at longitudinal assessments for up to 36 months of treatment with MTS. These data were compared with norms provided by the Centers for Disease Control. This study used a 12-hour patch wear time as opposed to the recommended 9-hour patch wear time of the currently marketed MTS.

Results: MTS treatment led to small but statistically significant delays in growth for height, weight, and body mass index. The latter two indices were affected in a dose-dependent manner. Children who had not received prior stimulant therapy and children who entered the study with above-average height, weight, and BMI were most likely to experience growth deficits during the trial. Effects on all parameters of growth were most apparent during the first year of treatment with significant attenuation over time suggesting that the effects of MTS on growth are not progressive or cumulative.

Conclusions: Consistent with prior studies of methylphenidate, our results suggest that treatment with MTS can lead to reductions in expected height, weight, and BMI that show some attenuation over the course of treatment. Growth of ADHD patients treated with MTS should be closely monitored, but in this study, deficits in growth in relation to MTS treatment were not a significant clinical concern for most children.

This work was supported by Shire Inc.

References:

NR661 Tuesday, May 22, 3:00 PM - 5:00 PM
Differences in Medication Adherence and Patterns of Use Among Newer and Older Antidepressant Agents for Depression and Anxiety Disorders
Matthew S. Keene, M.D. Scottsdale Center for the Advancement of Neuroscience (S.C.A.N.), Executive Director, 4114 Woodlands Parkway, Suite 500, Palm Harbor, FL, 34685, 9000, David V. Sheehan, M.D., Michael Eaddy, Ph.D., John E. Kraus, M.D., Ph.D., David J. Carpenter, M.S., Stan Krulewicz, M.A.

Educational Objectives:
Participants will review results of a retrospective database analysis conducted on claims data from the PharMetrics Patient-Centric Database (Watertown, MA) representing managed care patients initiating antidepressant therapy for the treatment of depression and/or anxiety between January 1, 2002 and September 30, 2004.

At the conclusion of this presentation, participants should be able to describe how medication adherence and therapy change rates compared among antidepressants launched on or after January 1, 2002 and those launched prior to this date.

Summary:
Introduction: Early discontinuation of antidepressant therapy has been linked to relapse, poor clinical outcomes, and increased healthcare costs. Newer antidepressants sometimes claim to be more effective and tolerable, leading to improved compliance with potentially better outcomes. The purpose of this study was to compare medication adherence and therapy change among older and newer antidepressants for the treatment of depression and/or anxiety.

Methods: Using claims data from the PharMetrics Patient-Centric Database, a retrospective database analysis was conducted on managed care patients initiating antidepressant therapy between January 1, 2002 and September 30, 2004. Adults diagnosed with depression and/or anxiety disorder within a 6-month period preceding or within 30 days after the initial prescription were included. Patients were defined as adherent if they filled 144 days of therapy with once-daily OROS® MPH.

Overall, therapy changes within 6 months occurred in 22% of patients receiving an OA compared to 18% on a NA (OR 0.73; 95% CI: 0.71 to 0.74; P < 0.0001). Among the NA, the percent of patients adherent to their medication was: venlafaxine XR (38%); paroxetine CR (35%); escitalopram (34%); duloxetine (33%); and bupropion XL (31%).

Conclusions: Patients receiving newer antidepressants experienced greater adherence and less therapy changes than patients who received older agents.

Collaborative Research Grant by GlaxoSmithKline
Transdermal Methylphenidate in Adults


References:

Human Pharmacology and Abuse Potential of Transdermal Methylphenidate in Adults

Donald R. Jasinski, Sr., M.D., Johns Hopkins University, Medicine, JHBMGC FL Bldg West Tower 2nd Fl, 5200 Eastern Avenue, Baltimore, MD, 21224, 9000, Mario A. Gonzalez, Ph.D., Kenyatta A. Peoples, Pharm.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
• Describe the subjective and hemodynamic effects of MTS.
• Compare the pharmacologic effects of MTS, subcutaneous MPH, and oral phentermine

Summary:
Objective: Compare the subjective and physiologic effects of methylphenidate transdermal system (MTS) with those of parenteral methylphenidate (MPH) and placebo.

Methods: An initial dose-ranging study determined the doses utilized in this double-blind, randomized, crossover trial. Healthy adults (n=18) currently abusing stimulants received MTS (three or six 55 mg patches), placebo, subcutaneous (sc) MPH (25 or 50 mg), or oral phentermine (30 mg) at a 48-hour interval. Plasma concentrations, liking and disliking scores on the Drug Rating Questionnaire, and vital signs were measured at baseline and over 24 hours.

Results: MPH plasma levels peaked around 10-11 hours for MTS and at 1-hour for sc MPH; phentermine levels peaked after 3 hours. Incidence of euphoria was highest and dose proportional with sc MPH (74% with 50 mg; 42% with 25 mg), whereas incidence was 42%, 21%, and 26% with 3 MTS, 6 MTS, and phentermine, respectively. Phentermine and sc MPH liking scores peaked within 1-2 hours of administration; a MTS liking effect appeared after 2-4 hours and peaked at 10-12 hours. Mean maximum euphoric response with MTS was not dose related (3.1 and 2.9 with 6 MTS and 3 MTS, respectively), was less than that of 50 mg MPH (8.3; P<.05) or 25 mg MPH (4.8), and similar to phentermine (3.4). Dysphoria with MTS peaked at 12 hours, but disliking scores remained high over 24 hours. Blood pressure increases occurred with all active agents, but peak effect was significantly delayed with MTS. No relationship between plasma concentrations of d- or l-MPH and degree of euphoria/dysphoria was reported.

Conclusions: Euphoric responses seen with MTS indicated some abuse potential. The relative abuse potential of MTS was not greater than oral phentermine. MTS responses were delayed and more dysphoric than those with sc MPH or phentermine. This work was supported by Shire Inc.

References:

Treatment Satisfaction after Conversion from Oral to Transdermal Methylphenidate

Jeanne M. Landgraf, M.A. HealthActCHQ, —, 8 Faneuil Hall 3rd Floor, Boston, MA, 02109, 9000, L Eugene Arnold, M.D., Michael J. McKay

Educational Objectives:
At the conclusion of this presentation, the participant should be able to:
• Describe the clinical use of the methylphenidate transdermal system (MTS) in pediatric subjects who were previously treated with oral extended-release methylphenidate.
• Discuss the use of ADHD ratings of quality of life and satisfaction in a naturalistic setting.

Summary:
Objective: To evaluate the efficacy, safety, and treatment satisfaction of methylphenidate transdermal system (MTS) use in children with attention-deficit/hyperactivity disorder (ADHD) previously treated with oral extended-release methylphenidate and abruptly converted to MTS.

Methods: A 4-week, prospective, multicenter, open-label conversion study of MTS was conducted in children (6-12 years) diagnosed with ADHD, as defined by DSM-IV-TR criteria, on a stable dose of oral extended-release methylphenidate (XR-MPH) and whose parent/legal guardian was considering a change in treatment. Subjects were abruptly converted to MTS based on their previous dose of oral XR-MPH using a predefined dose-transition schedule, were maintained on that dose for a week, and then entered a 3-week dose-adjustment period. Efficacy was assessed by change in ADHD Rating Scale-IV (ADHD-RS-IV) total scores from baseline to study end. Secondary measures included parent-rated quality of life (QoL) using the ADHD Impact Module-Children (AIM-C) and parent- and physician-rated satisfaction with MTS using the Medication Satisfaction Survey (MSS). The AIM-C was completed at baseline and, along with the MSS, at study end.

Results: In the intent-to-treat population (n=164), conversion to MTS resulted in lower ADHD-RS-IV mean total scores at study endpoint compared with baseline (P<.0001). Mean child and family impact scale scores improved from baseline to study endpoint regardless of previous oral XR-MPH treatment. Most physicians reported satisfaction with MTS based on clinical observation and information provided by subjects and their families. MTS was generally well tolerated. Four serious adverse events in 2 patients were reported.

Conclusions: Parents reported significant improvements in child and family QoL, as measured by the AIM-C. Physicians were satisfied with ease of use, effectiveness, subject compliance with MTS, and with MTS as an ADHD treatment. This work was supported by Shire Inc.

References:
NR663 Wednesday, May 23, 12:00 PM - 2:00 PM

Have Recent Food and Drug Administration (FDA) Warnings Affected Prescriptions of Medications Approved to Treat Attention Deficit Hyperactivity Disorder (ADHD)?

Karl M. Jacobs, M.D., Quintiles CNS Therapeutics, Medical Services, 10201 Wateridge Circle, San Diego, CA, 92212, 9000, Penny K. Randall, M.D., Douglas A. Kalunian, M.D., Susan Lenderts, B.A., Amir H. Kalali, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be familiar with the affect of recent FDA warnings on the prescription of approved medications to treat ADHD.

Summary:

Introduction: Recent reviews of published literature and manufacturer clinical trial data by regulators prompted a re-evaluation of risks associated with approved treatments for ADHD. In September 2005 the FDA introduced revised labeling for the non-stimulant medication atomoxetine to include a boxed warning and additional warning statements regarding increased risk of suicidal thinking in children and adolescents being treated with this drug.

Subsequently, in February 2006, reportedly alarmed by the rising trend in prescriptions, the FDA warned about cardiovascular risks and sudden death in children with ADHD taking stimulants.

To understand potential trends in the use of atomoxetine and stimulants in response to increased regulatory action, we examined Verispan retail pharmacy prescription data from January 2005 through October 2006.

Methods: The Verispan database captures more than 1.4 billion prescriptions per year, which is nearly half of all prescription activity in the U.S. Prescriptions for atomoxetine and stimulants were gathered and combined to obtain rolling quarterly figures, and we calculated an annual growth rate for each rolling quarter.

Results: Prescriptions for atomoxetine were already declining prior to the September 2005 warning, and this trend has continued at a similar rate following the warning.

The dip in the stimulant prescriptions observed immediately following the February 2006 warning is due to the cyclical nature of this market (i.e., lower prescribing in the summer, non-school months), and the prescription rate appears to have rebounded similarly compared to this time last year.

Conclusion: Neither the stricter labeling requirements for atomoxetine nor the FDA warnings concerning stimulants, issued in late 2005 and early 2006, respectively, have had any demonstrable impact on the rate of prescriptions for either of these agents.

References:

NR664 Wednesday, May 23, 12:00 PM - 2:00 PM

12-Month Efficacy and Tolerability of MTS in Children with ADHD

Frank A. Lopez, M.D., Children’s Developmental Center, — 600 South Orlando Avenue, Suite 102, Maitland, FL, 32751, 9000, Oscar G. Bukstein, M.D., Robert L. Findling, M.D., John M. Turnbow, M.D., Liza Squires, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to:
  - Demonstrate an understanding of the clinical use of the methylphenidate transdermal system (MTS) in pediatric subjects.
  - Discuss the long-term efficacy and safety of MTS, as seen in this trial.

Summary:

Objective: Evaluate the long-term (up to 12-months) efficacy and safety of the methylphenidate transdermal system (MTS) in the symptomatic treatment of pediatric subjects with attention-deficit/hyperactivity disorder (ADHD).

Method: This was a 12-month, multicenter, open-label, flexible dose extension of four trials of MTS in subjects previously exposed to MTS (range of 3 days up to 42 weeks), placebo or OROS MPH.

Children (6-12 years) diagnosed with ADHD by DSM-IV-TR criteria entered a MTS 4-week stepwise dose titration phase (if applicable) followed by an 11-month dose maintenance phase. Efficacy measures included ADHD-RS-IV, CGI and PAG, and were assessed weekly for the first 4 weeks, monthly for 2-6 and every 2 months thereafter. Safety (including adverse events, physical exams, vital signs, ECG, and laboratory tests) was assessed throughout the study.

Results: Of the 326 subjects randomized, 157 completed the study. In the intent-to-treat population (n=324), effectiveness was demonstrated by the overall mean change in ADHD-RS-IV total score from baseline to endpoint, -9.3 ± 18.29, (P<.0001). Clinician (CGI-I) and parent (PGA) assessments were rated as improved (“very much improved” and “much improved”) at end of study, (82% and 76%, respectively), P<.0001. The most common adverse events (>10%) included decreased appetite, headache, upper respiratory tract infection, cough, pyrexia and decreased weight. Most (98%) adverse events were mild or moderate in severity. Three serious adverse events were reported and all were considered unrelated to study drug.

Conclusion: In this 12-month open-label study, MTS demonstrated efficacy in pediatric subjects with ADHD. Reported adverse events were typical for MPH and the overall safety profile was consistent with previous MTS studies and other approved MPH products. These results indicate that long-term exposure to MTS, up to 12 months of treatment, is effective and generally well-tolerated in pediatric subjects with ADHD.

This work was supported by Shire Inc.

References:

NR665 Wednesday, May 23, 12:00 PM - 2:00 PM

Efficacy and Safety of MTS in Male and Female Pediatric Subjects with ADHD

Robert L. Findling, M.D., University Hospitals Case Medical Center, Psychiatry, 11100 Euclid Avenue, Suite 200, Cleveland, OH, 44106-5080, 9000, Samuel Boellner, M.D., John C. Bunsilde, M.D., Oscar G. Bukstein, M.D., MaryAnn Livolsi, M.S.N., R.N.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to:
  - Discuss the efficacy of MTS in the treatment of pediatric ADHD.
  - Discuss the safety profile of MTS in male and female pediatric subjects with ADHD.
Summary:

Objective: Evaluate the efficacy and safety of the methylphenidate transdermal system (MTS) in male and female pediatric subjects compared with placebo, using OROS methylphenidate as a reference therapy.

Methods: This was a randomized, double-blind, placebo-controlled, parallel-group study with a 5-week stepwise dose optimization phase and a 2-week maintenance phase. Children (6-12 years) diagnosed with attention-deficit/hyperactivity disorder (ADHD) by DSM-IV-TR criteria received MTS, OROS MPH or placebo. The primary efficacy measure was the ADHD-Rating Scale-IV (ADHD-RS-IV), and was assessed at each visit beginning at baseline.

Results: Two hundred and seventy-four subjects (182 male and 92 female) received study medication. At endpoint, ADHD-RS-IV scores in active treatment groups were significantly lower than placebo (P<.0001). Within treatment groups, scores were similar in male and female subjects at baseline and endpoint. Adverse events with MTS were comparable with those of OROS methylphenidate but had a slightly higher incidence. The most common (>10%) adverse events included decreased appetite, headache, insomnia, nausea and vomiting. Male MTS subjects showed a higher incidence (>10%) than female subjects (<3%) of vomiting, upper abdominal pain, tic, and affect lability. Gender differences in the incidence of adverse events were less frequent in OROS methylphenidate and placebo groups. Adverse events were generally mild (48.2% of subjects) or moderate (19.0% of subjects) in intensity and no serious adverse events were reported.

Conclusions: MTS and OROS methylphenidate improved ADHD symptoms compared with placebo and demonstrated similar efficacy. No apparent differences were observed between male and female subjects. Adverse events were comparable in MTS and OROS methylphenidate groups, and consistent with stimulant treatment; however, MTS-treated male subjects tended to have more adverse events than female subjects. MTS was a generally well-tolerated and effective non-oral treatment for male and female pediatric subjects with ADHD.

This work was supported by Shire Inc.

References:

NR666 Wednesday, May 23, 12:00 PM - 2:00 PM
Cardiovascular Effects of MTS in Pediatric Patients
Robert L. Findling, M.D. University Hospitals Case Medical Center, Psychiatry, 11100 Euclid Avenue, Suite 200, Cleveland, OH, 44106-5080, 9000, John C. Burnside, M.D., Samuel W. Boellner, M.D., Larry Xie, Ph.D.

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

- Demonstrate an understanding of the clinical use of the methylphenidate transdermal system (MTS) in pediatric subjects.
- Discuss the cardiovascular effects of MTS seen in this trial and their clinical implications.

Summary:
Objective: Assess the cardiovascular effects of methylphenidate transdermal system (MTS), using OROS methylphenidate (MPH) as reference therapy, in the symptomatic treatment of pediatric patients with attention-deficit/hyperactivity disorder (ADHD).

Method: This was a randomized, double-blind, placebo-controlled, parallel-group study with a 5-week stepwise dose optimization and 2-week dose maintenance phase. Children (6-12 years) diagnosed with ADHD by DSM-IV-TR criteria were randomized to MTS, OROS MPH or placebo. Maximum doses utilized were MTS 30 mg and OROS MPH 54 mg. Resting blood pressure (BP) and pulse were assessed at baseline and each weekly visit. Additionally, a 12-lead electrocardiograph (ECG) was performed at screening, baseline, week 5, and end of study. Changes from baseline for these parameters were examined.

Results: A total of 274 subjects were included in the safety population. Moderate, clinically insignificant mean increases in systolic and diastolic BP from baseline were noted for MTS (1.3 mmHg and 1.6 mmHg, respectively), and for OROS MPH (1.6 mmHg and 2.7 mmHg, respectively). Mean increases in pulse were generally similar between treatments at most visits but slightly higher with MTS (5.2 bpm) and OROS MPH (4.7 bpm) compared with placebo (1.0 bpm) at end of study. Active treatments were not associated with clinically significant abnormal changes in ECG indices. One subject in each of the three treatment groups had a >60 msec increase from baseline in QT or QTc. At Week 5, more subjects receiving MTS had a 30-60 msec change in QTc from baseline. No subject had a QT or QTc ≥500 msec at any assessment period.

Conclusion: When used over a 7-week period, cardiovascular changes were more frequent in active treatment groups than placebo; however, investigators deemed these changes clinically insignificant. MTS at doses of ≤30 mg was generally well-tolerated in children with ADHD.

This work was supported by Shire Inc.

References:

NR667 Wednesday, May 23, 12:00 PM - 2:00 PM
Using the CNS Vital Signs Computerized Battery for Assessing Neurocognition in Adults with Untreated ADHD
Grant L. Iverson, Ph.D. University of British Columbia, Department of Psychiatry, 2255 Wesbrook Mall, Vancouver, BC, V6T 2A1, 1220, Brian L. Brooks, Ph.D., Margaret D. Weiss, M.D., Ph.D., C. Thomas Gualtieri, M.D., Lynda G. Johnson, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to easily identify cognitive deficits commonly associated with ADHD in adults. Specifically, the participant should have an understanding of how to assess a patient’s neurocognitive abilities using a brief computerized assessment battery, recognize frank neurocognitive impairment that is associated with ADHD in adults, and interpret test results at the individual level.

Summary:
A significant proportion of children with Attention Deficit Hyperactivity Disorder (ADHD) will experience neurocognitive deficits through adolescence and into adulthood. Adults with ADHD perform more poorly on tests measuring attention and concentration, verbal learning, and executive functioning. The purpose of this...
study is to illustrate the clinical usefulness of the CNS Vital Signs battery for identifying neurocognitive deficits in adults with untreated ADHD. Participants were 60 adults with ADHD. Their average age was 34.4 years (SD=12.9) and their average education was 14.8 years (SD=2.0). The sample was 55% male and 88.3% Caucasian. All patients were medication-free at the time of their evaluation, which included computerized neurocognitive testing. They were compared to 60 healthy control participants selected from the CNS Vital Signs normative database who were individually and precisely matched to the adult ADHD sample on age, education, gender, and ethnicity. The two groups were compared on the five domain scores using multivariate analysis of variance followed by univariate ANOVAs. There was a significant multivariate effect [Wilks' Lambda=.80; F(5,114)=5.7, p<.001, partial eta squared=.20]. Pairwise comparisons revealed significantly worse neuropsychological test scores for those in the ADHD group on the Memory (Cohen's d=.74), Psychomotor Speed (d=.48), Reaction Time (d=.54), Cognitive Flexibility (d=.80), and Complex Attention domains (d=.82). When using two or more scores below the 5th percentile as the cutoff for frank neurocognitive impairment, 28.3% of the adults with ADHD and 1.7% of the control sample scored in this range [χ²(1)=16.7, p<.001; Odds Ratio=23.3, 95% CI=3.8-141.5]. Adults with ADHD were 23 times more likely to have two or more unusually low domain scores. Knowing the base rates of low scores in untreated ADHD and healthy control samples can facilitate interpretation of individual test scores in a busy clinical practice.

References:

Summary:
To understand the importance of comorbidity on ADHD subtype

Conclusions: The even distribution of ADHD subtypes among sexes in adulthood, as opposed to childhood, may be related to uneven distribution of comorbid mood and anxiety disorders.

References:

NR669 Wednesday, May 23, 12:00 PM - 2:00 PM 
Agreement Rates Between Parent and Self Report on Past ADHD Symptoms in an Adult Clinical Sample.
Paulo E. Matos, Ph.D. UFRJ, Institute of Psychiatry, Rua Paulo Barreto 91, Rio De Janeiro, 22280-010, 3510, Gabriela Dias, M.D., Gabrieli Coutinho, Daniel Segenreich, M.D., Eloisa Saboya, Psy.D., Vanessa A. Franco, M.D.

Educational Objectives:
Agreement rates between parent and self report on past ADHD

Conclusion: results suggest retrospective information provided by adults with ADHD has moderate agreement rates with parent's report for both domains.

References:

NR670 Wednesday, May 23, 12:00 PM - 2:00 PM 
Neuropsychological Performance in Adults With ADHD as a Function of Subtype and Sex Difference
Rosa Bosch Hospital Universitari Vall d'Hebron, Servicio de psiquiatría, Pg Vall d'Hebron, 119 -129, BARCELONA, 08035, 4700, J. Antoni Ramos-Quiroga, Mariana Nogueira, Sergi Valero, Yolanda Martinez, Nuria Gomez, Miguel Casas
There exists heterogeneity in neuropsychological performance in adults with Attention Deficit/Hyperactivity disorder (ADHD) and gender as principal factors and age and anxious-depressive symptoms (BDI and STAI-E) as covariates. The group of inattentive women showed the most impairment on the Arithmetic (F = 5.689, p = 0.019), Symbol Search (F = 4.026, p = 0.047) and Logical Memory I and II (F = 5.001, p = 0.027; F = 4.126, p = 0.044) subscales. In the CVLT (F = 4.040, p = 0.046; F = 4.733, p = 0.031) and Digit Span (F = 5.345, p = 0.023) gender was significant. Our results indicate that comorbidity, sex, age and ADHD subtype are relevant in the performance of neuropsychological functions. There exists heterogeneity in neuropsychological performance in adult ADHD patients relative to clinical variables. The development of more effective pharmacological and psychotherapeutic treatments is enhanced by targeting homogeneous subgroups.

**References:**


**NR671**  
Wednesday, May 23, 12:00 PM - 2:00 PM  
**Spanish Validation of the Adult ADHD Self-Report Scale-Version 1.1: A New Strategy Score Proposal**  
J. Antoni Ramos-Quiroga, M.D.  
Hospital Universitari Vall d’Hebron. Universitat Autonoma de Barcelona, Servicio de psiquiatría, Pq Vall d’Hebron, 119 -129, Barcelona, 08035, 4700, Rosa Bosch, Sergi Valero, Nuria Gomez, Yolanda Martínez, Miguel Casas

**Educational Objectives:**

At the end of this presentation, the participant should have an understanding of the psychometric properties of the World Health Organization Adult ADHD Self-Report Scale-Version 1.1 (ASRS v1.1) Spanish version.

**Summary:**

Adult attention deficit hyperactivity disorder (ADHD) has a prevalence up to 4% of the general adult population, however in Spain adult ADHD is underdiagnosed. Screening instruments can help clinicians to detect adult ADHD. The World Health Organization Adult ADHD Self-Report Scale-Version 1.1 (ASRS v1.1) is a 6-question scale designed to screen for adult ADHD. A validation of Spanish version of the ASRS v1.1 was performed. In addition, the score model proposed by the authors of the scale was compared with a new strategy, that the summation all 6-questions, with a range from 0 to 16 points. A case control study was carried out (adult ADHD vs non ADHD). ADHD evaluation was performed using Conners Adult ADHD Diagnostic Interview for DSM-IV (CAADID-II) and the diagnosis was compared with the ASRS responses. A logistic regression study was carried out to evaluate each score model in terms of sensitivity, specificity, positive and negative predictive values (PPV and NPV). Kappa coefficients of classification accuracy and area under curve (AUC) were calculated.

Sample consisted of 90 adult with ADHD and 90 controls. Average age was 31.6 (SD=10.09) and 57.8% of subjects were men (there were not significant differences between the two groups). Logistic regression analysis showed that the original score model is significant (χ²=129.36, p=0005); sensitivity (92.2%), specificity (95.6%), PPV (94.8%), NPV (84.3%), Kappa coefficient 0.78 and AUC 0.89. The new score strategy proposed by our group suggests that 12 points is the best cut-off: sensitivity (96.7%), specificity (91.1%), PPV (91.6%), NPV (96.5%), Kappa coefficient 0.88 and AUC 0.94.

In this study, the Spanish version of the ASRS v1.1 6-question is a valid scale to screen ADHD for adults. The new proposed score strategy (12 points cut-off) showed better results than the original dichotomized model.

**References:**


**NR672**  
Wednesday, May 23, 12:00 PM - 2:00 PM  
**Differences in Personality Traits in Adult ADHD Subtypes**  
Yolanda Martinez, Hospital Universitari Vall d’Hebron, Servicio de psiquiatria, Pg Vall d’Hebron, 119 -129, Barcelona, 08035, 4700, Rosa Bosch, Sergi Valero, Ana Ortin, Mariana Nogueira, J. Antoni Ramos-Quiroga, Miguel Casas

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to identify different personality traits in adults diagnosed with different subtypes of ADHD.

**Summary:**

Attention deficit/hyperactivity disorder (ADHD) is the most prevalent disorder in childhood and adolescence. It persists into adulthood in around 50% of the cases with a prevalence of 4% in adults. The comorbidity of ADHD and other psychiatric disorders is high (60-70%), and its co-occurrence with personality disorders is common. Some studies examine clinical and non-clinical personality traits in adults with ADHD. To our knowledge, no studies about the personality traits in each subtype of the disorder have been carried out.

To identify the presence of different personality traits in each subtype of ADHD in adults using Millon’s and Zuckerman’s personality models.
To establish the existence of a personality pattern that allows the discrimination between the clinical subtypes of ADHD.

Descriptive-comparative study with a sample of 82 adults with ADHD from the Integral Adult ADD Program of the Psychiatry Department at the Hospital Universitari Vall d'Hebron. The personality traits were assessed with two self-administered instruments: MCMI-II (Millon) and ZKPQ (Zuckerman).

The inattentive (37.3%) and combined (56.9%) subtypes were considered for the statistical analysis. The hyperactive/impulsive subtype was rejected due to its low prevalence in our sample. A logistic regression model was applied and two personality factors were obtained. Greater scores on the Histrionic scale of the MCMI-II and on the Impulsivity scale of the ZKPQ were associated to a greater probability of displaying the combined subtype of ADHD. The combination of both factors allowed the detection of 79% of the combined subtype and 79% of the inattentive subtype.

The combination of clinical and non-clinical personality models, particularly Histrionic and Impulsivity factors, allows for the discrimination between the inattentive and combined ADHD subtypes.

References:

NR673 Wednesday, May 23, 12:00 PM - 2:00 PM

Attention Deficit Hyperactivity Disorder (ADHD) Symptoms in Parents of a Brazilian ADHD Non-Clinical Sample

Daniel Segenreich, Sr. Rio de Janeiro's Federal University, Psychiatry Institute of Rio de Janeiro's Federal University, Rua Paulo Barreto 91 - Botafogo, Rio de Janeiro, 22280 - 020, 3510, Paulo E. Mattos, Gabriel Coutinho, Sr., Didi Fortes, Giuseppe Pastura

Educational Objectives:
At the conclusion of this presentation, the participant should be able to know about prevalence of ADHD symptoms in parents of a Brazilian ADHD non-clinical sample.

Summary:
Objective: Studies have demonstrated higher rates of ADHD symptoms among parents of ADHD children than parents of normal control children. The aim of the current study was to compare the prevalence of ADHD symptoms among parents of ADHD and control children from a non-clinical sample.

Methods: 36 parents (21 mothers and 15 fathers) of ADHD probands and 30 parents (18 mothers and 12 fathers) of non-ADHD probands were assessed through a self-report scale for ADHD symptoms (ASRS). The number of symptoms and the global score of ASRS (ASRS-G) were considered for comparisons. For the dimensional evaluation of the clinical picture severity described on ASRS, a score was associated to each answer of the questionnaire. The answer never got the value "0"; rarely the value "1"; sometimes was associated to "2", often to "3", and very often to "4". The global score was obtained by the sum of the 18 items' values. The comparisons were conducted considering parents' gender and the diagnosis of their children.

Results: 33.3% of the mothers of ADHD children reported six or more symptoms of either inattentiveness or hyperactivity, whereas none of the control children's mothers reported six or more symptoms of either ADHD dimension (attention and hyperactivity). 33.3% of the ADHD fathers reported ADHD symptoms above the threshold of six symptoms, whereas only 8.3% of the fathers of control children reported significant number of symptoms (six or more symptoms in either dimension). The average of ASRS-G among probands' mothers was of 30.57, whereas the controls' mothers average was of 22.06. The probands' fathers average was of 28.33 against 21.3 of the fathers of the control group.

Conclusion: Parents of ADHD probands presented more ADHD symptoms than control probands' parents. These results might correlate to the findings of previous studies that suggested the disorder is genetically influenced.

References:

NR674 Wednesday, May 23, 12:00 PM - 2:00 PM

Efficacy of Extended-Release Dexamethylphenidate in Children with Inattentive and Combined Subtype ADHD: A Pooled Analysis of Two 12-Hour Placebo-Controlled Laboratory Classroom Studies

Raul Silva, M.D. New York University School of Medicine, Division of Child and Adolescent Psychiatry, 550 First Avenue, NB215B, New York, NY, 10016, 9000, Rafael Muniz, M.D., Matthew Brams, M.D., Kevin McCague, M.S.

Educational Objectives:
At the end of this presentation, the participant should be able to:
• Understand the effects of extended-release dexamethylphenidate (d/-MPH-ER) in 6-12 year-old children with inattentive or combined subtype ADHD.
• Describe the comparative effects over 12 hours of d/-MPH-ER versus d/-methylphenidate-ER (d/-MPH-ER) among children with inattentive and combined subtypes of ADHD.

Summary:
Introduction: This pooled subanalysis assessed the efficacy of extended-release dexamethylphenidate (d/-MPH-ER) and d/-methylphenidate (d/-MPH-ER) in the treatment of children with inattentive and combined subtype attention-deficit/hyperactivity disorder (ADHD).

Methods: Data from two double-blind, crossover, placebo-controlled classroom studies were pooled and stratified according to ADHD subtypes. Children 6-12 years old with ADHD previously stabilized on 20-40 mg/day MPH or 20 mg/day d/-MPH were randomized to receive d/-MPH-ER 20 and 30 mg/day, d/-MPH-ER 36 and 54 mg/day, and placebo for 7 days each. The final dose of each treatment was administered in a laboratory classroom setting where blinded raters assessed participants over 12 hours. Efficacy measures included change from pre-dose to various timepoints post-dose on the SKAMP Combined score, Department/Attention subscores, and written Math tests.

Results: A total of 166 children with ADHD participated in the two studies (14 inattentive, 152 combined, 0 hyperactive-impulsive). Significant decreases (indicative of improvement) from pre-dose in SKAMP Combined scores were observed in patients with combined subtype ADHD with d/-MPH-ER and d/-MPH-ER compared to increases (indicative of worsening) with placebo (all p<0.001) from 0 to 12 hours post-dose (AUC0-12: d/-MPH-ER 20 and 30 mg/ day: -83.7 and -128.5; d/-MPH-ER 36 and 54 mg/day: -72.5 and -
tial avoidance, i.e. a strong tendency to avoid aversive inner experi-
ences, has been shown to be important for the development and
maintenance of psychiatric disorders. Therefore it is important to
develop interventions that help to reduce these tendencies. As
similar trends were observed for the inattentive subtype group, how-
er, results were inconclusive due to the small n.

Supported by Novartis Pharmaceuticals.

References:
1. Silva RR, Muniz R, Pestreich L, et al: Efficacy and duration of
effect of extended-release dexamfetamine versus placebo
in schoolchildren with attention-deficit/hyperactivity disorder. J
2. Wigal S, Gupta S, Guinta D, Swanson JM: Reliability and valid-
ity of the SKAMP rating scale in a laboratory school setting.

NR675 Wednesday, May 23, 12:00 PM - 2:00 PM
Effects of an Intensive Emotion Regulation Training on the Tendency to Avoid Situations that Trigger Negative Emotions in a Sample of CBT-treated Inpatients.

Matthias Berking, Ph.D. University of Washington, Department of Psychology, Box 351525, Seattle, WA, 98195-1525, 9000

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand a) why experiential avoidance contributes to the development and maintenance of psychiatric disorders and b) that an intensive emotion regulation skill training can be an effective intervention to reduce experiential avoidance.

Summary:
The objective of the presented research is to clarify how experiential avoidance can be reduced in psychiatric patients. Experien-
tial avoidance, i.e. a strong tendency to avoid aversive inner expe-
riences, has been shown to be important for the development and
maintenance of psychiatric disorders. Therefore it is important to
develop interventions that help to reduce these tendencies. As
deficits in emotion regulation skills can be seen as the cause of
experiential avoidance it was assumed that a treatment module
that focuses on enhancing these skills will help to reduce experien-
tial avoidance. In order to test this hypothesis 102 CBT-treated
patients suffering from diverse mental disorders where randomly
assigned to either treatment as usual plus a one week training of
emotion regulation skills, or to treatment as usual plus a one week
intensive physiotherapy (control) condition. The results showed
that the patients in the skills enhancement condition showed a
significantly stronger reduction in experiential avoidance than the
patients in the control condition. Thus emotion regulation skill
training can be seen as an effective means to reduce experiential
avoidance.

References:
1. Hayes AM, Beevers CG, Feldman GC, Laurenceau JP & Per-
iman C: Avoidance and processing as predictors of symptom
change and positive growth in an integrative therapy for depres-

Dimensional Approach to Diagnosis and Treatment. J Consult

NR676 Wednesday, May 23, 12:00 PM - 2:00 PM
Ideal: A 6-Month Placebo-Controlled Study of the
First Transdermal Patch in Alzheimer's Disease - Rivastigmine Patch Versus Capsule

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Floor, St. Louis, MO, 63104-1016, 9000

Educational Objectives:
At the conclusion of this presentation, the participant will under-
stand the potential efficacy and tolerability profile of a novel AD
treatment formulation that may be available in the US by the end
of 2007.

Summary:
Background: Transdermal delivery avoids the first pass effect
seen with oral administration, providing more even plasma con-
centrations, reduced Cmax and continuous exposure. The rivastig-
mine (Exelon®) patch is the first transdermal treatment to be de-
veloped for Alzheimer's disease (AD).

Objective: To compare the efficacy, safety and tolerability of
rivastigmine patches with conventional capsules and placebo.

Methods: IDEAL (Investigation of transDermal Exelon in ALzheimer's disease) was a 24-week, multicenter, randomized, double-
blind, double-dummy, placebo- and active-controlled evaluation
of once-daily rivastigmine patches versus twice-daily capsules in
1,195 patients with AD. Target patch sizes were 10cm² and 20cm²
(delivering 9.5 or 17.4mg/24-hr, respectively) and capsules were
6mg twice-daily. Patches (rivastigmine or placebo) were applied
to dry, hairless skin on the upper back every morning and worn
for 24 hours. Normal activities including bathing were allowed.
All patients also took a capsule (rivastigmine or placebo) twice-daily.

Primary efficacy measures were the AD Assessment Scale - cog-
nitive subscale (ADAS-cog) and AD Cooperative Study - Clinical
Global Impression of Change (ADCS-CGIC). Secondary outcome
measures assessed a range of symptom domains, including activi-
ties of daily living and caregiver preference for patch versus
capsule.

Results: Rivastigmine patches showed significant benefits ver-
sus placebo on measures of cognition, global impression of
change and activities of daily living. The 10cm² patch showed
similar efficacy to rivastigmine capsules, with placebo-like rates
of nausea and vomiting (5% vs 7.2% and 3.3% vs 6.2% for nausea
and vomiting, respectively). The 20cm² patch showed numerically
superior cognitive scores versus the 10cm² patch (p< ns), with
similar tolerability to capsules. Local skin tolerability was good.
Approximately 70% of caregivers expressed an overall preference
for rivastigmine patch versus capsules. Data from additional analy-
yses will also be presented.

Conclusion: A transdermal patch may prove to be the best way
to deliver rivastigmine in the treatment of AD.

References:
of a transdermal patch formulation of rivastigmine in healthy
volunteers: relative effects of body site application. J Clin Phar-
macol, in press.
2. Cevc G: Drug delivery across the skin. Expert Opin Investig

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NR677 Wednesday, May 23, 12:00 PM - 2:00 PM
Effectiveness and Safety of Donepezil in Patients with Severe Alzheimer’s Disease: Results From a 12-Week Open-Label Extension (OLE) of a 24-Week Double-Blind Placebo-Controlled Study
Sandra Black, M.D. University of Toronto, Cognitive Neurology Unit, LC Campbell Cognitive Neurology Research Unit, Sunnybrook Health Sciences Centre, Toronto, ON, M4N 3M5, 1220, Rachelle S. Doody, M.D., Honglan Li, Ph.D., Thomas M. Cawley, Ph.D., Yijun Sun, Ph.D., Yikang Xu, Ph.D., Sharon Richardson, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to demonstrate an understanding of the effectiveness and safety of donepezil in the treatment of patients with severe Alzheimer's disease (AD). Participants should also be able to make informed decisions on the most appropriate therapeutic strategies (treatment choice and timing of treatment) for their patients in the more severe stages of AD.

Summary:
Objective: To evaluate the effectiveness and safety of donepezil for severe Alzheimer's disease (AD).
Methods: Patients who completed a 24-week double-blind period were eligible to enter the OLE, and received donepezil 5 mg/day for 6 weeks, followed by 10 mg/day for 6 weeks. Outcome measures included the Severe Impairment Battery (SIB), Mini-Mental State Examination (MMSE), modified Alzheimer's Disease Cooperative Study-Activities of Daily Living Inventory for severe AD (ADCS-ADL-sev), Neuropsychiatric Inventory (NPI), Caregiver Burden Questionnaire (CBQ), and Resource Utilization for severe Alzheimer's Patients (RUSP). We compared Week 36 scores to baseline scores at the start of the double-blind period.
Results: Ninety-four percent of patients who completed the double-blind period entered the OLE (111 donepezil-treated [DON-DON group], 118 placebo-treated [PLA-DON group]) and, overall, 87% completed the OLE (90% DON-DON, 85% PLA-DON). At Week 36, mean SIB scores decreased from baseline by 1.52 points (DON-DON group) and by 4.68 points (PLA-DON group); MMSE scores remained near baseline levels and ADCS-ADL-sev scores declined by a similar extent in both groups; NPI scores improved relative to baseline in both groups; no changes were noted on the CBQ or RUSP in either group. Adverse event-related withdrawal rates in the open-label period were low for the DON-DON and PLA-DON groups (3.6% and 10.2%). With the exception of agitation (4 DON-DON patients; 7 PLA-DON patients) observed adverse events were consistent with the known donepezil safety profile.
Conclusions: In patients with severe AD, continued donepezil treatment was well tolerated over 36 weeks. At the end of this 36-week study, the PLA-DON group did not catch up to the DON-DON group on cognition, but no differences between groups were seen in measures of function, behaviour, caregiver burden, or resource use.

References:

NR678 Wednesday, May 23, 12:00 PM - 2:00 PM
Prevalence and Risk Factors for Depression and Anxiety in Hospitalized Cardiac Patients in Pakistan
Muhammad W. Azeem, M.D. CABHS, CABHS, CABHS, 11705 State Avenue, Brainerd, MN, 56401, 9000, Imtiaz A. Dogar, M.B.B.S., Imran Khawaja, M.D.

Educational Objectives:
1. The participants should be able to recognize the prevalence of depression and anxiety among hospitalized cardiac patients in Pakistan.
2. The participants will learn the various risk factors associated with depression and anxiety among hospitalized cardiac patients in Pakistan.
3. The participants will be able to recognize the need and importance of close monitoring for depression and anxiety in hospitalized patients with cardiovascular diseases in Pakistan.

Summary:
Introduction: Several studies have shown a strong association between cardiovascular diseases, depression, and anxiety. To our knowledge this is the first study done in Pakistan looking at the prevalence and risk factors for depression and anxiety in hospitalized cardiovascular patients.
Objective: To determine the prevalence and risk factors for depression and anxiety in cardiovascular patients in an inpatient tertiary care setting in Pakistan.
Methods: All patients admitted to a cardiac unit over a period of 8 weeks, who gave consent, were evaluated with DSM IV criteria, for diagnosing major depression and generalized anxiety disorder.
Results: 100 patients entered the study. Mean age for the entire sample was 52.2 ± 11.12 years, males 60 / females 40. Sixty eight (33 males/35 females) met the DSM IV criteria for major depression and generalized anxiety disorder or both (anxiety = 16, Males 3/ Females13, depression = 47, Males 28/Females19, and depression + anxiety = 5, Males 2 / Females 3). Mean age for patients meeting criteria for depression and anxiety was 50.81 ± 10.04, 83.3% were married and 4.4% single, 47% illiterate, 56% from lower and 34% from middle socioeconomic status, 75% living in urban areas, 34 (50%) were taking psychotropic medications. A total of 87.5 % (35/40) of the entire female sample met the criteria for depression and anxiety or both. The rates of anxiety and depression were extremely high among the widows, all females (8/ 10, 80%) and house wives (33/37, 89%).
Conclusions: 1. This study shows high prevalence of major depression and generalized anxiety disorder in cardiac patients in Pakistan.
2. Being female, house wife and widow are high risk factors associated with depression and/or anxiety in this population, requiring close monitoring.
3. Prospective control studies are needed involving larger sample size, multiple sites and follow-ups over longer period of time.

References:

NR679 Wednesday, May 23, 12:00 PM - 2:00 PM
Cross-Cultural Validity of a Quality of Life Instrument Using New Psychometric Approach -Comparison Between Brazil Versus Other Countries in Lido Study
Neusa S. Rocha, M.D. UFRGS-HCPA, Psychiatry, Avenida Iguacu, 119/201, Petropolis, Porto Alegre-RS, 90470-430,
Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize particularities of cross-cultural research in developing countries.

Summary:

Aims: The Longitudinal Investigation of Depression Outcomes (LIDO) was a study including 6 centers worldwide (Brazil, Australia, Russia, Spain, USA and Israel). Several measures were made during this study. One of them was quality of life using WHOQOL-bref. The main aim of this present research is to evaluate cross-cultural validity of this measure between Brazil and other countries involved in LIDO Study.

Methods: To range the purpose of the present study we use a differential item functioning (DIF) analysis from Rasch model. We investigated data from six countries, assessing quality of life and economic aspects of undiagnosed depression among primary care patients.

Results: We found that Brazil as a factor shown DIF in 13 of 26 items of WHOQOL-bref. The most affected domains were Psychological with DIF in 4 of 6 items, followed by Environment which shown DIF in 4 of 8, whereas, Physical domain shown DIF only in 2 of 7 items and Social domain 1 of 3 items.

Conclusions: These finding may be accounted by some cultural differences related to social economic resources (environment domain) and to the meaning of psychological suffering (psychological domain), which may differ among these cultures studied. Although WHOQOL-bref was constructed by some different cultures in the same time to ensure cross-cultural validity, it can not be demonstrated by this sophisticated statistical method. The quality of life may vary more strongly within some cultures than others. In this respect, Brazil is a country with a broad diversity of cultures, which can have a strong influence on its concept and understanding of quality of life.

References:


NR680 Wednesday, May 23, 12:00 PM - 2:00 PM ADHD Management In Hispanic and Caucasian Patients from a Large Health Plan

Eugenio M. Rothe, M.D. University of Miami, 1 Hoegi-dong, Dongdamoon-gu, Dept of Psychiatry, Seoul, 130-702, 5900, Yong Chul Park, M.D., Seokkyung Lee, M.D., AHRANG CHO, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will recognize that the management of ADHD varies greatly between Hispanic and Caucasian patients enrolled in a large, managed care health plan, with differences such as fewer prescriptions filled for ADHD medications and less treatment continuity among Hispanic patients.

Summary:

Objective: To evaluate attention-deficit/hyperactivity disorder (ADHD) management between Hispanic and Caucasian patients.
Results: Most data showed negative attitude for the families. However, they did not have enough evidences. There are also several articles against latchkey parents in journals. Even though investigators did in depth interview with them, the number of subject families was less than 20. Only two articles were positive for family and concluded there are prejudices about those families. Past separated families were supported by the government, nationalism, and recent separated are regarded as selfish. In general, separated families stemmed from parents' will to get financial base with family consent. It means that past separated families were supported by the government, nationalism, and recent separated are regarded as selfish.

Conclusions: Authors analyzed various sources about latchkey family and concluded there are prejudices about those families. In general, separated families stemmed from parents’ will to get better chance of education for children. Therefore, it does not seem as pathologic but spontaneous.

References:

NR682 Wednesday, May 23, 12:00 PM - 2:00 PM
Detection of Oral Cavity Early Injuries in Eating Disorders (ED) and Correlation With Flag Biological Markers and ED Behaviours
Oscar L. Meehan, Sr., M.D. The Royal College of Psychiatry, International Department. Gregoria Matorras 3660, Cerro de las Rosas, Cordoba - CAP, 5009, 3570, Rene Panico, Sr., Ph.D.

Educational Objectives:
- Early symptom identification and detection play a crucial role in prevention and early therapeutic interventions in any illness.
- The study aims at identifying prevailing injuries and physical signs of oral mucous membrane and their timing correlation with physical and biological flag markers: vitamin A and carotene plasma increase levels, amenorrhea, and eating disorder associated behaviours: self injury, laxative and diuretic misuse, dehydration and vegan type diet.

Summary:
- Methods and Material: Case-control study of 65 untreated outpatients of a national ED unit in Cordoba, Argentina, matched by gender and age with 65 healthy control group.
- Diagnosis based on The Diagnostic and Statistical Manual of Mental Disorders IV (DSM-IV) criteria for Anorexia and Bulimia Nervosa.
- Prior to the study subjects and control group had a thorough oral cavity examination at the Dental Medical School, a structured interview designed to identify eating habits, weight control methods, and psychological symptoms related to eating disorders, and the EDI-2 Scale.
- Inclusion Criteria: DSMIV Eating Disorders Criteria for Bulimia (BN) and Anorexia (AN)
- Exclusion Criteria: DSMIV Affective - Psychotic - Anxiety Disorders
- Physical examination of the oral cavity was conducted following a comprehensive set of clinical procedure instructions and guidelines of the Clinical Oral Cavity Examination Procedure and a dynamic examination of swallowing movements.
- Results and conclusions: In the observed group 61 subjects had oral mucosa lesions (94%) with 112 injuries in all, whereas less 18.5% of the controls had them, 15 injuries in all, and a positive correlation between lesions and newly onset ED symptoms, behaviours and biochemical evidence was also found.
- Typical lesions: desquamative queilitis n 28, 43% - lip erythema n 28, 43% - yellow palate n 22, 35% - purpura n 17, 26% - bitten mucosa n 12, 18% - palatal atrophy n 5, 8%.
- According to the Fisher’s Test there is statistical significance @ p<0.005 for each of the injuries in the observed group and in the controls.
- The description of these injuries and their correlation with time of onset of ED has not been previously published in the medical literature.

References:

NR683 Wednesday, May 23, 12:00 PM - 2:00 PM
Problems Applying the DSM-IV Eating Disorders Diagnostic Criteria in a General Psychiatric Outpatient Practice
Mark Zimmerman, M.D. Rhode Island Hospital, Psychiatry, 235 Plain Street, Suite 501, Providence, RI, 02905, 0000, Caren Francione-Witt, M.A., Iwona Chelminska, Ph.D., Diane D. Young, Ph.D.

Educational Objectives:
- At the conclusion of this presentation the participant should be able to describe the prevalence of DSM-IV eating disorders in psychiatric outpatients, and recognize the problems with the clinical applicability of the DSM-IV diagnostic criteria for eating disorders.

Summary:
- Background: A substantial number of patients treated in specialized eating disorder programs fail to meet criteria for anorexia nervosa or bulimia nervosa, the two eating disorders with specified criteria in DSM-IV. These patients are diagnosed with eating disorder not otherwise specified (NOS). We hypothesized that in a general psychiatric setting, where the severity of eating pathology is likely to be milder than in specialty programs, an even greater proportion of patients with disordered eating will fail to meet full criteria for one of the DSM-IV eating disorders and instead will be diagnosed with eating disorder NOS.
- Methods: Two thousand five hundred psychiatric outpatients were interviewed with the Structured Clinical Interview for DSM-IV (SCID) upon presentation for treatment.
- Results: Fourteen percent (n=354) of the patients were diagnosed with a lifetime history of an eating disorder. Almost half (n=165) of the patients with an eating disorder had it at the time of presentation, one-sixth (n=59) had an eating disorder in partial remission, and slightly more than one-third (n=130) had a past diagnosis. When binge eating disorder is combined with the other forms of eating disorder NOS, as it is in DSM-IV, then 89.1% (147/165) of the patients with a current eating disorder were diagnosed with eating disorder NOS.
- Conclusions: The preponderance of eating disordered patients in a general psychiatric setting were diagnosed with eating disorder NOS. This suggests that there is a problem with the clinical applicability of the diagnostic criteria in the DSM-IV eating disorder category.

References:
1. Turner H, Bryant-Waugh R: Eating Disorder Not Otherwise Specified (EDNOS): Profiles of clients presenting at a commu-


NR684 Wednesday, May 23, 12:00 PM - 2:00 PM
Rate of Weight Restoration as a Predictor of Early Clinical Deterioration in Patients With Eating Disorders
Brian C. Lund, Pharm.D., Laureate Psychiatric Clinic and Hospital, Laureate Research Center, 6855 S. Yale Avenue, Tulsa, OK, 74136, 9000, Craig L. Johnson, Ph.D., Elsa R. Hernandez, Ph.D., William R. Yates, M.D., Jeffrey R. Mitchell, M.D., Patrick A. McKee, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to: (a) consider the potential impact of weight restoration rate during inpatient eating disorder treatment, and (b) recognize the need to enhance and develop evidence-based interventions for patients with eating disorders.

Summary:
Introduction: Failure to achieve weight restoration above 90% of expected body weight is a predictor of relapse. However, little is known about the impact of weight restoration rate.

Methods: Data were obtained from the ongoing Laureate Outcomes and Genetic Initiative (LOGI). LOGI participants undergo extensive phenotypic assessment, DNA banking and long-term prospective follow-up. Participants in the eating disorder substudy of LOGI were recruited upon acute inpatient admission to a specialty eating disorders program. To date, 140 participants have been enrolled. Results reported here were derived from the first 37 participants who completed one year of follow-up and received weight restoration during inpatient treatment. Clinical deterioration was defined as an increase in the eating disorder Clinical Global Impression-severity score from discharge to year one follow-up. Multiple logistic regression was used to test for association with clinical deterioration and adjust for potential confounding factors, including demographics, eating disorder psychopathology, and psychiatric comorbidity.

Results: Weight restoration rates during inpatient treatment varied from one to three pounds per week. Within this range, slower rates were associated with increased risk of deterioration after discharge, specifically if below 1.75 pounds per week (69.6% vs 35.7%, \( \chi^2 = 4.06, p = 0.0438 \)). This association remained statistically significant even after adjusting for confounding factors. Other restoration-related variables, including discharge body mass index, weight gained, and length of stay were not significant predictors.

Discussion: Weight gain is closely controlled during inpatient eating disorder treatment. Within the typical range, however, we found that slower rates predicted risk for early clinical deterioration after discharge. These results support the APA guideline for restoring two to three pounds per week during inpatient treatment. It is unclear if more rapid weight gain causes favorable clinical outcome, or is simply a marker of the patient's physiological or psychological readiness to tolerate weight restoration.

References:


NR685 Wednesday, May 23, 12:00 PM - 2:00 PM
Eating Disorder Prevalence Correlates with Mean Annual Temperature
Michael J. Norden, M.D. University of Washington, Psychiatry, 18419 17th Ave NW, Seattle, WA, 98177, 9000, Timothy David Brewerton, M.D., David Haynor, M.D., Ph.D., David Avery, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that the relative point prevalence of anorexia nervosa (AN) and bulimia nervosa (BN) changes with ambient annual temperature. Specifically, that anorexia is relatively less prevalent and bulimia more prevalent in hotter climates. He or she should recognize that this correlation raises numerous unanswered questions concerning causation that deserve further exploration.

Summary:
Introduction: Assaults and violent suicides are known to correlate with elevated ambient temperatures (TEMP). It was hypothesized that bulimia nervosa (BN) may similarly involve a reduction of serotonin metabolism may also increase with heat. In contrast, in the case of anorexia nervosa (AN) there have been reports of positive responses to the therapeutic application of heat. We hypothesized that the ratio of AN to BN prevalence would decrease with increasing ambient TEMP.

Method: Most prevalence studies have been conducted on young, non-rural Caucasian females, and reported point prevalence. A literature search was conducted in Pubmed using the search terms (anorexia nervosa OR bulimia nervosa) AND prevalence, to identify potential studies. In addition references were checked in papers to broaden the search.

Inclusion criteria: studies used DSM-III-R, DSM-IV, or ICD-10 diagnostic criteria and reported point prevalence rates for young Caucasian females in areas not primarily rural.

Exclusion criteria: subjects selected in such a way as to clearly not be representative of the community — such as college students, medical patients, or psychiatric patients. Fifteen studies met these criteria, and twelve were from Europe. This group was analyzed separately as these comparisons have fewer cultural confounds. We collected data on average annual TEMP for all of the locales.

Results: The ratio of AN to BN was strongly and inversely correlated with average annual TEMP of the communities (Spearman correlation, rho = -0.805, p < 0.001). For just the twelve European studies the correlation was similarly strong (rho = -0.715, p < 0.01).

Discussion: This robust correlation deserves to be further investigated especially in light of the potential recently raised regarding the therapeutic use of heat in AN. The possible role of serotonergic mechanisms mediating environmental influence deserves exploration. These data also raise the possibility of gene-environment mechanisms involving environmental TEMP in the etiology of eating disorders.

References:

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NR686  Wednesday, May 23, 12:00 PM - 2:00 PM
Life Satisfaction, Health-Related Quality of Life, and Health Behaviors Among U.S. Adults
Tara W. Strine  Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, 4770 Buford Highway NE, Mailstop K-66, Atlanta, GA, 30341, 8000

Educational Objectives:
At the conclusion of this presentation, the participants should be able to describe the sociodemographic characteristics, quality of life, and health behaviors of U.S. community-dwelling adults who report dissatisfaction with life.

Summary:
Background and Objective: Life satisfaction is a predictor of longevity and psychiatric morbidity. In turn, it is related to other health predictors such as favorable self-reported health, social support, and positive health behaviors. Despite this, there have been no recent population-based U.S. studies regarding life satisfaction. Therefore, we examined health-related quality of life (HRQOL), and health behaviors by level of life satisfaction among community-dwelling adults residing in the U.S. and its territories.

Methods: Data were obtained from the Behavioral Risk Factor Surveillance System, an ongoing, state-based, random-digit telephone survey of the non-institutionalized U.S. population aged ≥18 years. In 2005, one life satisfaction question, 4 HRQOL questions, 2 disability questions, and 4 health behavior questions were administered in the 50 states, the District of Columbia, Puerto Rico, and the Virgin Islands.

Results: An estimated 5.6% of adults reported that they were dissatisfied/very dissatisfied with their lives. As the level of life satisfaction decreased, the prevalence of fair/poor general health, disability, and infrequent social support increased. Additionally, as life satisfaction decreased, the mean number of days of recent physical distress, mental distress, and activity limitation increased. Moreover, the prevalence of smoking, obesity, physical inactivity, and heavy drinking also increased with decreasing level of life satisfaction.

Conclusion: Our results suggest that the implications of life satisfaction are germane to public health and psychiatry. Further assessment of life satisfaction may identify both factors relevant to its utility as a theoretical construct in different populations, as well its potential in predicting mental illness.

References:

NR687  Wednesday, May 23, 12:00 PM - 2:00 PM
Nicotine Dependence Among Adults in Bucaramanga, Colombia: Prevalence and Associated Factors

Educational Objectives:
At the conclusion of this presentation, the participants should be able to recognize the prevalence and associated factors with nicotine dependence in Colombian people.

Summary:
Background: Nicotine dependence is the most common substance dependence in Colombian population. However, its factors associated are unknown.

Objective: To establish the prevalence and factors associated with nicotine dependence among adults in Bucaramanga, Colombia.

Method: A cross-sectional study was done with adults aged between 18 and 65 years. Participants completed the CAGE questionnaire, General Health Questionnaire (GHQ-12), and the Cigarette Dependence Scale (CDS) (daily cigarette smokers). Regression logistical was calculated for controlling confounding variables.

Results: A total of 2496 people participated in this reasearch.

Conclusions: Nicotine dependence is high among Colombian smokers. Smokers with nicotine dependence present more alcohol and coffee consumption, and mental common disorders than non-nicotine dependence smokers and non-smokers.

References:

NR688  Wednesday, May 23, 12:00 PM - 2:00 PM
A Comparison of Two Scales for Nicotine Dependence in a Sample From the General Population in Bucaramanga, Colombia
Adalberto Campo-Arias, M.D. Instituto de Investigación del Comportamiento Humano, Dirección de Investigaciones, Transversal 93 No 53-48, Interior 68, Bogotá, 57 1, 3010, Jaider A. Barros-Bermudez, M.D., German E. Rueda-Jaimes, M.D., Luis A. Díaz-Martínez, M.S.C., Francisco J. Diaz, Ph.D.

Educational Objectives:
At the end of this sesion, the attendants will be able to recognize the differences between the Fagerström Test for Nicotine Dependence and the Cigarette Dependence Scale.

Summary:
Background: The Fagerström Test for Nicotine Dependence (FTND) is the most popular scale for identifying nicotine dependence. However, the FTND has limited psychometric properties.
Recently, The Cigarette Dependence Scale (CDS) has been designed and appears to possess better properties than the FTND.

**Objective:** To compare some psychometric properties of the FTND and CDS in people from the general population of Bucaramanga, Colombia.

**Method:** One hundred twenty-six current smokers completed the FTND and CDS. They were aged between 18 and 65 years (mean=38.0; SD=13.8); mean scholarship was 7.7 years (SD=4.0); 52.4% were employees or self-employed; 52.4% were married; and 52.4% lived in middle- and 47.6% in low-class neighborhood. Cronbach alpha, sensitivity, specificity, predictive values, likelihood values, Cohen kappa, and ROC area were computed for each scale. The Composite International Diagnostic Interview for nicotine dependence applied by a psychiatrist was taken as the gold-standard.

**Results:** For the FTND Cronbach alpha was 0.72; sensitivity, 0.69; specificity, 0.71; positive predictive value, 0.90; negative predictive value, 0.40; positive likelihood ratio, 2.4; negative likelihood ratio, 0.43; Cohen kappa, 0.32; and ROC area, 0.74; and for the CDS, Cronbach alpha was 0.90; sensitivity, 0.77; specificity, 0.71; positive predictive value, 0.90; negative predictive value, 0.47; positive likelihood ratio, 2.8; negative likelihood ratio, 0.33; Cohen kappa, 0.40; and ROC area, 0.80.

**Conclusions:** The CDS seems to exhibit better psychometric properties than the FTND in Colombian smokers. These observations must be replicated in other and larger populations.

**References:**

**NR689  Wednesday, May 23, 12:00 PM - 2:00 PM**

Health Impact of Depression: Results From a Population-Based Study

Jose Luis Ayuso-Mateos, M.D. Hospital Universitario de La Princesa / UAM, Psychiatry, Diego de León 62, Madrid, 28006, 4700, Marta Nieto-Moreno, Psy.D., Patricia Gimeno-Blanco, Psy.D., Maria Cabello, Psy.D., Emese Verdes, Somnath Chatterji, M.D.

**Educational Objectives:**
- At the conclusion of this presentation, participants should be able to recognize the great negative impact that depression has on individual's health rate, especially when it is a co-morbid state of prevalent physical chronic disease. Secondly, participants should be aware of the public health burden of depression and of the need for the development of effective management strategies at the community level.

**Summary:**
- **Introduction:** Depression is one of the leading causes of disease burden globally. It is also frequently co-morbid with other chronic diseases. However, few studies have analyzed the effect of depression on overall health outcomes at the population level.
- **Objective:** To explore the impact of depression on individuals' health scores in the general population, and to compare these with the health scores of other prevalent chronic conditions.
- **Methods:** Data were derived from the World Health Organization, in which 6364 adult responders were assessed to study health, health-related outcomes, and their determinants. Prevalence of depression was estimated based on ICD-10 criteria, as well as the prevalence of four chronic physical diseases: angina, arthritis, asthma, and diabetes based on algorithms derived via a Diagnostic Item Probability Study. Mean health scores and mean health-related domains scores (cognition, affect, vision, pain, discomfort, self-care, interpersonal-skills, vision, sleep-energy) were compared across disease states.
- **Results:** One-year prevalence of ICD-10 depressive episode alone was 3.48% in the general population; for angina it was 0.68%; 3.91% for arthritis; 4.63% for asthma; and 3% for diabetes. Among 12.2% and 33.66% of participants with a chronic disease had co-morbid depression. Regarding mean health scores, major depression arises as the most disabling condition, followed by angina, arthritis, diabetes, and finally asthma. Co-morbid depression significantly worsened health scores in respondents.
- **Conclusions:** In the Spanish general population, depression is associated with a similar or higher negative drop in health rate compared with other prevalent chronic conditions. The co-morbid state of depression is responsible for worse health when compared with depression alone, with any of the chronic diseases alone, and with any combination of chronic diseases without depression. Depression is the most disabling disorder in terms of self-reported health rate and health-related domains.

**References:**

**NR690  Wednesday, May 23, 12:00 PM - 2:00 PM**

Fatal Reports in Intramuscular Versus Oral Antipsychotics in the FDA Adverse Event Reporting System (AERS)

Sebastian Sorsaburu, M.D. Eli Lilly and Company, Lilly Research Laboratories, Lilly Corporate center, Indianapolis, IN, 46285, 9000, Karen Holdridge, M.P.H., F. Patrick DeLisle, Meghan E. Jones, M.P.H., Kenneth Hornbuckle, D.V.M.

**Educational Objectives:**
- At the conclusion of this presentation the participant should be able to describe three different antipsychotics that have FDA-approved oral and rapid acting IM formulations, explain at least two possible reasons that acutely agitated patients may be at increased risk for serious adverse events, and describe two limitations of spontaneous data.

**Summary:**
- **Background:** Oral antipsychotics (AP) are used for acute and maintenance treatment of schizophrenia and bipolar disorder. Intramuscular (IM) forms are typically approved for acute agitation due to psychiatric conditions, but agitation might also present in patients with substance abuse, delirium, or other conditions and may be treated with IM AP. Differences in oral and IM populations may lead to different adverse event (AE) profiles. Three AP have FDA-approved oral and IM formulations: olanzapine (OLZ), ziprasidone (ZIP), and haloperidol (HAL).
- **Objectives:** To describe the proportion of cases with a fatal outcome among reports with IM vs oral administration of OLZ, ZIP, and HAL in the FDA AERS database.
- **Methods:** AERS is a publicly available database containing AEs spontaneously reported to FDA. All reported cases through March 2006 for OLZ, ZIP, or HAL were categorized by route of administration (injection and oral). The percent of fatal cases was calculated for each drug and formulation.
Results: In a large proportion of cases, route of administration was not reported. The numbers of identified IM/oral cases were OLZ: 35/4558, ZIP: 159/1867, and HAL: 1139/4085. The percent of cases with a fatal outcome was greater for IM relative to oral use across all AP (OLZ: 34% vs 11%; ZIP 38% vs 12%; HAL: 24% vs 15% for IM and oral, respectively).

Conclusions: The greater proportion of reported fatal outcomes in IM cases is consistent with the hypothesis that agitated patients may have a different baseline risk. Patients treated with IM AP may be at increased risk of serious AEs due to factors like the state of agitation, intoxication, medical comorbidities and concomitant treatments (physical restraints, polypharmacy, etc). Results must be interpreted in the context of known limitations of spontaneous data as well as the small numbers of IM cases for OLZ and ZIP.

References:
NR693  Wednesday, May 23, 12:00 PM - 2:00 PM
Risk Factors for Schizophrenia: Are They Specific?
Mark Weiser, M.D. Sheba Medical Center, Psychiatric, Sheba Medical Center, Tel-Hashomer, Ramat-Gan, 52621, 5081, Avi Reichenberg, M.D., Efrat Kravitz, B.A., Gadi Lubin, M.D., Jonathan Rabinowitz, Ph.D., Shlomo Noy, M.D., Michael Davidson, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand that many of the risk factors for schizophrenia are non specific.

Summary:
Background: Poor cognitive and social abilities, having a non-psychotic psychiatric diagnosis in adolescence (anxiety, depression, personality disorder), cigarette smoking, low socio-economic status (SES), and fewer years of formal education have been implicated as risk factors for schizophrenia. However, many of the studies on the topic indicate that these risk factors have relatively low specificity. We examined the specificity of these risk factors by assessing their effect on risk for going to jail during military service, as a proxy for an non-specific undesirable life event.

Methods: We identified 627,103 male adolescents assessed by the Israeli draft board, and examined the effect of these putative “schizophrenia” risk factors on the risk for going to jail for 7 days or more during military service. All potential risk factors were dichotomized to low (more than 1 SD below population mean or higher), and normal-high (1 SD below population means or higher) social cognitive functioning (OR=1.14), low cognitive functioning (OR=3.48), low SES (OR=2.09), less education (OR=6.26), having a non-psychotic psychiatric diagnosis (anxiety, depression, personality disorder, OR=2.01) and cigarette smoking (OR=3.55) were associated with going to jail.

Conclusions: Some of the risk factors associated with schizophrenia are associated with risk for undesirable life events such as going to jail during military service. One might hypothesize that in persons with these risk factors, the presence or absence of other environmental and/or genetic risk factors causes mental illness to manifest in some, while others have undesirable life events, such as going to jail, without suffering from psychosis.

References:

Summary:
Background: Early identification and treatment of impending psychosis might delay or attenuate the first psychotic episode, therefore it is of utmost relevance. The purpose of this study was to investigate if a psychological examination on treatment seeker adolescent soldiers can distinguish between individuals who will and will not be hospitalized for psychosis. Method: Using an historical prospective design on a population-based cohort followed for up to 6 years, 129,339 adolescents who had been examined by mental health professionals were followed for later hospitalization using a psychiatric hospitalization registry. Following each examination, the presence of psychiatric symptoms and signs is recorded. The findings of the examination of each adolescent later hospitalized for psychosis was compared with the results of 2 controls matched for age and gender, who had been examined by the same mental health professional, and were not later hospitalized.

Results: In adolescents hospitalized 14-64 days after the mental health examination (N=58), thought disorder (OR= 6.9, 95% CI: 1.1-42.5) and functional decline (OR=3.0, 95% CI: 1.2-7.4) were more common, While anxiety (OR=0.4, 95% CI: 0.2-0.9) was more frequent in controls. For adolescents hospitalized 65 days and more after examination (N=103), only disheveled appearance and abnormal behavior were associated with later hospitalization (OR= 3.0, 95%CI: 1.5-5.9), while suicidality (OR=0.4 95%CI: 0.2-0.9) and depressed affect (OR=0.4 95%CI: 0.2-0.6) were more common in controls.

Discussion: Most if not all treatment-seeking adolescents experience psychiatric signs and symptoms with some individual symptoms being more frequent in adolescents later hospitalized for psychosis. However, due to the relative rarity of hospitalization for psychosis, even those symptoms which were more common in adolescents later hospitalized were not clinically relevant in predicting impending psychosis. Although the assessment was not specifically focused on identifying later psychosis, these results underscore the difficulty of identifying among treatment seekers those with impending psychosis.

References:

NR695  Wednesday, May 23, 12:00 PM - 2:00 PM
Body Composition in Psychiatric Disorders
Suoma E. Saarni, M.D. University of Helsinki, Department of Public Health, P.O.Box 41, University of Helsinki, 00014, 4050, Samuli I. Saarni, M.D., Jaana Suvisaari, M.D., Antti Reunanen, M.D., Markku Heliovaara, M.D., Jouko Lonnqvist, M.D.

Educational Objectives:
At the end of this presentation the reader should have learnt how different psychiatric disorders are associated with overweight and body composition (i.e. abdominal obesity, fat percentage, muscle mass) at population level.

Summary:
Introduction: Overweight and psychiatric disorders are among the most important public health problems in western countries. Literature proposes association between obesity and other metabolic disorders and psychiatric disorders (Arch Gen Psychiat 2006; 63:824-30, Int J Obes 2006; 30:520-7). Abdominal obesity is a clinically relevant measure for the risk of cardiovascular and metabolic disorders.

NR694  Wednesday, May 23, 12:00 PM - 2:00 PM
Is It Possible to Identify Impending Psychosis Before the First Psychotic Episode? A Population-Based Study
Mark Weiser, M.D. Sheba Medical Center, Psychiatry, Sheba Medical Center, Tel-Hashomer, Tel Hashomer, Ramat-Gan, 52621, 5081, Abigail Livny-Ezer, B.A., Avi Reichenberg, Ph.D., Efrat Kravitz, B.A., Gadi Lubin, M.D., Moti Shmushkevitch, M.D., Michael Davidson, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand that many of the symptoms which are common in the prodrom of the first psychotic episode are very common in treatment seeking adolescents.
Objectives: To determine the prevalence of obesity and abdominal obesity, and the distribution of body fat and musculature in common psychiatric disorders.

Methods: General population sample of 8028 Finns aged over 30 years. Weight, height, waist circumference (WC) and body composition (segmental multi-frequency bioelectrical impedance analysis, using InBody 3.0) were measured. Psychiatric disorders were diagnosed according to DSM-IV-TR criteria using M-CIDI interview for 12-month prevalence of affective, anxiety and alcohol use disorders, and a using a consensus procedure based on SCID-I interview, case note and register data for lifetime diagnoses of psychotic disorders (Perälä J et al, Arch Gen Psychiatry; in press).

Results: BMI was obtained for 89.8% and bioimpedance for 72.6% of the population. Schizophrenia and other non-affective psychotic disorders (ONAP) were associated with increased risk for obesity and abdominal obesity (table 1). After adjustment for BMI, people with schizophrenia and ONAP still had larger WC and lower lean body mass. Affective psychoses did not affect body composition. Non-psychotic disorders were not associated with obesity but, after controlling for BMI, alcohol dependence and anxiety disorders were associated with increased WC and anxiety and depressive disorders with increased body fat percentage. Results concerning different anxiety and mood disorders, and the upper-lower-body balance of fat and muscle distribution will be presented.

Conclusion: Schizophrenia, non-affective psychotic disorders, alcohol dependence and anxiety disorders are associated with metabolically unfavourable body composition. Investigating only BMI is not sufficient to detect this.

References:

NR696 Wednesday, May 23, 12:00 PM - 2:00 PM
Alcohol Abuse and Dependence: Prevalence and Correlates Among a Tunisian Population of Primary Care Patients
Bechir BEN HADJ ALI, Sr., Psy D. Farhat Hached Hospital, Sousse, Rue Iman El Jazzar, Sousse, 4000, 7230, Mohamed Ali GORSANE, Jr., Psy.D., Selma BEN NASR II

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to recognise that the prevalence alcohol abuse and dependence among a Tunisian Muslim population is as important that found in western countries. The patient should be able to recognise that the importance of those troubles justify the development of adequate treatment and prevention strategies.

Summary:
Alcohol consumption is frequent, and according to WHO, there are about two billion people from all over the world who consume alcohol regularly. However, in Tunisia and in most of Muslim countries, this subject has remained taboo. In fact, a few studies have been interested in the prevalence of alcoholism, which instead should be regarded as a disease that has to be assessed, cured and prevented.

Objective: The aim of this study was to determine the prevalence of alcohol abuse and dependence in an adult primary care population in Sousse in Tunisia.

Methods: Sampling followed a stratified multistage probability cluster design from with a representative sample of adult primary care population of Sousse was obtained. The sample was composed of 1762 individuals aged 18 years or older. Individuals were interviewed by psychiatrists using the Composite International Diagnostic Interview (CIDI), which was translated to the Tunisian dialect and validated.

Results: The sample was made of 1762 patients: 77.2% are female (n=1360) and 22.8% are male (n=402). The study focussed on male patients given the rarity of alcoholism among female patients (one case only of alcohol abuse).

Prevalence of alcohol abuse affected 12.7% of the male population in a life time period, 2.7% per month, and 4.4% per year. Respectively, prevalence of dependence was as follows 1.7%, 1.9% et 3.2%.

Alcohol abuse was correlated with marital status (17.9% among the non married vs. 9.9% among the married; p=0.023). Similarly, we noticed that active population were more subject to alcohol abuse (15.8% vs. 7.4%; p=0.014).

Conclusion: This study has shown that in Tunisia the prevalence of troubles related to alcohol use, especially among male population, is as important as that found in western countries. Therefore, studying this issue in Tunisia seems to be well justified in order to develop adequate prevention strategies.

References:

NR697 Wednesday, May 23, 12:00 PM - 2:00 PM
Diagnostic Comorbidity in Psychiatric Outpatients Presenting for Treatment: Findings from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) Project
Mark Zimmerman, M.D. Rhode Island Hospital, Psychiatry, 235 Plain Street, Suite 501, Providence, RI, 02905, 9000, Joseph B. McGlinchey, Ph.D., Iwona Chelminski, Ph.D., Diane D. Young, Ph.D.

Educational Objectives:
At the conclusion of this presentation the participant should be able to identify the frequency of diagnostic comorbidity in patients presenting to an outpatient practice, and the different patterns of comorbidity associated with different Axis I disorders.

Summary:
Background: The largest clinical epidemiological surveys of psychiatric disorders have been based on unstructured clinical evaluations. However, several recent studies have questioned the accuracy and thoroughness of clinical diagnostic interviews; consequently, clinical epidemiological studies, like community-based studies, should be based on standardized evaluations. The Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project is the largest clinical epidemiological study using semi-structured interviews assessing a wide range of psychiatric disorders conducted in general clinical outpatient practice. In the present report we examined the frequency of DSM-IV Axis I diagnostic comorbidity in psychiatric outpatients.

Methods: Two thousand three hundred psychiatric outpatients were interviewed with the Structured Clinical Interview for DSM-IV (SCID) upon presentation for treatment.

Results: The mean number of current and lifetime DSM-IV Axis I disorders in the 2,300 patients was 1.9 (SD=1.5) and 3.0 (SD=...
The pattern of comorbidity varies by the principal diagnosis. Their important roles in risk assessment of coronary heart disease and the relationship between body weight and cholesterol measurements, and个性的完成 psychiatric diagnosis of posttraumatic stress disorder and bipolar disorder.

Conclusions: Clinicians should assume that psychiatric patients presenting for treatment have more than one current diagnosis. The pattern of comorbidity varies by the principal diagnosis.

References:

**NR699 Wednesday, May 23, 12:00 PM - 2:00 PM**

**Body Weight and Lipid Risk Factors in Predicting Risk for Coronary Heart Disease**

Ralph D’Agostino, Sr., Ph.D. Boston University, Mathematics and Statistics Department, 111 Cummings St, Boston, MA, 02215, 9000, Brian Cuffel, Ph.D., Antony D. Loebel, M.D., Cynthia Siu, Ph.D.

**Educational Objectives:**
1. The participant will have greater understanding of the relationship between body weight and cholesterol measurements, and their important roles in risk assessment of coronary heart disease (CHD)
2. The participant will have greater understanding of the Framingham Risk Score which is an important tool to guide assessment and management of risk for CHD

**Summary:**
Background: The Framingham Risk Score (FRS) provides an important tool to guide assessment and management of risk for coronary heart disease (CHD), but requires measurements of HDL and total cholesterol. Overweight and obesity have long been recognized as major, underlying risk for CHD, but body weight is not a component of the FRS due to its potential associations with lipid and other risk factors already included in the model (1). Incorporating easily obtained weight measures as substitution for laboratory measurements in a modified Framingham predictive model may facilitate the ability to monitor for risk of developing CHD.

Methods: In a randomized, double-blind, 6-week study of ziprasidone and olanzapine (2), we examined the relationship between body weight and cholesterol measurements, particularly total cholesterol and HDL (N=259). Using baseline data from this trial, a regression analysis was performed to evaluate the significance of these cross-sectional relationships.

Results: Baseline body weight or BMI was significantly related to baseline fasting serum measurements of total cholesterol (p<0.01), HDL (p<0.01), LDL (p<0.01) and triglycerides (p<0.05). Consistent pattern was observed for weight and lipid measurements after 6 weeks of treatment exposure (p<0.05).

Conclusions: These results suggest that a modified risk assessment tool incorporating body weight and other non-lipid components of Framingham Risk Score (e.g. age, blood pressure, and cigarette smoking) could be useful to predict risk for CHD without the need for laboratory measurements. Supported by funding from Pfizer Inc.

References:

**Use of Sodium Thiopental and Propofol for Anesthesia Induction during Electroconvulsive Therapy (ECT): A Comparison**

Pe Shein Wynn, M.D., M.P.H. Rockland Psychiatric Center, Department of Psychiatry, Rockland Psychiatric Center, 140 Old Orangeburg Road, Orangeburg, NY, 10962, 9000, Scott Clark, M.D., Jong Sun, M.D., Fabien Trémeau, M.D.

**Educational Objectives:**
At the conclusion of this presentation, the participant should be able to recognize -
- minimum effective dose of induction agent without interfering seizure duration
- a safer induction agent for anesthesia during electroconvulsive treatment (ECT)

**Summary:**
Introduction: Since its introduction in 1989, Propofol has been popular for inducing and maintaining anesthesia. Benefits include rapid clearance and favorable side-effect profile; however its potential anti-seizure quality potentially limits its uptake in ECT practice. This review compares impact on seizure duration of the use of Sodium Thiopental (STP) and Propofol (PPF) as induction agents for ECT.

Methods: Retrospective review of ECT treatments for 4 inpatients. Each patient received either STP (0.4mg - 2.75mg/kg) or PPF (0.4 mg - 1.1mg/kg) as an induction agent in each treatment.

Variables of interest included energy used, duration of EEG and EMG, body weight, dosages of agents used, and vital signs during treatments.

Results: A total of 4 subjects (2 male & 2 female) and 97 treatments (32 with STP and 65 with PPF) were reviewed. Mean age was 53±5.0 (M) and 41.5±9.5 (F) and body weight 88.3±16.6kg (M) and 56.21±10.06kg (F), respectively. Bi-frontal electrode placement was used in all treatments. Effects on EEG and EMG durations of the defined minimally hypnotic dose of PPF (0.75-0.85mg/kg) were not significantly different from that with the medium recommended dose of STP (>1.75mg/kg). There was a statistically significant increase (p<0.01) in diastolic blood pressure from pre-ECT baseline with STP compared to PPF, though no significant differences were noted for increase in systolic pressure and pulse rate during treatments.

Conclusion: PPF used at a minimally hypnotic dose is comparable to STP in its effect on seizure duration. There was significant post-stimulus increase in diastolic blood pressure with STP compared to PPF. With regard to hemodynamic effects, use of PPF (0.75-0.85mg/kg) may be superior to STP as an induction agent for ECT. Validation of these findings awaits further study with larger subject samples.

References:

**NR700** Wednesday, May 23, 12:00 PM - 2:00 PM

**Association of Antipsychotic Drugs with Diabetes Mellitus: An Analysis of the US FDA Adverse Event Reporting System (AERS) Database**

Ross A. Baker Bristol-Myers Squibb Company, Princeton, Bristol-Myers Squibb Company, Route 206 & Provinceline Road, Princeton, NJ, 08540, 9000, Artist Parker, Andrei Pikalov, Quynh Van-Tran, Tatya Kremenets, Ramin Arani

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to appreciate that the incidence of diabetes-related adverse events is greater with older atypical antipsychotics (clozapine, olanzapine, risperidone and quetiapine) than with the newer agents aripiprazole and ziprasidone, based on an analysis of the FDA adverse event reporting system (AERS).

**Summary:**

**Objectives:** The risk of diabetes-related adverse events (DRAEs) is increased by certain atypical antipsychotic agents such as olanzapine, risperidone and quetiapine. Newer atypical agents such as ziprasidone and aripiprazole are less likely to be associated with DRAEs. The present analysis was conducted to evaluate the potential association between any of the atypical antipsychotics or haloperidol and diabetes using data from the FDA adverse event reporting system (AERS).

**Methods:** An analysis of the AERS database was conducted for clozapine, risperidone, olanzapine, quetiapine, ziprasidone, aripiprazole, or haloperidol with 24 DRAEs from the Medical Dictionary for Regulatory Activities using a Multi-Item Gamma Poisson Shrinker (MGPS) data mining algorithm. Using MGPS, we calculated the Empiric Bayes Geometric Mean (EBGM) and 90% confidence intervals (EB05, EB95) to estimate the degree of association between drug-event combinations.

**Results:** All 7 drugs had an EB05 greater than or equal to 2 for at least one DRAE. The most common DRAE was diabetes mellitus with 1,745 cases reported. EBGM scores and 90% CIs (EB05; EB95) for diabetes mellitus were: olanzapine 5.8 (5.4, 6.2; 667 cases), clozapine 3.3 (3.0, 3.5; 453 cases), quetiapine 2.9 (2.6, 3.3; 167 cases), risperidone 2.5 (2.3, 2.8; 258 cases), ziprasidone 2.1 (1.7, 2.8; 51 cases), haloperidol 1.7 (1.5, 2.0; 108 cases) and aripiprazole 1.7 (1.3, 2.2; 41 cases).

**Conclusions:** The AERS database captures spontaneously reported AEs and less data is available for more recently introduced products. The quality/scope of such databases is limited, thus results must be interpreted with caution. Nevertheless, the present findings are consistent with recent epidemiological studies and the ADA consensus conference on diabetes risk with atypical antipsychotics.

**References:**


NR701 Wednesday, May 23, 12:00 PM - 2:00 PM

**Psychodynamicism of Parents of Children with Serious Asthma**

Wilze L. Bruscato, Ph.D. Santa Casa de Sao Paulo, Psychology Service, Rua Borges Lagoa, 1231, Vila Clementino, Sao Paulo, 04038-020, 3510, Adriana A. Fregonese, M.S., Wilma N. Forte, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to recognize that the clinical treatment provided by the health team is affected by parents' adhesion problems, especially by the asthmatic children's mothers.

**Summary:**

Asthma is a chronic disease that affects 10% of the Brazilian population and is a public health problem, resulting in high social cost due to hospitalizations, school absence, parcial ou total inability to work. It has a multifarious etiology, in which organic and/or hereditary factors join environmental and psychological ones. The clinical treatment provided by the health team is affected by parents' adhesion problems. Parents' emotional issues jeopardize the children's maturation process, blocking medical and psychological treatments. Both parents and society impede the asthmatic to become independent, and many children feel comfortable in that place, allowing parents to think, act and decide everything for them, maintaining a dependent relationship that may last for their hole life. This research investigate motherhood and fatherhood meaning, besides the association between the parents' psychodynamicism and children's respiratory allergy. The investigation instruments used were semi-guided interviews and two boards of Thematic Apperception Test (TAT). Through the analysis of the data and qualitative evaluation was possible to conclude that regarding motherhood, it was noticed the permanence of immature and less elaborated conflicts that are difficult to be solved. They tend to see their children as fragile and provide an exaggerated protection that keep the child attached to them. Most fathers had emotional problems on finding their places as partners and parents. They act as supplying of material resources and keep an affective distance. The parents' emotional issues affets the relationship with their children and the asthma assumes a communicative value for the parents-child triad. When the child realises the parents' weakness, it is possible to achieve everything that is desired, obtaining gains from the symptom. Parents can also obtain gains from children's asthma, because the crisis may take parents' attention away from conjugal conflicts, avoiding their facing and solving.

**References:**


NR702 Wednesday, May 23, 12:00 PM - 2:00 PM

**Elevated Levels of Plasma Interleukin-1 and Tumor Necrosis Factor-A Are Associated With Increased Depressive Symptomatology in Patients With and Without Chronic Hepatitis C**

Jennifer M. Loftis, Ph.D. Portland VAMC; Oregon Health & Sciences University, Mental Health and Neurosciences Division; Psychiatry, 3710 Southwest U.S. Veterans Hospital Road, P3MHAdm, Portland, OR, 97239, 9000, Marilyn Huckans, Ph.D., David J. Hinrichs, Ph.D., Peter Hauser, M.D.
NR703  Wednesday, May 23, 12:00 PM - 2:00 PM
The Protective Effect of Religiosity Under Terrorism
Robert Kohn, M.D. Brown University, Department of Psychiatry and Human Behavior, 345 Blackstone Boulevard, Providence, RI, 02906, 9000, Itzhak Levav, M.D., Miriam Billig, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the relationship between religion and ideology in response to a severe traumatic event, such as exposure to terrorism.

Summary:
Background: Religious observance has a protective effect on the mental health of individuals facing adverse events. Its role under terrorism has been less investigated. Gaza and West Bank settlers, both secular and those keeping different degrees of observance, have faced terrorism in recent years.

Methods: Respondents were interviewed by telephone (N = 764) regarding emotional distress, ideology, religious observance, and terrorism. We investigated their PERI-Demoralization mean scores following terrorist attacks controlling for confounding variables.

Results: The higher the religiosity of the respondent and the lower the demoralization mean score. This protective effect lessened when there was dissonance between the degree of religiosity of the respondent and the religious observance of the settlement of residence. This study found that the national-religious and the national-ultra-religious settlers had significantly lower levels of psychological distress than either the traditional or secular groups. Central to the aims of this inquiry we found that this difference persisted in situations of adversity, threat of removal and exposure to terrorism. Apparently, the differences we found in psychological distress between the groups could be explained by ideological factors, pro-disengagement and place attachment rather than by religiosity. In fact, these variables are so tightly interwoven in this population that it is rather impossible to deconstruct such a domain: to be more religious is to hold even more tightly the ideological stand that settling in Gaza, and especially in the West Bank constitutes an irrevocable Biblical mandate.

Conclusions: Religion as a down-regulator of stress, particularly with regard to illness and death and other crisis in life has been repeatedly shown in the literature to constitute a valuable psychosocial resource. For all stressors, religious concepts provide a schema that enables the person to find an explanation to their particular destiny, and that of the group.

References:

NR704  Wednesday, May 23, 12:00 PM - 2:00 PM
Escitalopram Reduces Hot Flashes in Non-Depressed Menopausal Women: An Open Label Trial
Roeanne DeFronzo Dobkin, Ph.D. Robert Wood Johnson Medical School, Psychiatry, 675 Hoes Lane, Room D-317, Piscataway, NJ, 08854, 9000, Matthew A. Menza, M.D., Lesley A. Allen, Ph.D., Humberto Marin, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that escitalopram may be a feasible and effective option for treating hot flashes in non-depressed, menopausal women.

At the conclusion of this presentation, the participant should be able to recognize that escitalopram may be a feasible and effective option for treating dysphoria, anxiety, and sleep disturbance in menopausal women.

At the conclusion of the presentation, the participant should demonstrate understanding that escitalopram is associated with improved quality of life in menopausal women experiencing vaso-motor symptoms.
Summary:

Introduction: Hot flashes are one of the most troubling manifestations of menopause, affecting as many as 80% of women. The goal of this study was to examine the impact of the SSRI, escitalopram, on hot flashes, mood, sleep, and quality of life in a healthy sample of non-depressed menopausal women seeking an alternative to HRT.

Methods: A total of 25 non-depressed women, with no significant medical or psychiatric history, who were experiencing at least 14 hot flashes per week were enrolled. All women were treated with escitalopram (10-20mg flexibly dosed) for 8 weeks. Given the high rate of placebo response in hot flash studies, the active treatment phase was preceded by a single blind placebo lead in; placebo responders (e.g., >25% reduction in hot flash frequency) were excluded from the active treatment trial. The frequency and severity of hot flashes (diaries), dysphoria (HAM-D), anxiety (HAM-A), sleep (diaries), and quality of life (MENQOL & Greene scale) were assessed bi-weekly in an academic medical center.

Results: A single-group, repeated measures pretest-posttest design was employed. In the group as a whole, there were significant decreases in both hot flash frequency F(1,24)=39.93, p < .001 and severity F(1,24)=38.38, p<.001, as well as improvements in dysphoria F(1,24)= 47.51, p<.001, anxiety F(1,24)=47.50, p<.001, total sleep time F(1,24)= 5.4, p=0.03, and quality of life (MENQOL: F (1,24)=27.81, p<.001 & Greene: F (1,24)= 52.11, p<.001). Improvements were noted by the second week of active treatment and maintained throughout the 8-week study.

Conclusion/Discussion: Non-hormonal approaches, such as escitalopram, may be feasible and effective options for treating hot flashes and other menopausal symptoms. The use of open-label escitalopram appeared to be both desirable and helpful for a non-depressed sample of women with vasomotor symptoms, who were interested in an alternative to hormone replacement.

References:

NR705 Wednesday, May 23, 12:00 PM - 2:00 PM
Desvenlafaxine Improves Mood in Women Treated for Vasomotor Symptoms: Effect of Baseline Mood Status

Meir Steiner, M.D., PhD, McMaster University, Psychiatry & Behavioural Neurosciences, 1280 Main Street West, Hamilton, Ontario, ON, L8S 4L8, 1220, Louis Kirby, M.D., Holly Yu, M.S.P.H., Joel Bobula, M.A., Sophie Olivier, M.D.

Educational Objectives:
At the conclusion of this presentation, participants should be able to:
1. Recognize that in postmenopausal women, DVS may improve mood symptoms along with alleviating vasomotor symptoms.
2. Recognize that the patients most likely to benefit are those with poorer than average mood scores.

Summary:
Objective: Desvenlafaxine succinate (DVS), a novel serotonin-norepinephrine reuptake inhibitor, improves hot flushes (HF) and mood in menopausal women with moderate-to-severe vasomotor symptoms (VMS). The objective of this analysis was to determine whether DVS improves mood differentially based on mood states at baseline

Methods: Postmenopausal women with ≥50 HF/wk were enrolled in 2 double-blind, placebo-controlled trials of DVS for VMS. Subjects completed the Profile of Mood States (POMS) at baseline and week 12. Data from the 2 trials were pooled, and subjects (n=843) from 100- and 150 mg DVS and placebo groups were stratified according to baseline POMS total mood disturbance (TMD) scores, using a normative mean score of 20 as the cut off point. POMS scores were analyzed using MANCOVA, adjusting for age, race, menopause type, and baseline values.

Results: Mean POMS TMD score at baseline was 27.8 with 51.7% of subjects scoring higher than the normative mean score of 20. Overall, POMS TMD scores improved significantly over 12 weeks of treatment for both DVS dose groups compared with placebo (P=0.0002 and P=0.0011, respectively). Stratification by baseline POMS TMD scores indicated that the effect was mainly driven by improvement in mood for subjects with baseline TMD scores higher than the normative mean. Women who scored ≥20 at baseline had significant improvements in POMS TMD scores after 12 weeks of DVS treatment compared with placebo (P=.0006 and P=.0066, respectively); those who scored <20 had no significant change from baseline for any treatment group. Subjects with higher baseline scores receiving either DVS dose showed significant improvement on anger/hostility, tension/anxiety, and depression/dejection subscales (all comparisons, P<0.006). The 100 mg DVS group also improved on the confusion/bewilderment subscale (P=0.0082). Improvement in mood for subjects with poorer baseline mood scores. Women who scored ≥20 at baseline had significant improvement.

Conclusion: For postmenopausal women experiencing moderate-to-severe VMS, DVS significantly improves mood in those with higher than average POMS scores at baseline.

References:
Background and Objective: Approximately 47 million adults aren't meeting the minimum amount of sleep estimated necessary to be fully alert the next day. We examined potential factors related to sleep insufficiency such as marital status and the presence or absence of children in the household.

Methods: Data were obtained from the 2002 Behavioral Risk Factor Surveillance System, an ongoing, state-based, random-digit telephone survey of U.S. adults residing in the community. The sleep insufficiency question was administered in 18 states and the District of Columbia (n=79,576).

Results: Both married men and women with children (26.7% and 33.9%, respectively) were significantly more likely to report insufficient sleep than their gender-matched counterparts without children (15.5% and 21.0%, respectively). The same was true of non-married men and women (30.6% and 35.7% respectively with children versus 24.9% and 26.8% respectively without children). Additionally, married women with children (33.9%) were significantly more likely to report sleep insufficiency than married men with children (26.7%). This was also true when comparing non-married women with children and non-married men with children (35.7% and 30.6%, respectively). Notably, married women without children (21.0%) were more likely to report sleep insufficiency than married men without children (15.5%) however, there was no significant difference in reported sleep insufficiency between unmarried women and men without children (26.8% and 24.9% respectively).

Conclusion: These data indicate that specific household compositions are associated with sleep insufficiency. Sleep insufficiency is more prevalent in households with children. Moreover, women with children are more likely to get insufficient sleep than their male partners. These findings suggest the need for sleep education among families with children - particularly mothers — and corroborate the importance of sleep as a facet of women's health.

References:

Educational Objectives:
At the conclusion of this presentation, the participant should be able to discriminate between the values of having an electronic diary to assess sexual desire in women with hypoactive sexual desire disorder (HSDD) compared with rating scales - i.e., they have high discriminant validity, convergent validity and good compliance rates. This may solve the problem of recall bias associated with retrospective rating scales. Participants should learn the difference in the frequency of sexual desire among women with no sexual disorder (about 15 days/month) and the frequency in women with HSDD (less than 5 days/month), as measured by an electronic diary.

Summary:
Introduction: Measuring the severity of Hypoactive Sexual Desire Disorder (HSDD) is complex. Numerous available ratings of symptoms and related distress (e.g., Female Sexual Function Index [FSFI]), Female Sexual Distress Scale (FSDS) can be criticized for recall bias. A valid electronic diary (e-diary) could address this issue.

Methods: A daily e-diary collected information on sexual events and attitudes in 3 clinical non-treatment studies, 511.73, 511.106 (both North American), and 511.85 (European), which recruited women with HSDD (n=381) and women with no female sexual dysfunction (no-FSD; n=260). Each study included a desire-related question; the e-diaries were used for 28 days and the mean results calculated. Standard rating scales were completed for reference: Changes in Sexual Function Questionnaire (CSFQ) and/or FSFI and FSDS and/or FSDS-R(revised).

Results: All 3 studies showed discriminant validity. 1) In study 511.73, 105 women with HSDD reported sexual desire on 4.6 days, compared with 13.6 days for women with no-FSD (p<0.0001). 2) Study 511.85 provided similar data, women with HSDD had sexual desire on 4.7 days compared with 13.3 days in the 120 women with no-FSD (p<0.0001). 3) In study 511.106,
women with HSDD rated their sexual desire as moderate or strong on 4.5 days/month compared with 17.4 days/month in women with no-FSD (p<0.001). Convergent validity was also shown; Pearson correlation between the FSFI desire subscale score and the e-diary sexual desire score (total points for the month) for all subjects (full analysis set; n=245) was high, 0.8179; the corresponding correlation for desire days moderate to strong was 0.8233. E-diary compliance was excellent; e.g., in 511.73, 77% of subjects missed 3 or fewer days of entries and only 5% of subjects missed entries for >10 days.

Conclusions: A simple daily e-diary question provides high discriminant validity, convergent validity, and compliance for assessing of sexual desire in women with HSDD.

Funding Source: Boehringer Ingelheim Pharmaceuticals, Inc.

References:

NR709 Wednesday, May 23, 12:00 PM - 2:00 PM
Differentiating Four Cognitive-Behavioral Types of Women with Decreased Sexual Desire
Lorraine Dennerstein, Ph.D. University of Melbourne, Department of Psychiatry, University of Melbourne, Parkville, 3010, 6021, Robert Pyke, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should realize that women's feelings towards decreased sexual desire and attitudes towards seeking help differ markedly within the study population and across countries. Women with decreased sexual desire were identified as belonging to four distinct clusters based on characteristics including their sexuality, partnership, health status and employment. As decreased sexual desire is frequently reported among women, it is important that healthcare practitioners are aware of these differences and that some groups of women may need more explanation than others about etiological factors and therapy options.

Summary:
Introduction: Decreased sexual desire is frequently reported among women. However, little is known about how women feel about their loss of desire. We conducted a study to look at the characteristics of women with decreased sexual desire.

Methods: 8,000 women in the USA, Germany and Italy, aged 18-65 and in a relationship, were identified from an existing database of women who had given consent to market research. The women were screened for decreased sexual desire using a SIDI-F-derived telephone questionnaire. Women in the USA (n=600), Italy (n=400), and Germany (n=400), identified as having decreased sexual desire, were surveyed using a 60-minute face-to-face questionnaire on partnership, sexuality, health status, employment, etc. Cluster analysis based on self-perception, sexual attitudes and sexual behavior was used to define 4 clusters, which were validated using convergent cluster analysis.

Results: Clusters were distinct in concern about decreased sexual desire, its perceived impact on their relationship, its cause, whether they would seek medical help, and social status:

*1 is disagree completely, 6 is agree strongly

Conclusions
This study indicated that there are four identifiable groups of women with decreased sexual desire, and that women's feelings towards decreased sexual desire and attitudes toward seeking help differ markedly within the population and across countries. The healthcare practitioner will be assisted by awareness of these differences and that some groups of women may need more explanation than others about etiological factors and therapy options.

Funding Source: Boehringer Ingelheim Pharmaceuticals, Inc.

References:

NR710 Wednesday, May 23, 12:00 PM - 2:00 PM
Validation of the Decreased Sexual Desire Screener' (DSDS): A Brief Diagnostic Instrument for Generalized, Acquired Hypoactive Sexual Desire Disorder in Women
Evan R. Goldfischer, M.D. Hudson Valley Urology, Director of Research, 1 Columbia Street, Suite 390, Poughkeepsie, NY, 12601, 9000, Anita Clayton, M.D., Irwin Goldstein, M.D., Robert Pyke, M.D., Diane Lewis-D'Agostino, R.N.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to appreciate the difficulty in diagnosing Hypoactive Sexual Desire Disorder (HSDD) in women using current methodology, which is often time consuming and poorly accessible. The Decreased Sexual Desire Screener (DSDS) is an accurate instrument to make such a diagnosis easier to the non-expert clinician, taking less than 15 minutes to complete, compared to the expert standardized interview, which takes approximately one hour. From this, the participant will learn that the DSDS should allow the identification of more women with this condition who may benefit from treatment.

Summary:
Introduction: The diagnosis of Hypoactive Sexual Desire Disorder (HSDD) relies on a time-consuming, extensive interview by an expert clinician. Many women with HSDD are undiagnosed and untreated due to limited access to such experts.

Methods: The Decreased Sexual Desire Screener (DSDS)® is a brief instrument to guide the diagnosis of HSDD, was assessed in two clinical studies in North America: a non-treatment validation study, 511.106 (n=263), and a treatment trial, 511.74 (n=921). Women were asked to complete the DSDS at their screening visit and their answers were reviewed with a non-expert clinician. Afterwards, a second clinician, certified as an expert in HSDD and unaware of the first clinician’s diagnosis, conducted an extensive, standardized interview to diagnose sexual disorders. In the analysis, the diagnoses of the two clinicians were compared. In addition, cognitive debriefing was performed in a sub-set of 89 women in the non-treatment trial and with all participating non-expert clinicians.

Results: In the non-treatment trial, the DSDS had a sensitivity of 83.6%, specificity of 87.8%, and accuracy of 85.2%. Cognitive debriefing demonstrated that each question and answer set was understood by, and acceptable to, the patients and non-expert clinicians. In the treatment trial, the DSDS had a sensitivity of 94.6%. Anecdotally, the expert, standardized interview was re-
portend to take approximately an hour to complete while the DSDS took less than 15 minutes.

**Conclusions:** While expert diagnosis of HSDD is often time-consuming, poorly accessible, and performed by few clinicians using current methodology, the DSDS enabled non-expert clinicians to diagnose generalized, acquired HSDD in women accurately and quickly. Additional research is needed to provide further validation of the DSDS in women outside North America.

**Funding Source:** Boehringer Ingelheim Pharmaceuticals, Inc.

**References:**

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**Summary:**

**Introduction:** No well validated scales exist for measuring distress associated with female Hypoactive Sexual Desire Disorder (HSDD). This study assessed validity of the Female Sexual Distress Scale (FSDS), which retrospectively ask women to rate their distress over the last 7 days or 30 days, or by electronic diary (e-diary), which keep a daily record of sexual distress. From this presentation the participant should learn that the FSDS-R, a revised version of the FSDS, and e-diaries all discriminate between women with HSDD and women with no sexual disorder.

**Results:**

For HSDD patients, all results confirmed reliability and validity of the SIDI-F. Test-retest reliability between day 0 and 28 was demonstrated with an intraclass correlation coefficient of 0.70 and a Pearson correlation coefficient of 0.72. Convergent validity was also demonstrated at day 0: Pearson's correlation to CSFQ-F was 0.70 and to FSFI was 0.62. Correlations were more pronounced across all subgroups. Low correlation of SIDI-F to MAS (0.02) showed divergent validity. SIDI-F showed more impairment of desire in HSDD (mean 21.1 ± SD 7.6) than in FSAD (26.8 ± 8.9, p<0.0001) or no-FSD (41.5 ± 5.6, p<0.0001) subjects. In contrast, CSFQ showed similar levels of impairment of desire in

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**Conclusions:** All measures of sexual distress clearly discriminated between HSDD and no FSD subjects. The FSDS and FSDS-R with 7-day recall discriminated as well as with 30-day recall. The e-diary showed high content validity and compliance.

**Funding Source:** Boehringer Ingelheim Pharmaceuticals, Inc.

**References:**

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**Summary:**

**Objective:** To determine the reliability and validity of the Sexual Interest and Desire Inventory - Female (SIDI-F), a 13-item clinician's rating with 30-day recall, to discriminate between patients with Hypoactive Sexual Desire Disorder (HSDD) and no female sexual dysfunction. Furthermore, as the study provides strong support for the reliability and validity of the SIDI-F as a specific measure of HSDD, the participants should be able to use the SIDI-F in assessing the severity of HSDD in their patients.

**Results:** For HSDD patients, all results confirmed reliability and validity of the SIDI-F. Test-retest reliability between day 0 and 28 was demonstrated with an intraclass correlation coefficient of 0.70 and a Pearson correlation coefficient of 0.72. Convergent validity was also demonstrated at day 0: Pearson's correlation to CSFQ-F was 0.70 and to FSFI was 0.62. Correlations were more pronounced across all subgroups. Low correlation of SIDI-F to MAS (0.02) showed divergent validity. SIDI-F showed more impairment of desire in HSDD (mean 21.1 ± SD 7.6) than in FSAD (26.8 ± 8.9, p<0.0001) or no-FSD (41.5 ± 5.6, p<0.0001) subjects. In contrast, CSFQ showed similar levels of impairment of desire in
HSDD (42.7 ± 7.0) and FSAD (41.8 ± 7.7), as did FSFI (22.1 ± 6.2 in HSDD and 20.4 ± 6.2 in FSAD). In both these scales women with no-FSD had a higher mean score: 55.3 ± 6.1 for CSFQ

and 31.6 ± 3.7 for FSFI. A SIDI-F cutoff score of 33 maximized sensitivity (94.7%) and specificity (93.4%) for identifying HSDD vs. no-FSD.

Conclusion: This study provides strong support for the reliability and validity of the SIDI-F as a specific measure of HSDD in North American women.

Funding Source: Boehringer Ingelheim Pharmaceuticals, Inc.

References:

NR713 Wednesday, May 23, 12:00 PM - 2:00 PM
Symptom Reduction in Women Treated with Desvenlafaxine for Menopausal Hot Flushes: Impact of Bothersomeness

Meir Steinier, M.D. McMaster University, Psychiatry & Behavioural Neurosciences, St. Joseph’s Hospital, 301 James Street S, Hamilton, ON, L8P 3B6, 1220, Cláudio N. Soares, M.D., Louis Kirby, M.D., Holly Yu, Joel Bobula, M.A., Sophie Olivier, M.D.

Educational Objectives:
At the conclusion of this presentation, participants should be able to:
1. Understand that the degree to which moderate-to-severe hot flushes are experienced as bothersome varies from woman to woman.
2. Recognize that hot flushes when perceived as bothersome may significantly impact mood.
3. Recognize that desvenlafaxine succinate may be more effective for alleviating vasomotor symptoms and their potential impact on mood in women who report their symptoms as bothersome.

Summary:
Objective: The degree to which individual women find menopausal hot flushes (HF) bothersome cannot necessarily be predicted by their frequency and severity: some women are relatively untroubled, while others find them extremely disruptive or debilitating.1 Our objective was to determine whether desvenlafaxine succinate (DVS), a novel serotonin norepinephrine reuptake inhibitor, improves menopausal symptoms differentially based on bothersomeness of HF at baseline.

Methods: Postmenopausal women with ≥50 moderate to severe HF/week were enrolled in a double-blind, placebo-controlled trial of 100 or 150 mg/day DVS. Subjects recorded HF daily and completed the Profile of Mood States (POMS)2 and Greene Climacteric Scale (GCS) at baseline and week 12. Subjects were stratified based on a GCS item rating bothersomeness of HF at baseline. Data were analyzed using ANOVA and ANCOVA.

Results: At baseline, 415 (86%) subjects described their HF as "Quite a bit" or "Extremely" bothersome ("bothered" group); 66 (14%) responded "Not at all" or "A little." The "bothered" subjects had slightly higher baseline frequency, but not severity, of HF compared with "non-bothered" subjects (10.7 vs 9.6, P<0.05). At baseline, the "bothered" group had poorer vasomotor subscale score of GCS (P<0.001) and POMS total score (P<0.01). At week 12, both DVS dose groups reduced HF frequency compared with placebo (P<0.05) with no significant differences between the "bothered" and "non-bothered" groups. In the "bothered" group, DVS at both doses achieved significant improvements over placebo in total POMS score (p<0.05) and vasomotor subscale of GCS (p<0.001) while the "non-bothered" group achieved much smaller improvements from baseline with no statistical difference between DVS groups and placebo.

Conclusion: DVS effectively improves vasomotor symptoms. Women with bothersome HF, will benefit not only from reduction in bothersomeness but also from improvement in mood.

References:

NR714 Wednesday, May 23, 12:00 PM - 2:00 PM
Atypical Antipsychotic Administration During Late Pregnancy: Placental Passage and Obstetrical Outcomes

D. Jeffrey Newport, M.D. Emory University, Psychiatry, 1365 Clifton Rd NE, Suite 6100, Atlanta, GA, 30322, 9000, Martha R. Calamaras, B.S., C. Lindsay DeVane, Pharm.D., Jennifer L. Donovan, Ph.D., Stephanie S. Winn, M.D., Adele C. Viguera, M.D., Zachary N. Stowe, M.D.

Educational Objectives:
At the conclusion of this presentation, attendees will be familiar with the placental passage of antipsychotic medications, including which medications were found to have the highest and lowest placental transfer, and the observed obstetrical outcomes associated with this in utero exposure.

Summary:
There is limited data regarding the use of atypical antipsychotic medications in pregnancy. The objectives of the current study were to quantify placental permeability to antipsychotic medications and document obstetrical outcomes for women taking these medications prior to delivery. Pregnant women enrolled in a prospective observational study that were treated with an atypical antipsychotic or haloperidol during pregnancy were included. Maternal and umbilical cord plasma samples collected at delivery were analyzed for medication concentrations. Placental passage was defined as the ratio of umbilical cord to maternal plasma concentrations (ng/ml). Obstetrical outcome was ascertained via maternal report and review of obstetrical records.

Fifty-four pregnant women with laboratory-confirmed antipsychotic use (i.e., detectable maternal serum concentrations) proximate to delivery were included in the analysis. Complete maternal-infant sample pairs were available for 50 participants. All four antipsychotics demonstrated incomplete placental passage (i.e., ratio < 1.0). The placental passage ratio (mean ± standard deviation) was highest for olanzapine (72.1% ± 42.0%), followed by haloperidol (65.5% ± 40.3%), risperidone (49.2% ± 33.9%), and quetiapine (23.8% ± 11.0%). There were trends toward higher rates of low birth weight (30.8%, p<.06) and NICU admission (30.8%, p<.09) among neonates exposed to olanzapine.

Quetiapine demonstrated significantly lower placental passage compared to the other antipsychotics. These novel data provide an initial quantification of the placental passage of antipsychotics.
and fetal exposure in humans, demonstrating significant differences between individual medications.

Supported by K23 MH-63507 and P50 MH-68036.

References:

NR715  Wednesday, May 23, 12:00 PM - 2:00 PM
Maternal Depression in Pregnancy Predicts Parenting Stress in the Postpartum Period
Shaila Misri, M.D. University of British Columbia, Psychiatry, 1081 Burrard Street, 2B Room 185, Vancouver, BC, V6Z 1Y6, 1220, Lianne M. Tomfohr, B.A., Tim F. Oberlander, M.D.

Educational Objectives:
At the conclusion of this poster presentation, the participants should be able to understand the relationship between antenatal depression and parenting stress in the postpartum period.

Summary:
Objective: To study the impact of antenatal depression on postpartum parenting stress.

Background: Studies have shown that postpartum depression is strongly associated with parenting stress which leads to insecure attachment, negative mother-baby interaction and impaired child development. However, the association between antenatal depression and postpartum parenting stress has not been investigated as of yet.

Methods: This study consisted of 95 pregnant women recruited as part of a larger study examining the effects of prenatal SSRI exposure on infants. The 96 subjects who participated in this study comprised three groups: (1) depressed pregnant mothers treated with SSRIs (n=40), depressed non-medicated pregnant mothers (n=13), and healthy pregnant controls (n=42). Mother's mood was prospectively monitored at 26 weeks of gestation and 3 and 6 months postpartum using the Hamilton Depression Scale (HamD).

Assessments of parenting stress were conducted with the Parenting Stress Index (PSI) at 3 and 6 months postpartum.

Results: Regression analysis showed that depressive symptoms at 26 weeks were significantly associated with postpartum parenting stress (p = .001) after controlling for current depression, medication use, age, education, ethnicity and number of children. Furthermore, for each 10-point increase on the HamD in pregnancy there was an average 12.44-point increase in postpartum PSI scores.

Conclusions: Antenatal depression is associated with postpartum PSI scores. The greater the severity of antenatal depression the higher the postpartum PSI scores.

References:

NR716  Wednesday, May 23, 12:00 PM - 2:00 PM
Paroxetine Controlled-Release versus Placebo in Symptomatic Midlife Women after Menopausal Hormone Therapy (MHT) Discontinuation
Claudio N. Soares, M.D., Ph.D. McMaster University, Dept. of Psychiatry, Women's Health Clinic, 301 James St South, FB#368, Hamilton, ON, L8P5B6, 1220, Hadine Joffe, M.D., MSc., Adele C. Viguera, M.D., M.P.H., Laura F. Petrillo, M.D., Brittny Somley, B.S., Lee S. Cohen, M.D.

Educational Objectives:
To understand the extent to which menopause-related somatic and psychological changes following menopausal hormone therapy (MHT) discontinuation may affect mood, sleep, and quality of life.

To examine the efficacy and tolerability of paroxetine CR for the treatment of symptomatic menopausal women after MHT discontinuation.

Summary:
With increasing concern about the safety of menopausal hormone therapies (MHT), many peri and postmenopausal women have discontinued hormone treatments.

Objective: This study examined the efficacy of paroxetine controlled-release (CR) versus placebo for the treatment of peri and postmenopausal women who present with menopause-related symptoms after discontinuing MHT.

Methods: Peri and postmenopausal women who developed vasomotor symptoms (VMS) after MHT discontinuation were enrolled into the study. Concomitant symptoms of depression and anxiety were allowed, but subjects meeting DSM-IV criteria for Mood or Anxiety Disorders were excluded. A one-week, single-blind, placebo lead-in phase, was used to obtain baseline diary data (hot flash frequency and severity) and to exclude placebo responders. Eligible subjects entered a six-week, double-blind phase, with paroxetine CR 12.5 mg/day or placebo. The primary outcome measure was change in vasomotor symptoms (hot flashes frequency/severity) over the 6-week period. Secondary outcome measures included changes in depressive and anxiety symptoms, quality of life and overall functioning. Analyses were conducted using non-parametric methods.

Results: Sixty-four women (aged 56.3 ± 5.5 years) were enrolled in this study, and 50 completed the 6-week trial. Subjects had used MHT for 77 months on average (interquartile range [IQR]=77-120), and had stopped MHT about 7 months (IQR=4-9 months) prior to study enrollment. Treatment with paroxetine CR was superior to placebo for the alleviation of VMS (mean reduction of 6.1 hot flashes per week; IQR=4.8-6.4; p=0.02). Depressive symptoms also showed superior improvement with paroxetine CR (p=0.01). Both placebo and paroxetine led to improvement of anxiety symptoms and overall functioning, with no differences between treatment groups.

Conclusions: Symptomatic peri and postmenopausal women who developed menopause-related complaints - particularly vasomotor and depressive symptoms - after MHT discontinuation benefitted from treatment with paroxetine CR.

References:

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NR717 Wednesday, May 23, 12:00 PM - 2:00 PM

Fourteen Year Interim Results from an International Observational Study of Pregnancy Outcomes Following Exposure to Lamotrigine

Thomas Thompson, M.D. GlaxoSmithKline, Department of Psychiatry, 8704 Kings Mill Place, Raleigh, NC, 27615-1883, 9000, Marianne Cunningham, John Messenheimer, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand pregnancy outcomes in women exposed to lamotrigine from an international registry established in 1992.

Summary:
Objective: Anticonvulsant medications are continued during pregnancy making it important to monitor their potential teratogenic effects. The international registry forms part of an epidemiologic safety program, established in 1992, monitoring pregnancy outcomes in women exposed to lamotrigine.

Methods: Physicians report exposure to lamotrigine during pregnancy and subsequent outcomes on a voluntary basis. Prospective reporting (prior to any knowledge regarding the possible outcome of the pregnancy) early in pregnancy is encouraged. Major congenital malformations (MCMs) are classified according to the Centers for Disease Control criteria and are reviewed by a pediatrician. The percentage of MCMs is calculated by trimester and according to monotherapy or polytherapy with/without valproate. Conclusions are developed and endorsed by a scientific advisory committee.

Results: As of March 2006, 23 MCMs were observed among 831 first trimester monotherapy exposures giving a risk of 2.8% (95% CI 1.8% - 4.2%). The observed risk among 128 lamotrigine and valproate polytherapy exposures was 11.7% (95% CI 6.9% - 18.9%) and was 2.8% (95% CI 1.3% - 5.7%) among 287 exposures to lamotrigine polytherapy without valproate. No dose-effect at first trimester monotherapy daily doses up to 400 mg was found. There was insufficient data at doses of 400 mg or more to confirm or refute a dose effect. No consistent pattern of malformation types was observed.

Conclusions: The current data do not indicate any substantial increase in the overall risk of major defects associated with prenatal lamotrigine exposure, though the sample size is insufficient to allow definitive conclusions regarding the safety of lamotrigine in pregnancy. The higher frequency of major malformations following lamotrigine-valproate polytherapy exposure is similar to that reported with valproate monotherapy. Continued registration of exposed pregnancies will enhance the statistical power of the study and allow physicians to assess the benefit-risk of lamotrigine use in pregnancy.

Funding provided by GlaxoSmithKline.

References:

NR718 Wednesday, May 23, 12:00 PM - 2:00 PM

Birth Outcomes Following Prenatal Exposure to Newer Antidepressant Medications

Maria R. Corral, M.D. St. Paul’s Hospital, Psychiatry, 1081 Burrard Street, 2B-139, Vancouver, BC, V6Z 1Y6, 1220, Shalia Misri, Diana Carter, M.D., Dierdre Ryan, M.D., Ladan Sadrehashemi, M.D., Andrea A. Wardrop, B.A.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize, in a sample of clinicians who attended an academic-based CME activity, first choice treatment preferences in the case of a pregnant, depressed patient.

Summary:
A significant minority of neonates exposed to antidepressants in utero is at heightened risk of developing transient symptoms after birth. We present data from birth charts of neonates exposed prenatally to citalopram, venlafaxine, bupropion and mirtazapine alone (Group 1, n=34) or in combination with other psychotropic medications (Group 2, n=13), and a non-exposed control group (Group 3, n=12). Mean gestational age was 38.64 weeks (SD=1.70) in Group 1, 38.43 weeks (SD=2.40) in Group 2 and 39.50 weeks (n=11) in the controls. Two neonates in each of Groups 1 and 2 (5.89%, 15.38% respectively) and 0 control infants were considered pre-term (gestational age <37 weeks). The mean birth weights were 3459.56 g (SD=522.24) and 3355.10 g (SD=503.10) in Groups 1 and 2 respectively, and 3504.58 g (SD=286.87) in the controls. One neonate in each of Groups 1 and 2 (2.94%, 7.69% respectively), and no control infants had low birth weight (<2500 g). Mean 5-minute APGAR scores were 8.76 (SD=0.61), 8.62 (SD=0.87), and 9.27 (SD=0.47) respectively. Mean stay in hospital was 2.94 (SD=2.81) and 2.92 (SD=1.71) days for Groups 1 and 2, and 1.91 (SD=1.0) for the controls. Ten infants in Group 1 (29.41%) were admitted to a special care nursery (SCN) during the hospital stay. Length of stay was recorded in 6 of these cases; all infants stayed ≤1 day. Five Group 2 infants were admitted to an SCN (38.46%), 3 of whom stayed ≥2 days. Two control infants (16.67%) had SCN admissions of <1 day. The most frequent reasons for admission were neurological or respiratory concerns, observation with absence of symptoms, maternal reasons, and jaundice in all groups. Symptoms in neonates exposed to these medications, alone or in combination, were more often reported than for non-exposed neonates. Poorer outcomes were found in infants exposed to multiple as opposed to single medications.

References:

NR719 Wednesday, May 23, 12:00 PM - 2:00 PM

Management of Depression during Pregnancy: First Choice Treatment Preferences

Timothy J. Petersen, Ph.D. Massachusetts General Hospital, Psychiatry, 55 Fruit Street, Bullfinch 449, Boston, MA, 02114, 9000, Anthony P. Weiss, M.D., Madeline B. Horwitz, Mark Blais, Psy.D., Jeff Huffman, M.D., Robert J. Birmbaum, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to more familiar with the range of neonatal symptoms associated with maternal use of newer antidepressants during pregnancy, either alone or in combination with other psychotropic medications. This knowledge will aid the participant in counseling patients about the possible consequences of using psychotropic medication in pregnancy.

Summary:
The current data do not indicate any substantial increase in the overall risk of major defects associated with prenatal lamotrigine exposure, though the sample size is insufficient to allow definitive conclusions regarding the safety of lamotrigine in pregnancy. The higher frequency of major malformations following lamotrigine-valproate polytherapy exposure is similar to that reported with valproate monotherapy. Continued registration of exposed pregnancies will enhance the statistical power of the study and allow physicians to assess the benefit-risk of lamotrigine use in pregnancy.

Funding provided by GlaxoSmithKline.

References:
The Impact of Comorbid Anxiety Disorders on the Course of Major Depressive Disorder in Pregnancy

Hope D. Courtney, B.S., Emory University, Psychiatry, 1365 Clifton Rd. NE, Clinic Building B Suite 6100, Atlanta, GA, 30322, 9000, D Jeffrey Newport, Elizabeth Z. King, Lee S. Cohen, Lori L. Altshtuler, Zachary N. Stowe

Educational Objectives:

At the conclusion of this presentation, the participant will be aware of the impact of comorbid anxiety disorders on maternal depressive symptoms in pregnancy.

Summary:

Factors affecting depressive symptoms and relapse of major depression (MDD) during pregnancy and the postpartum period are critical in the development of treatment guidelines. There is limited data on the course of most anxiety disorders in pregnancy, with considerable variation in the measures employed (Ross et al, 2006). Two hundred and four women from the Emory Women's Health Program with a SCID lifetime diagnosis of MDD were followed throughout pregnancy. Of these women comorbidity included: 1) 99/204 (48.5%) no comorbid anxiety disorder; 2) 76/204 (37.3%) had 1 comorbid anxiety disorder (Panic disorder, PTSD, or OCD); 3) 29/204 (14.2%) had ≥2 comorbid anxiety disorders. We compared the Beck Depression Inventory scores across pregnancy between these groups, using BDI ≥12 to identify significant depressive symptoms. Notably, 58.7% of the women with no comorbid anxiety disorders experienced significant depressive symptoms (BDI score 14.7±9.42). In patients with comorbid anxiety disorders depressive symptoms were significantly more common (F(2, 203)=3.841, p< .023), 1 anxiety disorder - 67.1% (BDI 18.2±10.34) and ≥ 2 anxiety disorders - 79.3% (BDI 19.4±10.5). With respect to the impact of specific comorbid anxiety disorders on depressive symptoms during pregnancy; 1) Comorbid Panic Disorder (n=59), mean BDI of 16.8±10.06 with 59.0% ≥12; 2) Comorbid OCD (n=19), mean BDI of 16.4±9.42 with 63.2% ≥12; and 3) Comorbid PTSD (n=18), mean BDI of 23.4±10.7 with 88.9% ≥12. These data indicate that comorbid anxiety has an adverse impact on the course of maternal depression during pregnancy. Diagnostic specific instruments - the Yale-Brown Obsessive Compulsive Scale, Panic Disorder Severity Scale, and PTSD Checklist - will be analyzed with respect to the course of anxiety disorders during pregnancy and the postpartum period. Further assessments will include mood state at conception, use of psychotropic medication during pregnancy, and treatment continuation/discontinuation.

Supported by P50 MH 68036, R01 MH 063979

References:


NR720

The Impact of Comorbid Anxiety Disorders on the Course of Major Depressive Disorder in Pregnancy

Kathryn A. Czarkowski, M.A., Yale School of Medicine, Psychiatry, 100 York St., Suite 2H, New Haven, CT, 06511, 9000, Deborah Ward-O'Brien, M.S.N., Ralitza Gueorguieva, Ph.D., C. Neill Epperson, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to appreciate the importance of early identification of postpartum depression for treatment, and the impact of lower socio-economic status on outcome of treatment.

Summary:

Introduction: This study examined whether the presence of known psychosocial risk factors for postpartum depression (PPD) predicted response to treatment in a small, randomized clinical trial of sertraline in the treatment of PPD.

Methods: Twenty-nine women with onset of major depression within three months of delivery of a healthy full-term infant were considered to be treatment responders. All others were considered non-responders. Risk factors of interest were age, parity, marital and employment status, education level, and approximate annual household income. Additionally, the impact of illness onset in...
that there were no demographic differences between women tested versus those who tested positive for unreported drug use were less educated (13.67 years versus 15.35, t=-2.381, p<.05) than those confirmed compliant. Multivariate analyses are currently underway and will be presented. These findings highlight the importance of obtaining comprehensive records from disparate sources when researching the effects of medication in pregnancy. Future obstetrical outcome studies should incorporate objective laboratory methods before drawing sweeping conclusions about the reproductive safety/teratogenicity of a particular compound. Supported by P50MH68036, R01MH063979, K23MH063507, R01MH071531

References:

**Validation of Maternal Drug Use in Pregnancy Using Objective Laboratory Methods**

Zachary N. Stowe, M.D. Emory University School of Medicine, Psychiatry & Behavioral Sciences, 1365 Clifton Road NE, Emory Clinic Bldg. B, Suite 6100, Atlanta, GA, 30322, 9000, Martha R. Calamaras, B.S., Adam Lorentz, James C. Ritchie, Ph.D., Bettina T. Knight, R.N., Stephanie S. Winn, M.D., Jeffrey Newport, M.D.

**Educational Objectives:**

At the conclusion of this presentation, participants should be able to identify different psychotropic treatment strategies to use with HIV/HCV coinfected patients beginning on treatment for Hepatitis C infection. The participant should be able to demonstrate knowledge of the prescribing patterns of expert clinicians treating hepatitis C in HIV/HCV coinfected individuals and of how these prescribing patterns differ among psychiatrists and non-psychiatrist providers.

**Summary:**

At the conclusion of this presentation, the participant should recognize the importance of incorporating objective laboratory methods in studies on medication safety in pregnancy, particularly in studies that address the safety/teratogenicity of particular medicines.

The use of psychotropic medications in pregnancy remains a controversial issue. Numerous investigations of obstetrical outcome related to psychotropic exposure have produced discrepant findings with respect to major malformations and delivery/neonatal complications. A seminal concern is the reliance on maternal self-report to identify fetal exposure. To validate maternal report, we measured urine cotinine in the 3rd trimester, urine drug screens, and maternal serum for medication concentrations.

A total of 845 pregnant women with a lifetime diagnosis of a mood or anxiety disorder were followed prospectively throughout pregnancy across several federally-funded investigations. Preliminary analysis confirmed our hypothesis that maternal self-report is not a viable proxy for actual fetal exposure, including: 1) 16.8% (35/208) of subjects denying cigarette exposure had detectable levels of urine cotinine; 2) 3.4% (15/440) tested positive for unreported drugs of abuse; and 3) 13.3% (72/536) had undetectable maternal medication serum concentrations (parent and metabolite compound) in pregnancy or at delivery. Further analysis showed that 1) there were no demographic differences between women with/without detectable urine cotinine; 2) participants who tested positive for unreported drug use were less educated (13.67 years versus 15.39, t=2.645, p<.01), had a greater parity (1.92 versus 1.01, t=-2.628, p<.01), were more likely to have an unplanned pregnancy (X^2=6.176, p<.05) and an undesired pregnancy (X^2=18.292, p<.01); and 3) women deemed noncompliant with their medication as determined by blood level were more likely to be African American (X^2=17.937, p<.01) and less educated (14.63 years versus 15.35, t=-2.381, p<.05) than those confirmed compliant. Multivariate analyses are currently underway and will be presented.

**References:**


**Psychotropic Medication Use in HIV/HCV Coinfected Patients Beginning Treatment for Hepatitis C Infection**

Jeffrey J. Weiss, Ph.D. Mount Sinai School of Medicine, Department of Psychiatry, Box 1228, New York, NY, 10029, 9000, Jack M. Gorman, M.D.

**Educational Objectives:**

At the conclusion of this presentation, participants should be able to identify different psychotropic treatment strategies to use with HIV/HCV coinfected patients beginning on treatment for Hepatitis C infection. The participant should be able to demonstrate knowledge of the prescribing patterns of expert clinicians treating hepatitis C in HIV/HCV coinfected individuals and of how these prescribing patterns differ among psychiatrists and non-psychiatrist providers.

**Summary:**

Introduction: HIV/HCV coinfected persons are being treated for HCV with pegylated interferon/ribavirin (PEG-IFN/RBV) in increasing numbers and data to guide clinicians on the use of psychotropic medication in this context is lacking.

Methods: Anonymous online survey of expert providers to assess psychotropic prescribing practice in managing HIV/HCV patients beginning PEG-IFN/RBV therapy.

Results: 70/160 providers targeted by email participated. 9/70 providers only prescribe PEG-IFN/RBV and refer to others to prescribe psychotropics. Of the 61 providers who prescribe psychotropics, 35 were ID specialists, internists or hepatologists; 16 were psychiatrists, and 10 were not physicians. Providers were asked about prescribing antidepressants in four scenarios: (1) No past or current depression; (2) History of depression but no current symptoms; (3) Current depression on antidepressants; (4) Current bipolar disorder on mood stabilizers. In scenario 1, 36% of the providers would consider using antidepressants prophylactically, with psychiatrists more likely to consider this (56%) than non-psychiatrists (29%) (p<.05). In scenario 2, 20% of providers would begin the patient on antidepressants, 57% would give the patient the option of doing so, and 23% would not begin antidepressants but monitor the patient closely. In scenario 3, there was strong agreement among providers (92%) to leave the patient on the...
current dose of antidepressants. In scenario 4, all psychiatrists and 78% of non-psychiatrists would leave the patient on the current dose of mood stabilizer. Of the providers who have also treated HCV monoinfected patients (77%), 21% of non-psychiatrists, but no psychiatrists, indicated that they would be more likely to use antidepressants in HIV/HCV coinfected patients than in HCV monoinfected patients.

Conclusions: In patients without current symptoms of depression, there is a lack of consensus among expert providers on the prophylactic use of antidepressants for HIV/HCV patients beginning PEG-IFN/RBV. Data to guide treatment decision making in this situation is urgently needed.

References:

NR724 Wednesday, May 23, 3:00 PM - 5:00 PM
Directly Observed Therapy to Treat Depression in the HIV-Positive Urban Poor

Dan H. Karasic, M.D. UCSF at San Francisco General Hospital, Psychiatry, 1001 Potrero Avenue, Suite 7M, San Francisco, CA, 94110, 9000, Gwendolyn P. Hammer, Ph.D., James L. Sorensen, Ph.D., Kathleen Ragland, Ph.D., Andrew R. Moss, Ph.D., David R. Bangsberg, M.D., M.P.H., James W. Dilley, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the effect of depression in medication adherence and health outcomes in the HIV-positive urban poor, and recognize the impact of directly observed antidepressant therapy in the treatment of depressive disorders in incompletely adherent and substance using populations.

Summary:

Depression in the HIV-positive urban poor is closely associated with antiretroviral non-adherence and disease progression; however, incomplete adherence and concurrent substance abuse complicate antidepressant treatment. We tested the effectiveness of directly observed antidepressant therapy (DOT) in this population.

Methods: Individuals diagnosed with current Major Depressive Disorder, Minor Depressive Disorder, or Dysthymia, by Structured Clinical Interview for DSM-IV criteria, were randomized to either DOT delivered at the study site or referral to community psychiatric care. The DOT group was administered daily fluoxetine for 1 month, then weekly fluoxetine for the next 5 months; for 3 months thereafter, weekly fluoxetine was self-administered. Augmenting medications were added if necessary to treat depression to remission. Participants in the control group visited the study site weekly as an attention control. Individuals in both groups were paid $25 per weekly visit. Primary outcomes were monthly Hamilton Depression Rating Scale (HAM-D), Hamilton Anxiety Rating Scale (HAM-A), Beck Depression Inventory (BDI), and the Clinical Global Impression (CGI), assessed blinded to treatment assignment. Outcomes were analyzed by treatment status over each 3-month interval using generalized estimating equations. Results: Of 1530 individuals screened, 103 participants were enrolled. Eighty-nine percent had a history of substance abuse. Fifty-one were nine controls (56%) reported taking antidepressants. DOT was more effective (P<0.01) than referral to usual community care at every three-month interval for HAM-D, HAM-A, and BDI. This difference was maintained for the 3 months of self-administered therapy following DOT. (See figure.)

Conclusion: Weekly DOT is more effective than referral to community care in the treatment of depressive disorders and is a promising strategy in a population in which incomplete adherence and substance use is common.

References:

NR725 Wednesday, May 23, 3:00 PM - 5:00 PM
Effects of Prenatal Exposure to Nitric Oxide Synthase Inhibitor on Behavioral Changes in Forced Swimming Test in Postnatal Rats

Young In Chung, M.D. Pusan National University Hospital, Psychiatry, 1-10 Ami-Dong, Sea-Gu, Pusan, 602-739, 5800, Gil Joong Kim, M.D., Sook Hyun Park, M.D.

Educational Objectives:

The aim of the study was to investigate the involvement of NO in the underlying mechanisms of biological vulnerability to depression. At the conclusion of the presentation, the authors suggest that the glutamate-NMDA-NO pathway may lead to a novel approach to the treatment of depression.

Summary:

Objective: It has been demonstrated that nitric oxide (NO) serves as an inter- and intra-cellular messenger in the brain. NO has been implicated in the regulation of monoaminergic neurotransmission and the neuronal growth and synaptogenesis. Recently, NO has been suggested to involve the pathogenesis of depression. Therefore, the aim of the study was to investigate the involvement of NO in the underlying mechanisms of biological vulnerability to depression.

Methods: The authors measured locomotor activities and postnatal behavioral changes in the forced swimming test (FST) in rats which were exposed prenatally to N^-nitro-L-arginine, a NO synthase (NOS) inhibitor. It was also investigated that paroxetine, a selective serotonin reuptake inhibitor, may affect the behavioral changes in the FST.

Results: Locomotor activities were significantly diminished and the immobility times in the FST were significantly prolonged in the rats which were exposed prenatally to NOS inhibitor compared with controls. Pretreatment with paroxetine blocked the prolongation of the immobility times in the FST.

Conclusion: These results indicate that postnatal behavioral changes due to prenatal exposure to NOS inhibitor in the rats may become a model of endogenous depression and the glutamate-NMDA-NO pathway can be involved in the pathophysiology of depression. It is indirectly suggested that serotonergic mechanism may be, in part, involved in the action of NO. This indicates that the glutamate-NMDA-NO pathway may lead to a novel approach to the treatment of depression.

References:

**NR726 Wednesday, May 23, 3:00 PM - 5:00 PM**

**Serum Pyridoxal Level in Patients With and Without Tardive Dyskinesia**

Vladimir Lerner, M.D. Ben Gurion University, Mental Health Center, P.O.Box 4600 Mental Health Center, Be’er Sheva, 84170, 5081, Chanoch Miodownik, M.D., Aviel Meoded, M.D., Ben-Ami Sela, Ph.D., Igor Libov, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to understand the connection between tardive dyskinesia and serum pyridoxal levels.

**Summary:**

The origin of tardive dyskinesia (TD) is not well understood. Vitamin B6 plays an essential role in the normal functioning of the central nervous system. Some researchers described motor disturbances which have been observed in vitamin B6-deficient animals. Clinical experiments showed that vitamin B6 may ameliorate different drug-induced movement disorders including TD. Since vitamin B6 plays an important role in the metabolism of all neurotransmitters, which assumed to take a part in the pathogenesis of TD, we decided to examine whether a difference between mean PLP serum levels in those two groups (with and without TD) may have correlation with presence or absence of TD symptoms.

**Methods:** For the aim of our study, we enrolled 41 schizophrenic inpatients, 19 males and 22 females, 20-66 years-old, suffering from TD (the study group), and 49 schizophrenic inpatients, 19 males and 30 females, 21-66 years-old without any symptom of motor disturbances (the control group).

Blood sample (5 mL) was drawn before breakfast. Measurement of the physiologically active vitamer of vitamin B6 pyridoxal-5-phosphate (PLP), is performed by high performance liquid chromatography (HPLC) separation according to Botticher and Botticher assessment method.

**Results:** Mean of serum PLP level significantly differed between the study and control groups: 17.7 ± 18.7 nmol/L and 26.3 ±13.5 nmol/L (p<0.014), accordingly. The difference between the groups was almost entirely attributable to the PLP levels of male patients: 12.4±11.4 nmol/L vs 29.0±12.9 nmol/L in males (p<0.001), and 23.9±13.6 nmol/L vs 22.3±13.6 nmol/L in females (p>0.5).

**Conclusions:** In general, serum PLP level is significantly lower in schizophrenic patients with TD. This statement is specially emphasized regarding male schizophrenic patients.

**References:**


**NR728 Wednesday, May 23, 3:00 PM - 5:00 PM**

**Is the Neurogenic Hypothesis of Depression a Myth? New Insights from the Bench to the Bedside.**

João M. Bessa, M.D. University of Minho, Life and Health Sciences Research Institute, Life and Health Sciences Research Institute (ICVS), Universidade do Minho, Campus de Guimarães, Braga, 4700, 4710, Ana R. Mesquita, Rui Silva, Ana Franky, Andreia Silva, João J. Cerqueira, M.D., Ph.D., Nuno Sousa, M.D., Ph.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to understand the importance of adult hippocampal neurogenesis in the pathophysiology of depression. Furthermore, he should be able to identify the differential modulation of hippocampal neurogenesis by chronic stress and antidepressive drugs in this animal model of depression. Finally he should be able to recognize that the effects of fluoxetine and imipramine on hippocampal neurogenesis are not necessary for the efficacy of these antidepressive agents thus providing a new insight on the neurogenic hypothesis of depression.

**Summary:**

Depression is amongst the most prevalent psychiatric disorders. Recent findings concerning the pathophysiology of this disease suggest that hippocampal adult neurogenesis plays a critical role in the action of antidepressant drugs, giving rise to a "neurogenic hypothesis" of depression. To further understand these phenomena, this study examined the effects of antidepressive drugs in animals exposed to a classical model of depression, in the presence or absence of the alkylation agent methylazoxymethanol (MAM) used to prevent the proliferation of neuroblasts. Fluoxetine (10mg/kg), Imipramine (10mg/kg) and vehicle (saline) were chronically administered alone or with MAM (7mg/kg), to male Wistar rats in the last two weeks of exposure to a Chronic Mild Stress (CMS) protocol of eight weeks.
Depressive-like behaviour was assessed with the forced swimming test (FST). Hippocampal cell proliferation and neurogenesis were assessed with immunocytochemical detection of BrdU incorporation and co-localization with neuronal markers. In the FST after exposure to CMS and drug treatment, immobility time was increased and latency to immobility decreased in the saline-treated group. Both Fluoxetine and Imipramine treatment were able to reverse these behavioural effects of CMS in the FST confirming their antidepressant effect in this animal model. The concomitant use of MAM with Fluoxetine, Imipramine or saline did not alter the behavioural profile in any experimental group. Moreover, CMS led to a decreased neurogenesis in the hippocampus whereas the use of Fluoxetine and Imipramine increased cell proliferation in this region; as expected, the use of MAM significantly reduced cell proliferation in all therapeutic groups.

In conclusion, these results suggest that neurogenesis is impaired in an animal model of depression (CMS) and is influenced by antidepressants. However, increased neurogenesis is not a necessary condition for the therapeutic effect of these drugs, thus calling for a re-appraisal of the role of hippocampal neurogenesis in depression.

References:

NR729 Wednesday, May 23, 3:00 PM - 5:00 PM
Use of a Biological Marker to Aid in the Diagnosis of Bipolar I Disorder and Attention Deficit Hyperactivity Disorder
Sharon A. Murphy, M.D. Private Psychiatry, Sole Proprietor, 9421 Hickory Limb, Columbia, MD, 21045, 9000, Douglas Woodruff, M.D.

Educational Objectives:
At the end of this presentation, the participant should be able to recognize that a new paradigm is imminent in Psychiatry; specifically, one in which biological markers are practical criteria aiding in the making of diagnoses, just as they do in other branches of medicine.

Summary:
It has been recognized in the literature since at least 1969 that abnormal regulation of ion distribution and variability in the functioning of the Na,K pump is associated with Bipolar Disorder. While using the membrane potential assay developed by Thiruvengadam and Chandrasekaran to identify Bipolar I Disorder (BPDI), we were intrigued because the emerging data suggested this membrane potential test is also sensitive to presumed malfunctioning of the Na,K pump in Attention Deficit Hyperactivity Disorder (ADHD). Testing 273 patients, of whom 123 were controls (negative), we found 55 to be BPDI and 95 to be ADHD. Confirmation of a diagnosis was by clinical response to medications appropriate for each diagnosis. The sensitivity of the test was comparable to the PSA test.

Assuming our findings are replicable in additional trials, this membrane potential assay is a potent clinical tool for clarifying the differential diagnosis between ADHD and BPDI as well as between unipolar (noncycling) recurrent depression and the depressive phase of BPDI. This membrane potential assay offers the possibility of reduced therapeutic misadventure, which can result from the possibility of clinical uncertainty in differential diagnosis using our current diagnostic criteria.

References:

NR730 Wednesday, May 23, 3:00 PM - 5:00 PM
Antidepressants and Suicide In Children and Adolescents in Virginia: Toxicology Findings
Antony Fernandez, M.D. McGuire Veterans Administration Medical Center, Psychiatry, 1201 Broad Rock Boulevard, Box 116A, Richmond, VA, 23249, 9000, Jose Mathews, M.D., Walter Victor Vieweg, M.D., Ananda K. Pandurangi, M.D.

Educational Objectives:
Antidepressants appeared more commonly among youths committing suicide than those dying by accident or homicide. SSRIs did not appear more commonly among youths committing suicide by poisoning than those committing suicide by gun or hanging.

Summary:
Interest in child and adolescent suicide remains intense. We describe post-mortem toxicology findings in a subset of youths who committed suicide We analyzed 'unnatural' deaths from Virginia's Medical Examiner Office for 1987-2003. There were 2818 unnatural deaths in children and adolescents. We grouped unnatural deaths as follows accident, homicide, and suicide. Toxicology was available for 753 cases of which 732 were Black or White youths.

Results: For all unexpected deaths, antidepressants were more commonly found among Whites than Blacks. Suicide by poisoning occurred more commonly among Whites. Recreational drugs were more commonly found among Blacks than Whites. Antidepressants were found in 39 Black and White suicides. There were 17 antidepressants (all tricyclic antidepressants_TCs) in suicide by poisoning. No other antidepressants were found in lethal levels in suicide by poisoning. SSRIs/venlafaxine appeared more commonly in the suicides (p < 0.0001) than in accidents or homicides. For suicides, SSRIs appeared no more commonly in poisoning than in gun or hanging deaths (p = 0.695).

Conclusions: Antidepressants appeared more commonly among youths committing suicide than those dying by accident or homicide. SSRIs did not appear more commonly among youths committing suicide by poisoning than those committing suicide by gun or hanging. Because our data are descriptive, they are subject to over-interpretation.

References:
Identification and Study of Attention Deficit Hyperactivity Disorder, Its Associated Comorbidity and Psychosocial Correlates in Primary School Children Studying in a Public School of a Metropolitan City in India

Vibhay Raykar, M.D.  B.Y.L.Nair Hospital, Psychiatry, Dr.A.L. Nair Road, Psychiatry Department, Mumbai, 400008, 5330, Ramesh R. Patel, M.D., Sanjeev M. Kamat, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that ADHD is prevalent in Indian primary school children, is associated with some psychosocial factors and comorbid conditions and they may experience significant functional problems.

Summary:
Objective: To study the prevalence of ADHD,socio-demographic profile,psychosocial factors,distribution of subtypes of ADHD,compare the subtypes of ADHD with respect to various psychosocial factors and assess the psychiatric comorbidity associated with ADHD in primary school children of a public school in a metropolitan city in India.

Method: Three thousand three hundred and fifty-six children between ages 5-9 years were evaluated. The parameters mentioned above were assessed using DSM-IV criteria for diagnosing ADHD, Weschler's Intelligence Scale for Children, Conners Teacher Questionnaire, Childhood Psychopathology Measurement Schedule, Parental Handling Questionnaire, Modified Kuppuswamy Socio-economic Status Scale. Data was analyzed using the chi-square test of significance.

Results: Prevalence of ADHD in primary school children between ages 5-9 years was 1.22% and it was more common in age group of 7-9 years (73%) and boys (83%). Poor school performance was seen in 24% of the children, 56% of the children had average school performance and 19.5% performed well academically. A high incidence of family history of ADHD (53.7%) was observed. Statistically significant greater number of children (56.1%) belonged to hyperactive type than combined (36.6%) and inattentive type (7.3%). All children of inattentive type were in age group of 7-9 years and 43.5% of children of hyperactive type were in age group of 5-7 years. The combined and hyperactive types were more common in boys while the inattentive type was more common in girls. Highest comorbidity found in the ADHD children was anxiety (60.5%) followed by conduct disorder (41.5%), physical symptoms due to emotional problems (46.3%) and depression (2.4%).

Conclusion: ADHD is prevalent even in Indian primary school children and is associated with number of comorbid disorders such as anxiety disorders and conduct disorders. Children with ADHD also experience significant functional problems such as poor school performance and academic underachievement.

References:

Neurocognitive Outcome of Lamotrigine in Pediatric Bipolar Disorder

Mani N. Pavuluri, M.D.  University of Illinois at Chicago, Psychiatry, 912 South Wood St, UIC M/C913, Suite 239, Chicago, IL, 60612, 9000, Megan M. O'Connor, Ph.D., John A. Sweeney, Ph.D.

Educational Objectives:
1. Understand the neurocognitive profile of pediatric bipolar disorder
2. Understand the effects of lamotrigine on neurocognition
3. Learn about developmental differences in outcome

Summary:
Background: The antiepileptogenic mechanism of action of lamotrigine may result in improvement in neurocognitive functioning in pediatric bipolar disorder (PBD). This is the first prospective lamotrigine study to examine the comprehensive neurocognitive profile in PBD with an aim to primarily identify the effects of pharmacotherapy.

Methods: There were 65 subjects aged 13± 3 years including PBD patients (n=32) and healthy controls (HC) (n=33) matched on age, sex, race, socioeconomic status, IQ and reading ability. Patient population belonged to bipolar type I and II, with manic or mixed episodes. All subjects completed tests on attention, executive function, attention, verbal learning, working memory and emotion recognition before and after 16 weeks of trial period. PBD patients received lamotrigine partial doses during the initial ramp up phase of 8 weeks and full and stable dose for the latter 8 weeks. Results: On the clinical outcome measures, PBD patients significantly improved from baseline to the end point scores on young mania rating scale (Pre- test score: 21.74; Post- test score:8.35; p<.001) and on child depression rating scale (Pre-test score: 51.5; Post- test score:24.7; p<.001). Working memory and executive function deficits present at baseline were significantly improved by lamotrigine treatment in younger age group compared to adolescents. No deterioration was evident after treatment in any domain. Facial emotion recognition improved with treatment in patient group, especially for happy child faces relative to angry faces or any adult faces.

Conclusion: Lamotrigine monotherapy resulted in no decline in neurocognitive functioning in PBD patients. There is significant improvement in working memory and executive function with lamotrigine therapy in younger PBD patients. There is distinct improvement in facial emotion recognition with treatment in both children and adolescents.

References:
Educational Objectives:

At the end of the presentation, participants should be able to describe the role of catechol-O-methyltransferase polymorphisms in the response of children with Attention Deficit Hyperactivity Disorder to methylphenidate treatment.

Summary:

Objective: Do catecholamine-O-methyltransferase (COMT) polymorphisms, which have been associated with ADHD, affect dose responsiveness to methylphenidate (MPH) in ADHD children?

Methods: As part of ongoing grant sponsored by the American Academy of Child and Adolescent Psychiatry, 45 children ages 7-15 years with the clinical diagnosis of ADHD, confirmed by NIMH DISC-IV-P, were enrolled in this blinded prospective study. Buccal samples were examined for genetic polymorphisms. Children were treated with gradually increasing doses of MPH using a structured schedule based on serial responses to Conners Global Index-Parent and Teacher Scale. The endpoints were the dose of MPH to achieve a 10 point CGI-PT improvement and the dose of MPH to normalize (T-score < 60).

Results: Among the 45 children with ADHD, 18 (40%) had Val-Val polymorphism, 5 (11%) had Met-Met polymorphism, and 22 (49%) were heterozygous Val-Met. There were no differences in the dose of MPH for a 10 point CGI improvement between groups (Val-Val 25mg, Met-Met 33mg, Val-Met 22mg, Log-rank 4.03, df=2, p=0.13). Similarly, there was no difference in the dose of MPH among groups to achieve a normalization T-score (Val-Val 36mg, Met-Met 40mg, Val-Met 33mg, Log-rank 1.29, df=2, p=0.52). Sufficient power (>80%) to detect a 10 mg difference in both analyses was present.

Conclusion: Unlike our previous study which noted an effect on mph dose by DRD4-7repeat allele status, this study did not identify an influence on clinical outcomes based on Comt Polymorphism status.

References:

NR735 Wednesday, May 23, 3:00 PM - 5:00 PM
Changes in Prolactin in Adolescents with Schizophrenia or Bipolar Disorder I during Treatment with Olanzapine: A Pooled Analysis of 4 Studies
Carol Robertson-Plough, D.V.M. Eli Lilly and Company, Lilly Research Laboratories, Lilly Corporate center, Indianapolis, IN, 46285, 9000, Gabrielle A. Carlson, M.D., Melissa P. DelBello, M.D., Robert L. Findling, M.D., Robert A. Kowatch, M.D., S. Charles Schulz, M.D., Ludmila Kryzanovskaya, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should have a better understanding of the changes in prolactin levels that occur in olanzapine-treated adolescents with schizophrenia or bipolar disorder.

Summary:

Introduction: Previous research suggests increases in prolactin (PRL) may occur in adolescents during antipsychotic treatment.1,2 PRL data from adolescents treated with olanzapine are presented.

Methods: Data from 454 adolescents (13-18, mean=15.9 yrs) with schizophrenia or bipolar mania were pooled from 4 olanzapine (2.5-20mg/day) studies (4-32 weeks; 2 double-blind, placebo-controlled studies [combined for acute phase endpoint PRL levels] with open-label extensions; 2 open-label studies). Age- and sex-specific Covance reference ranges defined normal PRL; categorical increases were based on multiples of the upper limit of normal (ULN). Baseline-to-endpoint PRL changes in adolescents were...
compared with data pooled from 84 olanzapine clinical trials in adults with schizophrenia or bipolar disorder.

Results: Olanzapine-treated adolescents had mean PRL increases at both the acute (11.4 μg/L) and open-label endpoints (4.7 μg/L). Of those patients with normal PRL levels at baseline (N=311), high PRL occurred in 54.7% at anytime; 32.2% at endpoint. The percentage of patients in which PRL levels shifted from normal-to-abnormal was smaller at endpoint than at anytime during treatment: 26.7% shifted to a higher category. Among patients with normal baseline PRL, 32.7% remained ≤1X ULN; 32.3% increased to 1-<2X; 6.0%, >2-<3X; and 1.2%, >3X at anytime; 4.6% had at ≥1 potentially PRL-related adverse event. Adolescents with schizophrenia or bipolar I disorder were pooled from 4 olanzapine studies (4-32 weeks). Changes in metabolic parameters in adolescents were compared with those of standardized growth curves.

Conclusion: Incidence of high PRL was significantly higher, and mean increases in PRL were significantly greater in adolescents versus adults. Mean increases and high PRL incidence were lower at the open-label compared with the acute phase endpoint.

References:

NR736 Wednesday, May 23, 3:00 PM - 5:00 PM Changes in Metabolic Parameters in Adolescents with Schizophrenia or Bipolar I Disorder During Treatment with Olanzapine: A Pooled Analysis of 4 Studies

Ludmila Kryzanovskaya, M.D., Eli Lilly and Company, Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN, 46285, 9000, Gabrielle A. Carlson, M.D., Melissa P. DelBello, M.D., Robert L. Findling, M.D., Robert A. Kowatch, M.D., S. Charles Schulz, M.D., Carol Robertson-Plouch, D.V.M.

Educational Objectives:
At the conclusion of this presentation, the participant should have a better understanding of the metabolic changes that occur in olanzapine-treated adolescents with schizophrenia or bipolar disorder.

Summary:
Introduction: Changes in metabolic parameters have been reported in adults treated with olanzapine. Methods: Data from 454 adolescents (13-18, mean=15.9 years) with schizophrenia or bipolar disorder were pooled from 4 olanzapine (2.5-20.0 mg/day) studies (4-32 weeks). Changes in metabolic parameters in adolescents were compared with those of olanzapine-treated adults (pooled from 84 clinical trials); changes in weight and BMI were compared with US age- and sex-adjusted standardized growth curves.

Results: Olanzapine-treated adolescents had significant increases from baseline-to-endpoint in fasting glucose (p<.001); total cholesterol, LDL, and triglycerides (p<.001); and significant decreases in HDL (p<.001). Significantly more adolescents gained ≥7% of their baseline weight compared with adults (65.1% vs. 35.6%, p<.001); mean change from baseline-to-endpoint in weight was significantly greater in adolescents (7.0 vs. 3.3 kg, p<.001). Adolescents had significantly lower mean changes from baseline-to-endpoint in fasting glucose (0.3 vs. 0.1 mmol/L, p=.002) and triglycerides (0.3 vs. 0.2 mmol/L, p=.007) compared with adults. Significantly more adults experienced treatment-emergent normal-to-high changes at anytime in fasting glucose (4.8% vs. 1.2%, p=.033), total cholesterol (6.9% vs. 1.1%, p=.001), LDL (5.8% vs. 1.5%, p=.014), and triglycerides (25.7% vs. 17.4%, p=.030). Compared with standardized growth curves, olanzapine-treated adolescents had greater increases from baseline-to-endpoint in weight (1.0 vs. 1.7 kg, p<.001), height (0.5 vs. 0.7 cm, p<.001), and BMI (0.2 vs. 2.2 kg/m², p<.001).

Conclusion: Olanzapine-treated adolescents may gain significantly more weight compared with adults, but may have smaller changes in other metabolic parameters. Clinicians may want to consider both efficacy and changes in metabolic parameters when selecting treatment options for individual adolescent patients.


NR737 Wednesday, May 23, 3:00 PM - 5:00 PM A Population Pharmacokinetic Model to Characterize the Disposition of Oral Olanzapine in Adolescent Patients with Schizophrenia or Bipolar I Disorder

Evelyn Lobo, Ph.D., Eli Lilly and Company, Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN, 46285, 9000, Tonya Quinlan, B.S., Jason T. Johnson, M.S., Quan Hong, Ph.D., Carol Robertson-Plouch, D.V.M.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the pharmacokinetics of oral olanzapine in adolescents with schizophrenia or bipolar I disorder, sources of interpatient variability in olanzapine exposure, important factors that affect olanzapine exposure, and how olanzapine pharmacokinetics in adolescents compare with adults.

Summary:
Objective: The pharmacokinetics of a drug may differ in pediatric and adults. Therefore, the pharmacokinetics of olanzapine were investigated in adolescents with schizophrenia and bipolar I disorder and compared to adults.

Methods: One-hundred seven adolescents with schizophrenia or bipolar I disorder (13-17 years) received 2.5-20.0 mg/day oral olanzapine. Four steady state blood samples were obtained from each patient. Olanzapine plasma concentrations were determined using a validated HPLC method, with electrochemical detection. A pharmacokinetic model was developed using a nonlinear mixed-effect modeling program. The distributions of pharmacokinetic parameters for olanzapine in adolescents were compared to those in adults using Kolmogorov-Smirnov two-sample test.

Results: The pharmacokinetics of oral olanzapine in adolescents were adequately described by a one-compartment model. The model estimates for oral clearance (CL/F) were 13.6 L/hr for females and 17.5 L/hr for males; oral volume of distribution (V/F) was 899 L. The interpatient variability in CL/F and V/F was 40.5% and 65.4%, respectively. Weight and sex had a significant influence on CL/F; in the weight range of 41 - 148 kg, there was a 3.6 fold increase in CL/F, and CL/F was 30% lower in females than males. The major of adolescents and adults had comparable CL/
justed odds ratios >1) were males, naive to therapy, or had taken the dose range of 2.5-20.0 mg in adolescents. Given the small magnitude of covariate effects and the interpatient variability, dose adjustments based on weight or sex are not necessary. The pharmacokinetics of olanzapine in adolescents are similar to those of adults.

References:

NR738 Wednesday, May 23, 3:00 PM - 5:00 PM
Treatment Initiation with Atomoxetine vs. Stimulants for Adults with ADHD in Medicaid Settings

Wenyu Ye for Adults with ADHD in Medicaid Settings

Educational Objectives:
At the conclusion of this presentation, participants will learn the prescribing trends for late adolescents and adults with ADHD, the factors associated with treatment selection for ADHD in Medicaid care setting, and the importance of risk adjustment when comparing treatments in observational data.

Summary:
Objective: To determine factors associated with initiation of atomoxetine (ATX), stimulants (STIM), or long-acting stimulants (LA-STIM) in adults with ADHD using Medicaid.

Methods: Data were from the IMS Health LRx Database. Patients covered by Medicaid age > 18 years were selected if they initiated treatment with an ADHD medication categorized as ATX, any STIM, or LA-STIM between Jan. 2005 and Dec. 2005. Initiation was defined as first use of a medication preceded by 120 days without a prescription in the same category. Contrasts of most-recent initiations of ATX vs. LA-STIM or ATX vs. LA-STIM, were modeled via stepwise logistic regression. Factors considered were age, gender, prior ADHD medications, initiation type (treatment, switch, add-on, reintroduction), concomitant medications, provider specialty, and line of therapy.

Results: 8,672 patients (58.04% female) most recently initiated treatment with ATX, 27,574 (59.72% female) with STIM, and 15,958 (57.02% female) with LA-STIM. Patients who were more likely to initiate ATX than STIM (lower confidence bound of adjusted odds ratios > 1) were males, naive to therapy, or had taken different ADHD medications in history prior to the current initiation, had prescriptions from primary care physicians or nurse practitioners, had previous use of ATX, or had concomitant use of antidepressants, anxiolytics, antipsychotics, anticonvulsants, or sleep aids. Conversely, STIM initiation was more likely for patients switching or being reintroduced to therapy, patients with prior use of stimulant, having concomitant use with anxiolytics, or receiving their prescription from neurologists. The model factors selected for initiation of ATX vs. LA-STIM were consistent with those for the comparison with STIM.

Conclusions: The factors significantly associated with initiation of ATX vs. STIM or LA-STIM suggest that therapy with ATX and STIM are addressing different patient treatment needs. The findings suggest that ATX is preferentially prescribed for patients with psychiatric comorbidities.

References:

NR739 Wednesday, May 23, 3:00 PM - 5:00 PM
Long-Term Effectiveness and Safety of Lisdexamfetamine Dimesylate (LDX) in Children Aged 6 to 12 Years With Attention-Deficit/Hyperactivity Disorder

Ann C, Childress, M.D., Center for Psychiatry and Behavioral Medicine, Inc., Psychiatry and Behavioral Medicine, 7351 Prairie Falcon Road, Suite 160, Las Vegas, NV, 89128, 9000, James J. McGough, M.D., Suma Krishnan, M.S., Robert L. Findling, M.D.

Educational Objectives:
At the end of this presentation, the participant should be able to:
1. Evaluate the effectiveness of long-term treatment with lisdexamfetamine dimesylate in children aged 6 to 12 years with attention-deficit/hyperactivity disorder (ADHD).
2. Evaluate the safety and tolerability of long-term treatment with lisdexamfetamine dimesylate in children aged 6 to 12 years with ADHD.

Summary:
Objectives: To evaluate the effectiveness and safety of long-term treatment with lisdexamfetamine dimesylate (LDX) in children aged 6 to 12 years with attention-deficit/hyperactivity disorder (ADHD).

Methods: This long-term, open-label, single-arm study enrolled children aged 6 to 12 years with DSM-IV-TR® diagnosis of ADHD (combined and hyperactive/impulsive subtypes) who were previously enrolled in a double-blind clinical study and who may or may not have received prior LDX treatment. Subjects were titrated to 30 mg/d, 50 mg/d, or 70 mg/d LDX over 4 weeks at the physician’s discretion, and treatment was maintained for up to 11 more months, during which time the dose could be adjusted to maintain optimal effectiveness and tolerability. The primary effectiveness measure was the ADHD Rating Scale (ADHD-RS); the secondary effectiveness measure was the Clinical Global Impression (CGI) scale. Safety assessments included adverse events (AEs), physical examinations, vital signs, laboratory evaluations, and electrocardiogram results.

Results: The intent-to-treat (ITT) population consisted of 272 subjects (189 boys, 83 girls). At endpoint, their mean (±SE) change in ADHD-RS total score from baseline was -27.2 (±12.8) (P<.0001), a >60% reduction from the baseline value of 43.3 (±7.7). Reductions from baseline were observed at each post-baseline visit, through Week 4. No differences were found between subjects who were or were not previously treated with LDX. At endpoint, investigators rated >80% of the ITT subjects as improved on the CGI scale. Treatment was generally well tolerated. Most AEs (>95%) were mild to moderate in severity and occurred during the first 8 weeks of treatment. The most common AEs were decreased appetite, insomnia, weight decrease, headache, abdominal pain, irritability, and upper respiratory tract infection.

Conclusions: Long-term treatment with 30 mg/d, 50 mg/d, and 70 mg/d LDX resulted in persistent improvements in ADHD symptoms and was generally well tolerated in children.

References:
References:

NR740  Wednesday, May 23, 3:00 PM - 5:00 PM
Lisdexamfetamine Dimesylate as a Treatment for ADHD: Dosage Formulation and pH Effects
Amir Shojaei, Pharm.D.

Educational Objectives:
- At the end of this presentation, the participant should be able to evaluate the effect of environmental pH on the solubility and oral pharmacokinetics of LDX.

Summary:
**Purpose:** Lisdexamfetamine dimesylate (lysine conjugated d-amphetamine [LDX]) is a novel prodrug designed to deliver d-amphetamine upon in vivo biotransformation. The lack of dependency of the oral pharmacokinetic (PK) profile on dosage formulation as well as the effect of pH on solubility and oral PK are presented.

**Methods:** The pH solubility profile of LDX in buffered aqueous solutions was determined using a high pressure liquid chromatography assay method specific for LDX. Saturated solutions ranging in pH from 1 through 13 were prepared and drug content was determined. Dosage formulation effect was studied in a 3-treatment, 3-period, single-dose, open-label, crossover PK study in healthy adult volunteers.

A single dose of 70 mg LDX was administered to each subject as an intact oral capsule, a solution, or an intact capsule after a high-fat meal.

**Results:** The solubility at pH 1 was 1027 mg/mL, remaining relatively unchanged through pH 8 with solubility of 935 mg/mL. Increasing the pH beyond 8 resulted in a modest solubility reduction such that at pH 13 solubility was 506 mg/mL. Dosage formulation also had no effect on the rate or extent of absorption. Mean C_max for the capsule and the solution were 48.0 and 45.6 mg/mL for LDX, and 69.3 and 68.4 mg/mL for d-amphetamine, respectively. The AUC trimmed for the capsule and the solution were 66.84 and 55.10 ng•hr/mL for LDX, and 1110 and 1074 ng•hr/mL for d-amphetamine, respectively. T_max was also similar for the capsule and the solution. Furthermore, systemic exposure to d-amphetamine (fed AUC trimmed of 1038 ng•hr/mL, and C_max of 65.3 ng/mL) was bioequivalent when taken with or without food.

**Conclusions:** Neither environmental pH nor dosage formulation (ie, capsule or solution) affects the intrinsic oral pharmacokinetics of LDX. The pharmacokinetic profile of LDX is inherent to its chemical prodrug nature such that dosage formulation dependencies are eliminated.

References:

NR741  Wednesday, May 23, 3:00 PM - 5:00 PM
Tolerability of Aripiprazole in the Treatment of Adolescents with Schizophrenia
Robert L. Findling, M.D. Case Western University, Child and Adolescent Psychiatry, 11100 Euclid Avenue, Suite 200, Cleveland, OH, 44106-5080, 9000, Margaretta Nyilas, M.D., Phillip Ruby, M.D., Suresh Mallikaarjun, Ph.D., Robert D. McQuade, Ph.D., Ronald N. Marcus, M.D., William H. Carson, Jr., M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to understand the outcome of clinical trial data, particularly with regard to the tolerability of aripiprazole as it was used for the treatment of adolescents with schizophrenia.

Summary:
**Introduction:** Optimal management of schizophrenia in adolescents has been limited by the lack of effective and safe therapies. Aripiprazole is a first-in-class, dopamine partial agonist approved in adults for treatment of schizophrenia and bipolar disorder.

**Methods:** This 6-week, double-blind, randomized placebo-controlled trial was conducted at 101 centers in 13 countries, with an independent safety monitoring board. After a 3-day antipsychotic washout period, 13-17 year-old patients with a DSM-IV diagnosis of schizophrenia confirmed by the K-SADS-PL and with a PANSS total score >70, were randomized 1:1:1 to placebo, or a fixed dose of 10mg or 30mg of aripiprazole reached after a 5 or 11 day titration, respectively, and maintained for a minimum of 2 weeks. Primary safety measures included incidence of adverse events and discontinuation from study due to adverse events. AIMS, SAS, and BARS were included to measure EPS related events. Weight change, ECG, and serum prolactin were also measured. Efficacy was assessed using the PANSS and CGI Improvement scales.

**Results:** Over 85% of patients completed the 6-week study (n=302, mean age=15.5). Overall incidence of discontinuation due to AEs was 4.3%, with similar discontinuation rates in the aripiprazole and placebo groups (10mg, 7%; 30mg, 3.9%; placebo, 2%). The most common AEs associated with aripiprazole were extrapyramidal disorder, somnolence and headache. Incidence of clinically significant weight gain (>7% increase) was minimal in aripiprazole-treated patients (10mg, 4.8%; 30mg, 6.0%) compared to placebo (1%). Mean prolactin levels were decreased relative to baseline in aripiprazole treated patients (10mg, -12 ng/ml; 30mg, -17 ng/ml; Placebo, -9 ng/ml). Both doses showed significant improvement relative to placebo on the PANSS total score.

**Conclusions:** Aripiprazole was generally well tolerated, with few discontinuations due to adverse events.
- Aripiprazole 10 mg and 30 mg doses are superior to placebo at week 6.

References:

NR742  Wednesday, May 23, 3:00 PM - 5:00 PM
Efficacy of Aripiprazole in the Treatment of Adolescents with Schizophrenia
Adelaide S. Robb, M.D. Child National Medical Center, Psychiatry, 111 Michigan Avenue N.W., Washington, DC,
20010, 9000, Phillipe Auby, M.D., Margareta Nyilas, M.D., Robert A. Forbes, Ph.D., Suresh Mallikarjun, Ph.D., Ronald N. Marcus, M.D., William H. Carson, Jr., M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the outcome of clinical trial data, particularly with regard to the efficacy and tolerability of aripiprazole as it was used for the treatment of adolescent patients with schizophrenia.

Summary:
Introduction: Optimal management of schizophrenia in adolescents has been limited by the lack of available therapies. Aripiprazole is a first-in-class, dopamine partial agonist approved in adults for treatment of schizophrenia and bipolar disorder.

Methods: This 6-week, double-blind, randomized placebo-controlled trial was conducted at 101 centers in 13 countries, with an independent safety monitoring board. After a 3-day antipsychotic washout period, 13-17 year-old (mean age 15.5) patients with a DSM-IV diagnosis of schizophrenia confirmed by the K-SADS-PL and with a PANSS total score ≥70, were randomized 1:1:1 to placebo, or a fixed dose of 10mg or 30mg of aripiprazole reached after a 5 or 11 day titration, respectively, and maintained for a minimum of 2 weeks. The primary endpoint was mean change from baseline to endpoint (week 6 LOCF) on the PANSS total score. Key secondary endpoints included the PANSS positive and negative subscales, and CGI Improvement score.

Results: Over 85% of 302 randomized patients completed the 6-week study. The mean baseline PANSS score for patients was 94.5. By week 1, patients randomized to 30 mg had PANSS scores that were statistically significantly different from placebo. At end of study, both the 10 mg and 30 mg doses showed significant differences from placebo (-26.7 and -28.6, respectively; placebo -21.2). Both doses showed statistically significant improvement on the PANSS positive and CGI-I scales compared to placebo and 10 mg dose was superior to placebo on PANSS negative score. Approximately 5% of aripiprazole patients discontinued due to adverse events. Weight gain and changes in prolactin were minimal.

Conclusions: Both 10 mg and 30 mg of aripiprazole were superior to placebo at week 6 on PANSS-total score. Both doses showed statistically significant improvement relative to placebo on the PANSS positive and CGI-I scales, and the 10 mg dose was superior to placebo on PANSS negative score.

References:

NR744 Wednesday, May 23, 3:00 PM - 5:00 PM
Psychiatric Disorders in Homeless Iranian Adolescent Girls
Mohamad Reza Eskandari, M.D. Zanjan University of Medical Sciences, Beheshti Hospital, Psychiatry, Beheshti Hospital, Arq Square, Zanjan, 45136, 5070, Soghra Karami, M.S.C., Ali Reza Aghajanlou, M.D.

Educational Objectives:
1) understand the epidemiology of the current methamphetamine abuse epidemic and its impact on rural families and communities.
2) recognize associations between adult substance abuse, overburdened communities, and child mental health.
3) recommend potential prevention or treatments for methamphetamine-abusing parents or their at-risk children.

Summary:
Over the last decade “crystal meth” has become a crisis across the USA. It profoundly impairs parenting and is now a major reason for rural children entering foster care and receiving psychiatric treatment. This study examines relationships between juvenile misbehavior and adult substance abuse. The relative lack of urban meth is in contrast to the deluge in rural counties.

Objectives: The temporal changes and the contrast between rural/urban counties may reveal relationships between adult addiction and adolescent mental health problems. This multivariate analysis is an extension of our ongoing qualitative studies of children's mental health and parent methamphetamine abuse.

Methods: Illinois, Wisconsin, Minnesota, Montana, and Washington were examined. Datasets included US-Census, USDOJ, State Police. We also examined public records on juvenile probation, school violence, and juvenile addiction. As proxy for adult addiction, we used county arrests for clandestine methamphetamine laboratories and workplace toxicology. We also examined county population, income, education. For example, Illinois has 19 urban and 81 rural counties. In 2002, our IL sample included 27812 petitioned juveniles and 730 meth labs.

Results: SPSS multivariate analysis breaks out region, urban vs. rural, with trends over time. IL meth labs went from 27 in 1997 to a total of 6138 by 2005. The rate of growth in rural counties was 2.5x that of urban, even with 9x greater population. Poor urban areas and rural Native American communities have stable juvenile misbehavior. However, higher juvenile probation rates are seen in the rural counties with the most clandestine meth labs. No significant pattern exists for school violence.

Conclusions: The recent emergence of the meth epidemic in rural communities has imposed a staggering burden on families and society. By comparing juvenile justice and drug enforcement data, we have indirect evidence that children in rural counties are acting-out in response to this community stress.

References:

NR743 Wednesday, May 23, 3:00 PM - 5:00 PM
Juvenile Probation Rates and Clandestine “Crystal Meth” Laboratories: Potential Associations of Adult Addiction And Adolescent Psychiatric Problems
James E. Black, M.D., Ph.D. Southern Illinois University School of Medicine, Department of Psychiatry, 901 West Jefferson, P.O. Box 19642, Springfield, IL, 62794-9642, 9000

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

1) understand the epidemiology of the current methamphetamine abuse epidemic and its impact on rural families and communities.
2) recognize associations between adult substance abuse, overburdened communities, and child mental health.
3) recommend potential prevention or treatments for methamphetamine-abusing parents or their at-risk children.

Summary:
Introduction: Run away Behavior in young girls is a complex social problem in Iranian adolescents. Psychiatric disorders may play an important role in run away behavior in young girls.
NR745  Wednesday, May 23, 3:00 PM - 5:00 PM  
Prevalence of Psychiatric Co-morbidities in Children with ADHD

Mohamad Reza Eskandari, M.D. Zanjan University of Medical Sciences, Beheshti Hospital, Psychiatry, Beheshti Hospital, Arq Square, Zanjan, 45136, 5070, Soghra Karami, M.S.C., Ali Reza Aghajanlou, M.D.

Educational Objectives:  
At the conclusion of this presentation, the participant should be able to aware that prevalence of Psychiatric Co-morbidities in Children with ADHD is high and some one of these children needs special treatments.

Summary:  
Introduction: Attention Deficit Hyperactivity Disorder (ADHD) is one of the most common psychiatric disorders in children. ADHD represents a frequent and highly comorbid disorder in children and adolescents. Not only comorbidity differs according to ADHD subtype and gender but also has been reported to have a direct effect on the severity of ADHD. Present study aimed at determining the prevalence rate of psychiatric disorder in ADHD children who were 4-14-year-old.  
Method: This study conducted on 70 Cases during 6 months on the 4-14-year-old children with ADHD referring to counseling center through 2 questionnaires containing Rutter test for evaluating Mood-Conduct disorder and a second questionnaire for Enuresis-Encopresis-tic and Nail Biting. The statistical method used was SPSS.  
Results: The present study indicates that 56% of the ADHD children suffered from Enuresis of which 49.2% reported to be night Enuresis also, 17% of them Suffered from Encopresis, 17% Nail Biting, and 20% Tic disorder of which 15.7% had motor tic. The analysis of Rutter test showed that 75% of the children had behavioral disorders of which 28.6% had Conduct disorder, 8.3% Mood disorder, 8.6% both of the above mentioned disorders, and finally 40% suffered from other types of behavioral disorders.  
Conclusion: Due to high prevalence of Enuresis-Encopresis-tic and Nail Biting in ADHD children studied, compared with general Population, more attention should be directed to those children with the mentioned diagnosis. Similarly, because of high prevalence of other unidentified behavioral disorders the use of other tests such as Child Behavior Check List (CBCL) with greater number of ADHD children is highly recommended.

References:  

NR746  Wednesday, May 23, 3:00 PM - 5:00 PM  
The Standardization of SNAP-IV in Korean Version

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Educational Objectives:  
If we understand that SNAP-IV is useful tool for ADHD screening in Korean patient, this tool can be used widely in clinical practices.

Summary:  
We conducted the standardization study to analyze the reliability and validity of SNAP-IV on purpose to determine whether SNAP-IV is adequate test for screening ADHD patient in Korea. SNAP-IV was administered to 605 control subjects and 94 ADHD patients. The test-retest reliability, internal consistency and split half reliability were performed to examine reliability. The criterion validity, factor analysis and discriminant analysis were performed to examine validity. The test-retest reliability coefficient was above 0.8 in both inattention and hyperactivity/impulsivity subscale. The Cronbach α coefficient representing internal consistency was above 0.8 and split-half reliability coefficient was above 0.7 in both subscales. The criterion validity of SNAP-IV with SNAP was from 0.582 to 0.802 and that of SNAP-IV with CPRS was from 0.656 to 0.778 in control subjects. In factor analysis, we identified 3 factors which were inattention, impulsivity and hyperactivity. The discriminant ability between ADHD and control subjects was 81.5%. By examining reliability and validity, we found that Korean SNAP-IV was reliable and valid. It also has high discriminant ability. Thus Korean SNAP-IV is useful tool for screening ADHD in Korean subjects.

References:  
Educational Objectives:

We investigated the temperament and characteristics in a normal control group, internet addiction group and substance abuse group with temperamental and character inventory (TCI) based on Cloninger’s theory. By doing this, we come to realize the specific social and interpersonal impairments of problematic internet users.

Summary:

Objective: Internet addiction is thought to belong to behavioral addiction disorders. Individuals with internet addiction do not have any known direct physical consequences as do substance abusers such as alcohol. Substance abuse is the typical reference for addictive behavior. We investigated the temperament and characteristics in a normal control group, internet addiction group and substance abuse group.

Method: We recruited participants from the three different groups. A survey was performed at a high school located southeast of Seoul. We also enrolled respondents from internet centers and collected responses from respondents who visited substance-abuse consultation office. We recruited 487 high school students, 89 individuals from the internet centers, and 45 from substance-abuse consultation office. Basic epidemiological data and the Korean version temperament and character inventory (TCI), Korean internet addiction scale and Korean Adolescent Drug addiction screening test (KOADAST-2) were used with all participants.

Results: The normal group had 375 (60.4%) responders. Problematic internet users had 127 (20.5%) responders from high-school and PC internet center according to the Korean internet addiction scale. The problematic drug user group included 18 (2.9%) from the substance-abuse consultation office by KOADAST-2. We compared the 3 groups using the Korean TCI. Our findings showed that the 3 groups were significantly different in novelty seeking (NS), reward dependence (RD), self-directedness (SD), cooperativeness (CO), and self-transcendence (ST). The differences between groups were most noticeable for the problematic internet users and problematic drug users on the basis of RD, SD, CO.

Conclusion: Although problematic drug users and internet users share the characteristic of addiction, they differ in regard to certain characteristics identified in personality profiles. Our findings suggest that we should pay more attention to the social and interpersonal impairments of problematic internet users.

References:


NR748 Wednesday, May 23, 3:00 PM - 5:00 PM

Comparative Efficacy and Safety of Lisdexamfetamine Dimesylate (LDX) in Stimulant-Naïve for Past 12 Months and Previously Treated Children Aged 6 to 12 Years With Attention-Deficit/Hyperactivity Disorder: A Secondary Analysis

Joseph Biederman, M.D. Massachusetts General Hospital, Pediatric Psychopharmacology, 55 Fruit Street, Warren Building 705, Boston, MA, 02114, 9000, Suma Krishnan, M.S., Jack Schreckengost, Ph.D., Robert L. Findling

Educational Objectives:

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

1. Evaluate the efficacy of short-term treatment with lisdexamfetamine dimesylate as a function of previous stimulant treatment in children aged 6 to 12 years with attention-deficit/hyperactivity disorder (ADHD).

2. Evaluate the safety and tolerability of short-term treatment with lisdexamfetamine dimesylate as a function of previous stimulant treatment in children aged 6 to 12 years with ADHD.

Summary:

Objectives: To conduct a secondary analysis comparing the efficacy, tolerability, and safety of lisdexamfetamine dimesylate (LDX) in stimulant-naïve for 12 months prior to study and prior stimulant-treated 6- to 12-year-old children with attention-deficit/ hyperactivity disorder (ADHD).

Methods: The primary study was a Phase III, randomized, multicenter, double-blind, parallel-group trial in 6 to 12 year olds meeting DSM-IV-TR criteria for ADHD (combined or hyperactive-impulsive subtype). Following screening and a 1-week washout period, subjects were randomized 1:1:1:1 to 4 weeks of treatment with placebo or 30 mg/d, 50 mg/d, or 70 mg/d LDX. The primary efficacy measure was the ADHD Rating Scale (ADHD-RS). Safety assessments included adverse events, physical examinations, vital signs, laboratory evaluations, and electrocardiograms. Stimulant-naïve children were defined per protocol as those not prescribed stimulants for the previous year.

Results: Of 290 subjects, 72, 71, 74, and 73 were randomized to placebo, 30 mg/d LDX, 50 mg/d LDX, and 70 mg/d LDX, respectively; of these, 48 (66.7%), 44 (62.0%), 49 (66.2%), and 54 (74.0%), respectively, were considered stimulant-naïve (n=195).

At treatment endpoint, LS mean (±SE) changes in ADHD-RS from baseline for stimulant-naïve children randomized to placebo, 30 mg/d LDX, 50 mg/d LDX, and 70 mg/d LDX were -6.85 (±2.06), -22.35 (±2.22), -24.64 (±2.07), and -25.96 (±1.90), respectively, whereas LS mean (±SE) changes in ADHD-RS from baseline for stimulant-treated children were -3.26 (±2.70), -18.09 (±2.60), -20.73 (±2.58), and -26.16 (±3.01), respectively. Compared with placebo, ADHD-RS improvement was statistically significant for each LDX dose in both groups. Adverse events were reported by 77.3% to 90.7% of subjects receiving LDX in the stimulant-naïve group, compared with 21.1% to 68.4% of subjects receiving LDX in the stimulant-treated group.

Conclusions: LDX-associated improvements were not related to previous stimulant treatment. In general, adverse events were reported more frequently in stimulant-naïve children compared with stimulant-treated children.

References:


NR749 Wednesday, May 23, 3:00 PM - 5:00 PM

Efficacy and Safety of Lisdexamfetamine Dimesylate (LDX) in Non-Caucasian Children Aged 6 to 12 Years With Attention-Deficit/Hyperactivity Disorder: A Secondary Analysis

Joseph Biederman, M.D. Massachusetts General Hospital, Pediatric Psychopharmacology, 55 Fruit Street, Warren Building 705, Boston, MA, 02114, 9000, Suma Krishnan, M.S., Yuxin Zhang, Ph.D., Robert L. Findling

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**Educational Objectives:**

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

1. Evaluate the efficacy of short-term treatment with lisdexamfetamine dimesylate in non-Caucasian children aged 6 to 12 years with attention-deficit/hyperactivity disorder (ADHD).

2. Evaluate the safety and tolerability of short-term treatment with lisdexamfetamine dimesylate in non-Caucasian children aged 6 to 12 years with ADHD.

**Summary:**

**Objectives:** To conduct a secondary analysis comparing the efficacy and safety of lisdexamfetamine dimesylate (LDX) versus placebo in non-Caucasian children aged 6 to 12 years with attention-deficit/hyperactivity disorder (ADHD).

**Methods:** The primary study was a phase III, randomized, multicenter, double-blind, parallel-group trial in children of all ethnic backgrounds aged 6 to 12 years meeting the DSM-IV-TR® criteria for diagnosis of ADHD (combined or hyperactive-impulsive subtype). Following 1-week screening and 1-week washout periods, subjects were randomized in a 1:1:1 ratio to 4 weeks of treatment with placebo or 30 mg/d, 50 mg/d, or 70 mg/d LDX. The primary efficacy measure was the ADHD Rating Scale (ADHD-RS). Safety assessments included adverse events (AEs), physical examinations, vital signs, laboratory evaluations, and electrocardiogram results.

**Results:** Two hundred ninety subjects were randomized, 72, 71, 74, and 73 to placebo, 30 mg/d LDX, 50 mg/d LDX, and 70 mg/d LDX, respectively; of these children, 29 (40.3%), 34 (47.9%), 40 (54.1%), and 32 (43.8%), respectively, were non-Caucasians (total number, 133). At treatment endpoint, LS mean (±SE) changes in ADHD-RS from baseline for non-Caucasians randomized to placebo, 30 mg/d LDX, 50 mg/d LDX, and 70 mg/d LDX were -10.12 (±2.81), -18.53 (±2.51), -20.21 (±2.43), and -25.13 (±2.67), respectively. Compared with placebo, the improvement in ADHD-RS for non-Caucasians was statistically significant for each LDX dose (P<.05 per model-based t-test). Overall, LDX was well tolerated in this population. Most treatment-emergent AEs were mild to moderate and occurred during the first week of treatment. The most common AEs reported in this population were decreased appetite, insomnia, and headache. Ten subjects discontinued due to adverse events.

**Conclusions:** Treatment with LDX significantly improved ADHD symptoms in non-Caucasian children aged 6 to 12 years. LDX was generally well tolerated in this population.

**References:**


**NR750**

**Wednesday, May 23, 3:00 PM - 5:00 PM**

**Efficacy of Adjunctive Divalproex Sodium for Stimulant-Refractory Aggression among Children with ADHD**

**Objectives:**

To conduct a secondary analysis comparing the efficacy and safety of lisdexamfetamine dimesylate (LDX) compared with mixed amphetamine salts (MAS XR) in children aged 6 to 12 years with attention-deficit/hyperactivity disorder (ADHD).

**Methods:** This Phase II, randomized, multicenter, double-blind, 3-treatment and 3-period crossover study evaluated the efficacy and safety of LDX (30 mg/d, 50 mg/d, or 70 mg/d) compared with MAS XR at equivalent d-amphetamine base doses (10 mg/d, 20 mg/d, or 30 mg/d) or placebo in children with ADHD. Subjects were titrated to optimum dose of MAS XR, and each medication was administered in a randomized fashion for 1 week. At the last visit of the double-blind period, blood was drawn predose and at 1, 2, 3, 4.5, 6, 8, 10, and 12 hours postdose for measurements of plasma drug concentration and pharmacokinetic parameters. Pharmacokinetic parameters were calculated using noncompartmental methods.

**Results:** Safety and efficacy results have been presented previously. Pharmacokinetic data were available for 8 patients administered 70 mg/d LDX and for 9 administered 30 mg/d MAS XR. The mean (±SD) Cmax, Tmax, and AUCinf of dextroamphetamine following 70 mg/d of LDX were 155 ± 31.4 ng/mL, 5.06 ± 0.78 hr, and 1326 ± 285.8 ng hr/mL, respectively, with percent coefficients of variation (%CV) of 20.34%, 15.38%, and 21.56%, respectively. For 30 mg/d MAS XR, the mean ± SD Cmax, Tmax, and AUCinf of dextroamphetamine were 119 ± 52.5 ng/mL, 6.56 ± 3.46 hr and 1019 ± 436.2 ng hr/mL, respectively, with %CV of 43.96%, 52.77%, and 42.83%, respectively.

**Conclusions:** These results indicate that interpatient variability in dextroamphetamine pharmacokinetics following LDX is considerably lower than that observed following MAS XR. These results are most likely due to the use of a prodrug in delivering the active moiety compared to an extended release drug delivery formulation.

**References:**


**Summary:**

**Background:** Preadolescents with highly aggressive behavior typically fulfill diagnostic criteria for a disruptive disorder. ADHD is highly comorbid with these conditions. Stimulant medication is first-line treatment for ADHD and frequently ameliorates aggression. Nonetheless, aggressive behavior and affective volatility remain significant impairments for many, leading clinicians to layer additional mood stabilizers or antipsychotics hoping to diminish aggressive dyscontrol. However, there is no evidence to support any medication combination strategy for aggressive children with ADHD. This study evaluated a stepped pharmacotherapy strategy, in which children 6 to 14 years-old, shown prospectively to have aggression under-responsive to stimulant monotherapy, participated in a randomized, double-blind, placebo-controlled trial of extended-release divalproex sodium (DVPX-ER).

**Methods:** Each subject participated in an open lead-in intended to optimize stimulant treatment via flexible titration based on response and tolerability. Children whose aggressive behavior persisted after stimulant treatment was optimized, were then randomized to receive either DVPX-ER or placebo for an eight-week trial. Principal outcome was the Modified Overt Aggression Scale completed by parents. Response was categorized as a score <= 15, which represented negligible aggression.

**Results:** Sixth-four children began the open stimulant lead in, 53% of whom experienced remission of aggression by the end of stimulant titration. The remaining 47% (n=30) who entered the randomized phase had DVPX-ER or placebo titrated to a target dose of 20 mg/kg. Final mean DVPX-ER dose was 585 mg, mean PBO dose was 700. Children on active DVPX-ER had a final mean serum valproate level of 75.1 mL/L. Half of those randomized to DVPX-ER fulfilled the criterion for response, compared with 10% of those randomized to placebo.

**Conclusions:** Although subjects had histories of stimulant treatment, well-supervised titration produced marked response for many subjects. Among children whose severe aggressive behavior was refractory to stimulant monotherapy, adjunctive DVPX-ER was substantially more efficacious than placebo.

**References:**


**NR753**

**Wednesday, May 23, 3:00 PM - 5:00 PM**

**Impact of FDA Black Box Warning on Clinicians’ Beliefs about the Safety of Antidepressant Usage in Pediatric Patients**

**Educational Objectives:**

1. At the conclusion of the presentation, the participant should be able to recognize, in a sample of pediatric psychopharmacologists, the impact that the FDA black box warning has had on beliefs about the safety of pediatric antidepressant use.
2. At the conclusion of the presentation, the participant should demonstrate an understanding of provider characteristics that are associated with the nature of the above beliefs.

**Summary:**

**Background:** In September of 2004, a FDA joint advisory committee recommended a “black-box” warning be required for antidepressant drugs, indicating that they increase risk of suicidal thinking and behavior in pediatric patients. While it appears that this warning has had an effect on the general public’s level of trust in antidepressant treatments, it is not clear to what extent this warning has affected prescribing beliefs and behaviors on community-based providers.

**Methods:** Survey questions, administered to 628 pediatric psychopharmacologists participating in a Massachusetts General Hospital Annual Pediatric Psychopharmacology review course, were analyzed to determine the extent to which the FDA black...
box warning influenced beliefs about the safety of antidepressant use in children and adolescents.

Results: 318 (50.6%) participants completed the survey questions. Mean age of participants was 52.8 years, 56.9% were female, 77% were physicians and 23% other licensed prescribers, and respondents had been practicing for a mean of 19.8 years. 42.2% of respondents indicated that the black-box warning has decreased their likelihood of prescribing antidepressants for children and adolescents: respondents indicated that 24.4% of patients they have treated with antidepressants have experienced a worsening of suicidality; and 21.9% of respondents indicated that certain medications are more associated with potential worsening of suicidality than others (with two thirds naming an SSRI). Conversely, 60.9% of respondents indicated that certain treatments are more associated with improvement in suicidality than others, and respondents estimated that 25.7% of patients treated with an antidepressant experience an improvement in suicidality.

Conclusion: Data from this clinician sample suggest that the FDA black box warning concerning antidepressant use in pediatric patients has impacted prescribing beliefs. Certain practice and provider characteristics may be associated with these beliefs. Further research is needed to establish whether belief changes result in actual changes in clinical care provided to depressed children and adolescents.

References:

NR754 Wednesday, May 23, 3:00 PM - 5:00 PM
Validity and Reliability of the Center for Epidemiological Studies-Depression (CES-D) in Adolescent Students from Colombia.
German E. Rueda, M.D. Universidad Autonoma de Bucaramanga, Psychiatry, calle 157 No 19-55, Bucaramanga, 1642, 3010, Paul A. Carmacho, M.D., MSc., Jose F. Latorre, M.D., MSc., Alvaro A. Navarro, M.D., Mauricio Escobar, M.D., MSc., Jorge Franco, M.D.

Educational Objectives:
1. At the conclusion of this presentation, the participant should be able to recognize the validity and reliability of the Center for Epidemiological Studies-Depression Scale (CES-D) in adolescent students, for the screening of depressive symptoms.

Summary:
Introduction: In Colombia, the lifetime prevalence of depression in adolescents is of 13.3% and 20.1% of 12 to 15 and 16 to 19 years old, respectively. However there are not validated scales in this population.

The aim of this study was to assess the validity and reliability of the CES-D in adolescent students, for the screening of depressive symptoms.

Methods: A validation study with a cross-sectional sampling was design, 3468 eligible adolescents from nine schools in Bucaramanga (Colombia) were evaluated both with CES-D and with the semi-structure clinical interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition (SCID-I) independently and blindly, the instrument was re-applied 2 - 3 weeks later. A statistical analysis was made considering the conditional probabilities through of tetracoric tables to determine the predicting diagnoses from CES-D, Lin's concordance correlation coefficient, principal components and the calculation of Cronbach's alpha.

Results: A total of 390 adolescents were surveyed. The mean age of the population was 14.77 ± 1.22 years and 44.36% were men. The prevalence of major depression episode based on the SCID-I was 11.54% [CI 95%: 8.54% - 15.13%]. Factor analysis revealed four factors (depressed affect, interpersonal relationships, positive affect and somatic complains) that explained 77% of variability. Cronbach's alpha for the total scale was 0.85. The test-retest reliability was satisfactory (Lin's R 0.75 for total score). The sensitivity was 73.33% [IC95%:57.79% - 84.99%], specificity 73,62% [IC95%: 68.58% - 77.13%] and the area under ROC curve was 0.815 [CI 95%: 0.748 - 0.881] for a cut-point equal or higher than twenty three in the score of CES-D.

Conclusions: The validity and reliability of the Spanish translation of the CES-D are similar to those reported in the international literature. It is a useful scale for the screening of depressive symptoms in Colombian adolescent students.

References:

NR755 Wednesday, May 23, 3:00 PM - 5:00 PM
The Utility of Brief Teacher Ratings in the Identification of Developmental Coordination Disorder
John Cairney, Ph.D. University of Toronto, Psychiatry, 33 Russell Street, Toronto, ON, MSS 251, 1220, Scott Veldhuizen, B.A., Cristina Spironello, B.S.C., Paul Kurdyak, M.D., John Hay, Ph.D., Brent E. Faught, Ph.D.

Educational Objectives:
1) Review diagnostic criteria for Developmental Coordination Disorder (DCD)
2) Review basic epidemiology of DCD
3) Review literature on screening for DCD in children
4) Present results of a short screen for DCD designed for teachers
5) Discuss clinical and research implications

Summary:
Objective: Developmental coordination disorder (DCD), a DSM-IV syndrome characterized by poor motor skills, is thought to be relatively common but is rarely diagnosed. In this study, we evaluated the usefulness of brief teacher ratings in the identification of DCD.
Method: 695 students aged 9 to 11 from the Niagara region of Ontario, Canada were assessed for coordination problems using the short form of the Bruininks-Oseretsky test of motor proficiency (BOTMP-SF). Classroom teachers completed a new 10-item questionnaire on students' general aptitude for and enjoyment of physical activity, the teacher evaluation of activity form (TEAF). Agreement between the TEAF and the BOTMP-SF was assessed using receiver operating characteristic analysis.
Results: 36 students were identified by the BOTMP-SF as probable cases of DCD, a prevalence of 5.2% (95%CI, 3.8% to 7.1%). Area under the curve for the TEAF total score was 0.77 (95%CI, 0.69 to 0.86). Performance was close to identical for male and female students. Several individual items dealing with general aptitude for physical ability had performance equivalent to the full scale.
**Discussion:** The level of agreement between teacher ratings and formal assessments for DCD is not adequate for identification of cases, but may be sufficient for screening efforts. The brevity of the TEAF relative to instruments such as the Movement Assessment Battery for Children Checklist may help make large-scale teacher or multiple-perspective screening practical. The reasonably good performance of individual items suggests that even shorter instruments may be useful.

**References:**

**NR756**

Wednesday, May 23, 3:00 PM - 5:00 PM

Real World Impact of Second Generation Antipsychotics on Weight Gain in an Adolescent Population

Qayyim Said, Ph.D. University of Utah, Pharmacotherapy, 421 Wakara Way, Room 208, Salt Lake City, UT, 84108, 9000, Lisa C. Rosenblatt, M.D., Myoung S. Kim, Ph.D., Diana I. Brixner, Ph.D.

**Educational Objectives:**
This work provides a foundation for the understanding of how second generation antipsychotics impact weight gain in adolescent patients treated in a real-world environment as opposed to a clinical trial. This information is useful in initiating SGA therapy in patients where weight gain may have a negative impact on patient outcomes.

**Summary:**

**Purpose:** Second generation antipsychotics (SGAs) are associated with weight gain in adolescent populations. Body mass index (BMI) has been studied in clinical trials with limited comparison between drugs. Using a national electronic medical record (EMR) database, the real-world impact of SGAs on BMI in adolescents taking antipsychotics was evaluated.

**Methods:** This was a retrospective database analysis employing data from a consortium of 5,000 physicians using GE Healthcare CPO EMR to document care for five million patients. NaUve monotherapy patients (12-19 years) receiving an antipsychotic prescription between February 2001 and March 2006 were identified; patients on clozapine or depot antipsychotic were excluded. Baseline BMI recorded within less than 180 days prior to first prescription and closest to index date was compared with maximum BMI obtained within 365 days after first antipsychotic prescription. Regression analysis was used to estimate adjusted mean differences between baseline and post prescription BMI for each SGA compared with all first generation antipsychotics (FGAs), controlling for age, gender, psychiatric diagnosis, baseline BMI, weight gain medications, and geographic region of residence.

**Results:** A total of 572 eligible patients were identified; mean age was 15.6 years and 55% were female. The sample contained 31% patients on any FGA (mean baseline BMI [MBB] 25.8), 8% on aripiprazole (MBB 25.1), 16% on olanzapine (MBB 25.3), 22% on quetiapine (MBB 25.1), 21% on risperidone (MBB 24.3), and 2% on ziprasidone (MBB 30.6). Compared with FGAs, patients on olanzapine had a statistically significant mean increase in BMI of 1.0 kg/m² (95% confidence interval [CI], 0.41-1.59). Aripiprazole (CI, -0.78-0.70), quetiapine (CI, -0.85-0.23), and risperidone (CI, -0.28-0.80) did not show any significant increase in BMI.

**Conclusions:** Antipsychotics differ in propensity to cause weight gain in adolescents. Antipsychotics without weight gain potential should be considered especially in adolescents who are overweight or at risk for overweight.

**References:**
issues, particularly the use of concomitant medications, made it difficult to attribute risk to specific agents. Mean weight gains were not adjusted for the normal weight increases of childhood and adolescence. Gender-specific body mass index (BMI) for age growth charts have been recommended to determine weight changes and determine clinical significance. Given the health risks of obesity, further research is recommended.

References:

NR758 Wednesday, May 23, 3:00 PM - 5:00 PM
Exploring internal consistency and factor structure of a scale for identifying bullying among Colombian high-school students

David Fortich Universidad del Sinú, Psychology School, Pie de la Popa, Calle 30 No 20-71, Cartagena, 57 5, 3010, Manuel Noreña, Adalberto Campo-Arias, M.D.

Educational Objectives:
At the end of this presentation, assistants will know Cronbach alpha and factor structure of a new scale for identifying bullying in Colombian high-school students.

Summary:
Background: Bullying is a common concern among adolescent students. There is a Spanish 50-item scale to identify this problem. However, the item number limits its psychometric properties.
Objective: To compute Cronbach alpha and know the factor structure of a new shorter self-rating scale for bullying in high school students of Cartagena, Colombia.
Method: A probabilistic sample of 91 high-school students with ages between 14 and 19 years. 67% were girls completed the 50-item self-rating bullying scale. Cronbach alpha was computed and factor structure explored by principal component method for different groups of items.
Results: Twenty items were retrained. The new and shorter self-rating bullying scale showed Cronbach alpha coefficient of 0.86 and three factors that explained 49.4% of the variance.
Conclusions: The new self-rating bullying scale presents an acceptable internal consistency and three dimensional structure. Further researches are needed to corroborate this finding.

References:

NR759 Wednesday, May 23, 3:00 PM - 5:00 PM
Is Type A Behavior a Factor of Resilience in Cardiovascular Disease?

Pinoit Jean-Michel, Sr., M.D. Teaching Hospital, Psychiatry and Addictology, 3 Rue du faubourg raines, Hôpital Général, Dijon, 21000, 4279, Chauvet-Gelinier Jean-Christophe, Sr., M.D., Bonin Bernard, Sr., Ph.D., Gieselmann Andre, Sr., Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to determine the importance of depicting type A behavior with Bortner test after a cardiac event.

The participant should know the interest of psychotropic treatment after myocardial infarction.

Summary:
Aim: Type A behavior is described as a common psychological coronary risk factor, but its effect on results of cardiac rehabilitation remains unknown. The aim of our study was to study the impact of type A behavior on anxiety and depression, and on physical performance during cardiac rehabilitation in outpatients.
Methods: When patients were referred for cardiac rehabilitation following a cardiac event, their personalities were assessed using the Bortner scale and the Zigmond and Snalh Hospital Anxiety and Depression scale (HAD). They once again were assessed by the same scores at the end of the 5 week comprehensive cardiac rehabilitation program. An ergonomic bicycle stress test was performed in each patient at the beginning and at the end of the cardiac rehabilitation program.
Results: 261 patients, 217 men, 44 women were included in this descriptive and prospective study. At the beginning and at the end of the rehabilitation program, type A subjects (n=95) were significantly (p<0.001) more anxious and more depressed than type B subjects (n=112). During their cardiac rehabilitation program, patients' physical capacities (in Watt) improved by an average of 33.82% on the stress tests. The performance of patients with major type B personality (Bortner score inferior to 140) improved by only 26.95% whereas that of patients with major type A behavior (Bortner score superior to 230) improved by 40.8%, and a significant statistical difference between these two groups was revealed (p=0.046).
Conclusions: Our study confirmed that type A behavior could increase anxiety and depression after a cardiac event. But paradoxically it also showed the resilience of type A subjects who managed to improve their physical condition to a greater degree. This may be due to a sort of “fighting spirit” associated with type A behavior.

References:

NR760 Wednesday, May 23, 3:00 PM - 5:00 PM
Type of Dialysis in Chronic Renal Failure and Its Association With Dyadic Adjustment, Body Perception, Sexual Function, Depression and Anxiety Levels

Demet Gulpek, M.D. Ataturk Training and Research Hospital, Psychiatry, Izmir Ataturk Training and Research Hospital, Baszmır Turkey, İzmir, 35100, 4890, Demet Güleç Oyekcin, M.D., Almila Erol, M.D., Levent Mete, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize depression and anxiety levels in patients with chronic renal failure on hemodialysis and peritoneal dialysis. In addition, the effect of the type of dialysis on patients' sexual life (dyadic adjustment and sexual satisfaction) and body perception will be recognised.

Summary:
Objective: Chronic renal failure (CRF) is a life threatening disorder that causes various complications. Dialysis may cause medical, social and psychological complications. Among all, depression
is the most widely studied complication. In patients on dialysis, depressive mood is associated with high mortality. Surgical interventions that change body appearance may disturb body perception and sexual life. In patients with CRF, changes in body perception is thought to be associated with invasive treatment interventions. In addition sexual problems are common in patients on dialysis. In this study, patients with CRF who are on hemodialysis or peritoneal dialysis are investigated for depression and anxiety levels, body perception, sexual satisfaction and dyadic adjustment.

**Method:** 54 patients on hemodialysis, 36 patients on peritoneal dialysis and 30 healthy controls are included in the study. All the subjects were assessed with SCID-I (Structured Clinical Interview for DSM-IV), Body Cathexis Scale, Beck Depression Inventory, Beck Anxiety Inventory, Glombok-Rust Inventory for Sexual Satisfaction and Dyadic Adjustment Scale.

**Results:** Comapred to peritoneal dialysis group, depression and anxiety levels were significantly higher in hemodialysis group. In peritoneal dialysis group as depression and anxiety levels increased body perception was disturbed and sexual satisfaction decreased. In peritoneal dialysis group body perception was better than hemodialysis group and was not different from controls. In hemodialysis group as depression and anxiety levels increased body perception was disturbed. In both groups, long-term dialysis disturbed body perception.

**Conclusion:** Depression and anxiety are common in patients on dialysis. Compared to patients on peritoneal dialysis, patients on hemodialysis had higher levels of depression and anxiety and more disruption about body perception. There were no significant differences between hemodialysis and peritoneal dialysis groups for dyadic adjustment and sexual satisfaction. It can be concluded that peritoneal dialysis has advantages over hemodialysis for depression, anxiety and sexual satisfaction.

**References:**

**NR761 Wednesday, May 23, 3:00 PM - 5:00 PM**

**The Psychosocial and Environmental Factors Affecting the Physical Health of Patients with Stomach Cancer: Confirmatory Factor Analysis of World Health Organization Quality of Life-Brief Form (WHOQOL-BREF)**

Yang-Whan Jeon Our Lady of Mercy Hospital, The Catholic University of Korea, Department of Psychiatry, 665 Bupyeong-Dong, Bupyeong-Gu, Inchon, 403-720, 5800, E-Jin Park, Sang-Ick Han

**Educational Objectives:**
Using the World Health Organization Quality of Life-brief form (WHOQOL-BREF), we explore how psychosocial and environmental factors affect the physical health of patients with stomach cancer.

**Summary:**
151 patients with stomach cancer from the outpatient clinic (60 males, 91 females, age: 58 ± 10.8 years) were recruited. The Korean version of WHOQOL-BREF including a total of 26 items was applied to those patients with stomach cancer and confirmatory factor analysis was employed. The psychosocial, environmental, and physical factors were established as the three main intrinsic factors, and a correlation diagram was used to determine the intimate relationship among these factors. The significant reliability was shown in every item of WHOQOL-BREF scale. The environmental factor (ENV) showed strong correlation with physical factor (PHY) and psychosocial factor (PSY) (PHY vs. PSY 0.764, PHY vs. ENV 0.638, PSY vs. ENV 0.835). Also, there was found to be a high impact on the vitality of everyday life and self-satisfaction. The Korean version of the WHOQOL-BREF was found to be applicable to stomach cancer patients and also that psychological and environmental factors formed a significant level of correlation. For stomach cancer patients, not only was psychiatric therapeutic intervention found to be a warranted significant need, but further concrete research is needed on the influences of psychiatric therapeutic intervention for these patients' physical health.

**References:**
presented a direct significant correlation with the SF-36 Pain domain and with the KPS. Regarding the MELD, a direct correlation was found only with the BDI.

Conclusions: Transplanted patients showed an improvement in their physical capacity and quality of life regarding the physical component, even though they had higher depression scores, however, demonstrated a worsening regarding their psychosocial condition.

References:

NR763 Wednesday, May 23, 3:00 PM - 5:00 PM Psychosocial Profile and Psychiatric Morbidity in Patients with Acromegaly: A Study From North India

Nitin Gupta, M.D. South Staffordshire Healthcare NHS Foundation Trust, General Adult Psychiatry, Margaret Stanhope Centre, Belvedere Road, Burton-Upo-Trent, DE13 ORB, 2410, Surendra Kumar Mattoo, M.D., Anil K. Bhansali, D.M., Sandeep Grover, M.D., Ramma Malhotra

Educational Objectives:
At the conclusion of this presentation, the participant should be able to [1] demonstrate the need of cross-cultural research in psychological/psychiatric issues related to endocrinological disorders, and [2] highlight the importance of identifying and managing psychiatric and psychosocial morbidity in Acromegaly, thereby helping clinicians to access appropriate and humane care for the psychological needs of patients with Acromegaly.

Summary:
Objective: To study the psychosocial profile and psychiatric morbidity in patients with a diagnosis of Acromegaly

Methods: A prospective cross-sectional study was carried out. A purposive sample of patients with acromegaly (N=24) attending the endocrinology out- or in-patient services at a multi-specialty teaching hospital in North India was taken up. The Acromegaly patients were group-matched for age, sex, education, locality and marital status with Healthy Controls who scored $<$2 on GHQ-12 (N=21). The patients were administered socio-demographic and clinical profile sheets, Presumptive Stressful Life Events Scale, Social Support Questionnaire, Coping Strategies CheckList, Dysfunction Analysis Questionnaire, WHO Quality of Life (QOL) Scale-Bref, General Health Questionnaire-12 (GHQ-12). Those with a GHQ-12 score of $>$2 were further assessed with Comprehensive Psychopathological Rating Scale and presence of psychiatric diagnoses as per the International Classification of Diseases-10th Revision (ICD-10) was determined. The GHQ $>$2 (GHQ Positive; N=8) and GHQ $<$2 (GHQ Negative; N=16) subgroups were compared as regards their psychosocial profile.

Results: The GHQ Positive and the GHQ Negative Acromegaly subgroups were similar for demography and illness variables, and social support and coping strategies. GHQ Positive subgroups had significantly higher - total life events in lifetime, disability, and impairment of QOL. Psychiatric morbidity was 33% (8 out of 24) in the GHQ positive subjects; ICD-10 diagnoses being Nil Psychiatry (N=2) depressive disorders (N=6, including 3 with prolonged adjustment disorder, 2 with psychotic depression, and 1 with other mood disorders).

Conclusions: Acromegaly is associated with considerable psychiatric morbidity which appears to be related to the impact of the disease in terms of the disability, coping strategies utilized, and impaired QOL.

Funding: This study was carried out as part of the Institute (PGIMER) Research Scheme and was supported by funding provided by the Institute-Postgraduate Institute of Medical Education and Research (PGIMER), Chandigarh, India.

References:
An Empirically Derived Adult Patient Self-Report Instrument for the Provisional Diagnosis of Multiple Non-Psychotic Psychiatric Disorders
Paula T. Trzepacz, M.D., Eli Lilly and Company, Neuroscience, Lilly Corporate Center, DC 6161, Indianapolis, IN, 46285, 9000, John P. Houston, M.D., Douglas E. Faries, Ph.D., Jonna Ahl, Ph.D., Sandra Malcolm, B.S., Caroline C. Doebbeling, M.D., Kurt Kroenke, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the development of self-assessment instruments and their utility in assisting the primary care provider in identifying patients who may need psychiatric care.

Summary:

Introduction: Accurate diagnoses of mood disorders using self-report instruments and primary care diagnostic tools can be com-

Diagnostic Differentiation Using Self-Report Measures for Mood and Anxiety Disorders in a Primary Care Population
Caroline C. Doebbeling, M.D. Indiana University School of Medicine, Internal Medicine and Psychiatry, RT 449, 535 Barnhill Road, Indianapolis, IN, 46202, 9000, John P. Houston, M.D., Douglas E. Faries, Ph.D., Jonna Ahl, Ph.D., Paula T. Trzepacz, M.D., Sandra Malcolm, B.S., Kurt Kroenke, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the utility patient self-assessment in assisting the primary care provider in identifying patients who may need psychiatric care.

Summary:

Introduction: Self-report instruments that are readily available to assess patients for single psychiatric disorders may overlook other diagnoses with similar symptoms. We utilized data from the initial phase of an instrument development protocol to construct a self-report instrument based on DSM-IV symptomatic diagnostic criteria for major depressive episode (MDE), mania, generalized anxiety disorder (GAD), and attention deficit hyperactivity disorder (ADHD).

Methods: Patients completed a self-report questionnaire with candidate symptom questions prior to being assessed by trained telephone interviewers for MDE, mania, ADHD, and GAD and for ADHD by SCID-RV and ACDS-V1.2 respectively. Using the diagnoses obtained via the telephone interview as the ‘gold standard’ reference, the optimal set of candidate items were selected for each diagnosis to construct an instrument for provisional diagnosis. The ‘optimal set’ was defined two ways: the set maximizing sensitivity plus specificity, and the set maximizing sensitivity under the condition that the specificity was at least 0.90.

Results: 343 patients completed both the set of candidate items and the telephone diagnostic interview. Based on the telephone diagnoses, 89 met DSM-IV criteria for a MDE, 64 for ADHD, 24 for GAD, and 24 for mania. The observed sensitivities/specificities calculated based on agreement between provisional diagnosis using the constructed self-report instrument and telephone interview were: 61/90 for MDE, 63/91 for past or present mania, 54/91 for ADHD, and 54/92 for GAD. Of the DSM-IV symptom diagnostic criteria 3 items were used for MDE, while 4 items were used for each of the other diagnoses.

Conclusions: A self-assessment instrument with potential utility for several common non-psychotic psychiatric diagnoses was constructed with similar sensitivities/specificities to that of individual instruments assessing these disorders. Formal field validation of the resulting instrument is necessary to confirm the psychometric properties of the empirically derived instrument.

References:

Do We Agree on When the Patient is Psychotic?
J. Nielsen Aalborg Psychiatric Hospital, Unit for Psychiatric Research, psyk.jin@nja.dk, Aalborg, 9000, 4099, K. Stage, A. Lindhardt, K. Martini, B. Mogensen, Jens K. Larsen, A. Bertelsen

Educational Objectives:
At the conclusion of this presentation the participant should be aware of doctors, psychologists and caregivers but whether they use the term in the same situations is unclear. Whether the patient is psychotic or not can be of crucial importance when deciding whether to use e.g. compulsory admission, antipsychotic treatment or sentence to prison. In Denmark the ICD-10 diagnostic criteria are used, but a broader legal psychotic definition is also used interchangeably.

Method: Doctors, psychologists and caregivers from eight hospitals in Denmark were asked to fill out a questionnaire with 11 cases and demographic variables. From the description of the cases they had to decide whether they found the patient psychotic or not.

Results: Two-hundred-forty-three answered the questionnaire. Doctors used the term psychotic more often than psychologists and caregivers (ANOVA, P < 0.001). Psychiatrists did not use the term psychotic more often than doctors (t-test, non-significant). Psychologist had more correct answers than doctors (t-test, p<0.005 df=120) according to the ICD-10. No correlation was found between the use of the term psychotic and the degree of biological conviction (r=0.03).

Conclusion: Doctors seem to use the term psychotic more often than psychologists and caregivers. Doctors might use the term psychotic more broadly due to the legal aspects of restraint and compulsory treatment.

Other professionals might tend to use the ICD-10 definition more strictly.

References:
plex, as many patients have multiple disorders or report symptoms common to multiple disorders and most instruments only diagnose a single disorder. We utilized data from the initial phase of a protocol designed to develop an instrument for use by adult primary care patients for self-assessment of common psychiatric disorders, to examine symptom overlap, and to differentiate diagnoses.

Methods: Patients completed a self-report questionnaire with candidate symptom questions prior to assessment by blinded, trained telephone interviewers using DSM-IV SCID-RV criteria for GAD, MDE, and mania, and ACDS-V1.2 for adult ADHD. For multiple diagnoses, stepwise logistic regression was utilized to determine self-report items that best differentiated between the diagnoses. The utility of self-report symptoms in differentiating between diagnoses was further assessed by examining correlations between scale scores and differences in the score distributions by diagnosis.

Results: Of 143 patients with at least one diagnosis, 46 (32%) met criteria for at least 2 diagnoses. Overlapping symptoms for paired diagnoses had rating scores that were at least moderately correlated (range: .38 to .82). For each diagnosis, all scale scores from patients with the diagnosis were significantly different than those from patients without the diagnosis. For differentiating patients with MDE from those with GAD, stepwise regression identified three predictive items: ‘having no interest or enjoyment’, ‘having no appetite or uncontrolled eating’, and ‘feeling restless or on edge’. Items differentiating ADHD from bipolar disorder were ‘trouble wrapping up final details’ and ‘extremely active and productive’. Optimal cutoff scores for the differentiating items and total scores from self report scales were also determined.

Conclusions: In primary care, utilization of this patient self-report instrument may have utility for diagnostic differentiation. Additional testing is needed to confirm these results.

References:

NR768 Wednesday, May 23, 3:00 PM - 5:00 PM
Sleeplessness Despite Remission in Depressed Outpatients
Suhayl J. Nasr NASR Psychiatric Services PC, Behavioral Medicine, 2814 South Franklin Street, Michigan City, IN, 46360-1843, 9000, Burdette J. Wendt

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that insomnia often times persists, even in patients who are otherwise in remission. The QIDS-SR16 is a useful, easy to use tool to help measure and identify depressive symptoms.

Summary:
Background: Sleep is an important symptom in mood disorders. Most medications used to treat these disorders have an impact on sleep. The QIDS-SR16 is a self-report depression questionnaire that includes three insomnia questions and one hypersomnia question.
Method: 145 consecutive outpatients were asked to complete the QIDS-SR16 just prior to their office visit. Their current diagnoses and medications were recorded, in addition to their demographics. Medications were classified as generally sedating (e.g. trazodone, mirtazapine, benzodiazepines, quetiapine, etc.), stimulating (modafinil, methylphenidate, amphetamines, etc.) or other (e.g. SSRI's, levothyroxine, ziprasidone, etc.)

Results: The average QIDS-SR16 score was 11.1 (±6.7). Most of the residual symptoms were accounted for by the first three sleep items (early, middle, and late insomnia). These three questions made up 21% of the questions on the test, but 38% of the score among all patients. 80 patients had a score of 10 or less (full remission to mild symptoms). Yet the three insomnia questions produced 45% of their score (50% in the remitted patients and 42% in the mildly depressed patients). Sedating medications were associated with lower total scores (11.2 vs. 12.0), but higher insomnia scores than were non-sedating medications (3.7 vs. 3.3). Patients on both a sedating and a stimulating medication had the lowest insomnia scores (2.0). The three insomnia questions correlated positively with restlessness, appetite change, and energy questions (p<0.01).

Conclusions: Sleep items significantly contribute to the total QIDS score. Insomnia is a persistent symptom in depressed patients, even when they achieve either recovery or remission.

References:
Conclusions: A cyclothymia score of 4 or more on the TEMPS short version is correlated with likelihood of a bipolar diagnosis and poorer response to treatment. The short version TEMPS is a useful addition to the identification of bipolarity in patients presenting with depression.

References:

NR770 Wednesday, May 23, 3:00 PM - 5:00 PM
Use of the Adult ADHD Investigator Symptom Rating Scale (AISRS) as an Instrument to Measure the Impact of Methylphenidate Therapy on Adult Signs and Symptoms of ADHD
Thomas J. Spencer, M.D. Harvard Medical School, Department of Psychiatry, 725 ACC, 55 Fruit Street, Boston, MA, 02114, 9000, Lenard Adler, M.D., Joseph Biederman, M.D., Diane D. Harrison, M.D., M.P.H., Brenda Zimmerman, M.S.

Educational Objectives:
At the conclusion of this presentation, the participant will recognize that the Adult ADHD Investigator Symptom Rating Scale (AISRS) is a sensitive instrument for detecting methylphenidate treatment effects and ADHD symptom improvement in adults with the disorder.

Summary:
Objective: The validated Adult ADHD Self-Report Scale (ASRS) was developed with questions consistent with DSM-IV criteria for childhood-onset ADHD diagnosis but which addressed the manifestations of ADHD symptoms in adults. The ASRS was modified for investigator use as the AISRS to more accurately reflect the impact and severity of ADHD in adults. The objective of this analysis was to investigate the effectiveness of the Adult ADHD Investigator Symptom Rating Scale (AISRS) in the evaluation of ADHD symptom improvement in adults treated with methylphenidate (MPH).

Methods: AISRS assesses 18 symptoms of adult ADHD, including work life balance, executive function, work responsibilities, employment history, and present behavior patterns, on a severity grid (0 = not present to 3 = severe) and has been used in studies as the primary outcome measure. To review the efficacy of the instrument in detecting treatment effects in adults with ADHD, this analysis assessed results from 2 published randomized, placebo-controlled studies of MPH that used the AISRS (Spencer. Biol Psychiatry. 2005;57:456-463; Biederman. Biol Psychiatry. 2006;59:829-835).

Results: The AISRS was sensitive to medication effects in adults with ADHD: 40% of placebo-treated, 60% of immediate-release (IR) MPH-treated, and 69% of OROS® MPH-treated patients attained a 30% reduction in AISRS scores, with statistically significant treatment effects compared with placebo for IR MPH and OROS MPH (P<0.001). Therefore, AISRS was selected as the primary rating scale for a randomized, 7-week, double-blind, placebo-controlled, dose titration, parallel study of OROS MPH 36, 54, 72, 90, or 108 mg/d versus placebo in 229 adults with ADHD.

Conclusions: The AISRS is an instrument that adequately and sensitively measures the impact of methylphenidate treatment on adult signs and symptoms of ADHD.

References:

NR771 Wednesday, May 23, 3:00 PM - 5:00 PM
Willingness to Screen for Depression/Distress: Preferences of Oncologists and Psychiatrists Compared
Alex J. Mitchell Leicester Partnership Trust, Liaison Psychiatry, Leicester General Hospital, Leicester, LE5 4PW, 4120, Stephen Karr

Educational Objectives:
At the conclusion of this presentation, participants should be able to understand the merits of short screening methods. They should be able to weigh the pros and cons of long vs short methods. They should gain an understanding of what proportion of psychiatrists and oncologists wish to use each screening method. They should try and understand the barriers to accurate detection of depression in clinical practice.

Summary:
Introduction: Several screening tools have been used to improve the detection rates, but their value remains unclear often due to problems with implementation. A significant issue is also whether health professionals are willing to formally screen for distress and if so, what length of tool do they prefer? Recent recommendations from the NCCN recommend screening for distress using short tools such as the distress thermometer.

Methods: An initial literature review revealed little has been published on this topic before. We designed a new questionnaire of clinicians attitudes to distress screening and conducted a survey of health professionals working in cancer care. We distributed 300 questionnaires and received 216. Typical questions were “Do you routinely screen for psychological distress in your patients?” and “How much time would you be willing & able to allocate to detecting distress per appointment?”

Results: 63% of oncologists and 76% of psychiatrists “always or regularly” tried to detect depression/distress but 14% never tried. Most (64% of oncologists and 68% of psychiatrists) relied on their clinical acumen alone but a quarter used 1,2, or 3 simple questions instead. Only 8% of cancer clinicians used a formal screening questionnaire in their typical practice. We then asked about ideal screening preferences for each clinician in their service. About one third preferred 1,2,3 simple questions and one third preferred a short formal questionnaire. Less than 10% in each group wanted to use a standard questionnaire like the HADS, BDI, Hamilton or similar.

References:
**NR772** Wednesday, May 23, 3:00 PM - 5:00 PM

**Detecting of Cancer Related Distress, Depression and Anxiety: Accuracy of the Distress Thermometer Compared to the HADs**

Alex J. Mitchell
Leicester Partnership Trust, Liaison Psychiatry, Leicester General Hospital, Leicester, LE5 4PW, 4120

**Educational Objectives:**

At the conclusion of this presentation, participants should be able to understand the merits of visual-analogue screening methods. They should be able to weigh the pros and cons of distress thermometer vs the HADs. They should try and understand the barriers to accurate detection of depression, distress and anxiety in cancer care.

**Summary:**

*Purpose:* The distress thermometer has been recommended by the NCCN as a simple method of detecting distress, anxiety or depression in cancer settings. However, its diagnostic accuracy has not been previously examined in a systematic fashion. The Hospital Anxiety and Depression Scale is the most widely used reference scale in cancer settings.

*Results:* 10 diagnostic validation studies of the DT versus the HADs were found involving a total of 3626 patients.

Four studies involving 2216 patients examined the validity of the DT in relation to the HADS-D. The cut-off chosen was 7 / 8 on the HADs and 3 / 4 on the DT. Overall 334 cases were detected on the DT out of 411 on the HADS-D giving a pooled sensitivity of 81.3%. 774 non-cases were misidentified out of 1805 giving a specificity of 57.1%. The PPV was 30.1% and the NPV 93.1%.

Four studies involving 2215 patients examined the validity of the DT in relation to the HADS-A. Overall 652 cases were detected on the DT out of 843 on the HADS-A giving a pooled sensitivity of 77.3%. 596 non-cases were misidentified out of 1372 giving a specificity of 56.6%. The PPV was 52.2% and the NPV 80.25%.

Four studies involving 1026 patients examined the validity of the DT in relation to the HADS-T. Overall 216 cases were detected on the DT out of 293 on the HADS-T giving a pooled sensitivity of 73.7%. Conversely 222 non-cases were misidentified out of 733 giving a specificity of 69.7%. The PPV was 49.3% and the NPV 86.9%.

*Conclusion:* The DT performed well in ruling out depression, distress and anxiety. However, it does not perform well as a case-finding (rule-in) instrument.

**References:**


**NR774** Wednesday, May 23, 3:00 PM - 5:00 PM

**The Integral Inventory for Depression (IID), a New Clinimetric Tool for the Emotional and Physically Painful Dimensions of Depression**

Hector J. Duenas
Sanatorio Durango, Psychiatry, Avenida Durango 290-409 Roma, Mexico City, 06700, 2010, Eduardo Angel Madrigal De Leon, Antonio Celis-Perdomo, Carmen Lara, M.D.

**Educational Objectives:**

At the end of this presentation, the participants should be able to recognize the Integral Inventory for Depression (IID) as a reliable and valid instrument for the evaluation of the emotional and painful dimensions of depression.

**Summary:**

*Introduction:* Pain is a major complaint in depressed patients. IID has been validated for detecting and evaluating severity of both the emotional (ED) and physically painful (PPD) dimensions of Major Depressive Disorder (MDD).

*Methodology:* 121 patients with MDD (according to DSM-IV TR criteria) and 88 non-depressed patients who attended psychiatric consultation. After signing their ICD and before their consultation, they answered the IID-P (Patient version) and the SCL-90. Straight afterwards the investigators evaluated those who presented MDD symptoms with the IID-I (Investigator version) and the HAMD-17. 1) Internal Consistency was determined with Cronbach’s Alpha; 2) External Consistency was calculated with the Pearson’s correlation coefficient between IID-P and IID-I, 3) Convergent Validity was calculated with Pearson’s correlation coefficient between IID and Ham-17 and SCL (Depression subscale) and 4) Construct
Validity with the differences between depressed and non-depressed patients. 5) Size effect was calculated after antidepressant treatment.

Results: 1) Cronbach's Alpha was 0.86 and 0.82 for both subscales (P-version) and 0.81 and 0.79 (I-version); 2) Correlation coefficient between the patient's and investigator's was: 0.88 for ED and 0.91 for PPD. 3) Correlations between HAMD-17 and ED-P and ED-I were 0.35 and 0.42 respectively. Correlations between HAMD-17 and PPD-P and PPD-I were 0.21 and 0.31. Correlations between the depression subscale of the SCL-90 and ED-P was 0.77 and -0.60 for the PPD-P. 4) Differences between depressed and non-depressed patients were statistically significant (12.87 for ED-P and 29.9 for PPD-P vs. 19.6 for ED-P and 35.4 for PPD). Similar results were obtained with the I-version. (p<0.0001). 5) Size effect was from 1.26 for PPD-P to 2.74 for ED-I.

Conclusions: I/D is a valid and reliable tool for detecting and evaluating severity in both the ED and the PPD of MDD.

References:

NR775 Wednesday, May 23, 3:00 PM - 5:00 PM
Internal Consistency and Factor Structure of the Zung'Self-Rating Anxiety Scale in Colombian University Students
Adalberto Campo-Arias, M.D. Human Behavioral Research Institute, Research Direction, Transversal 93 No 55-48 Interior 68, Bogota, 57 1, 3010, Elsa S. de la Ossa, Yuleima Martínez

Educational Objectives:
At the conclusion of this presentation, the participants should be able to recognize the internal consistency and factor structure of the Zung'self-rating anxiety scale in Colombian university students.

Summary:
Background: The Zung'self-rating anxiety scale (SAS) has been used in various Colombian researches. Although, its internal consistency and factor structure has not been reported.
Objective: To calculate the internal consistency and explore the factor structure of the SAS among Colombian university students.
Method: Two-hundred twenty-one medicine and psychology students of a private university in Cartagena were invited to complete the SAS. Students were aged between 18 and 32 years (Mean=20.5, SD=6.18) 64.4% were women, and 54.3% studied medicine. Cronbach alpha was computed and exploratory factor analysis (EFA) was done. Factors with eigenvalue higher than 1.41 were retracted.
Results: The Cronbach alpha coefficient was 0.77, and EFA exhibited two salient factors. Factor one (appraisal expectation) accounted for 24.0% of the variance; and factor two (somatic anxiety), 9.1%.
Conclusions: The SAS presents acceptable internal consistency. However, its two-dimensional structure that accounts for only 33.1% of the variance. It is necessary to design a better scale to recognize anxiety disorders in university students.

References:

NR776 Wednesday, May 23, 3:00 PM - 5:00 PM
Association Study of Dopamine D2 Receptor Gene TaqI A Polymorphism and Reward Related Personality Traits in Healthy Korean Young Females
So Hee Lee, M.D. National Medical Center, psychiatry, 18-79, Ulchiro 6-ga, Jung-gu, Seoul, 100-798, Byung-Joo Ham, M.D., Youl-Hee Cho, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize positive association between dopamine D2 receptor gene TaqI A polymorphism and reward related personality.

Summary:
Genetic factors significantly contribute to the determination of human personality traits. Gray's Reinforcement Sensitivity Theory (RST) measures behavioral sensitivity to reward and punishment. We aimed to investigate the possible relationship between Dopamine D2 receptor (DRD2) TaqI A polymorphism and the reward related personality traits as measured by the Carver and White BIS/BAS (the behavioural inhibition system / behavioural approach system) scales and Cloninger's TCI (The Temperament and Character Inventory).

The sample consisted of 267 female healthy unrelated university students (age: M=23.12, SD=3.22) and they filled out BIS/BAS scale and TCI scale. Genomic DNA was isolated from whole blood and genotyped with fluorescence polarization detection method. The effect of the independent variables (DRD2) on the dependent variables: TPQ personality factors (NS, HA, RD, PS) and BIS/BAS (BIS, BAS-RR, BAS-FS, BAS-D) were analyzed by multivariate and subsequent univariate ANOVA (SPSS for Windows) and a P value of less than 0.05 was regarded as significant.

The DRD2 TaqI gene polymorphisms was in Hardy-Weinberg equilibrium (χ²=0.45, d.f.=1, p=0.501). Allele Frequency of DRD2 A1(0.41) was considerably different from those in Caucasians (0.15-0.20) and were similar in Korean cases (0.42-0.43). We found significant associations between the A1 allele of the DRD2 TaqI A polymorphism and high BAS-RR (reward responsiveness). No significant association was observed between DRD2 polymorphisms and other factors of the BIS/BAS and TCI.

These findings suggest the notion that DRD2 TaqI A polymorphism contributes to high reward sensitivity that is considered to be a feature of substance use and binge-eating disorders.

References:
Educational Objectives:

At the conclusion of this presentation, the participant should have a better understanding of possible associations of several common genetic variants with olanzapine/fluoxetine combination and lamotrigine response in the treatment of bipolar I depression.

Summary:

**Objective:** To evaluate common genetic variations for association with treatment response of bipolar I depression with olanzapine/fluoxetine combination (OFC) or lamotrigine (LMG).

**Methods:** We assessed response in 108 OFC-treated and 103 LMG-treated bipolar I depressed patients in the seven-week acute period of a randomized, double-blind study comparing OFC (6/25, 6/50, 12/25, or 12/50 mg/day; N=205) with LMG (titrated to 200 mg/day; N=205). Single nucleotide polymorphisms (SNPs) were genotyped in a set of candidate genes corresponding to known sites of activity or reported predictors of response for olanzapine, fluoxetine, and lamotrigine, as well as others previously associated with psychiatric disease states. Primary outcome was baseline-to-endpoint reduction in Montgomery-Asberg Depression Scale (MADRS) total score, and analysis utilized repeated measures analysis with terms for visit, genotype, genotype by visit interaction, and baseline score as a covariate.

**Results:** SNPs within the dopamine-D2 receptor, histamine H1 receptor, and glucocorticoid receptor (NR3C1) genes were associated with statistically significant differences in response to lamotrigine. SNPs within the Dopamine-D3 receptor gene, including the coding ser-9-gly SNP rs6280 previously associated with psychotic symptom response to olanzapine in schizophrenia, and neuronal NPAS3 transcription factor gene were significantly associated with response to OFC.

**Conclusions:** SNPs in specific candidate genes differentially predicted response to OFC or LMG treatment of bipolar I depression. Replication in other datasets is needed.

**References:**


NR779 Wednesday, May 23, 3:00 PM - 5:00 PM

Interaction of ADRA2A Gene and ADRB3 Gene on Bone Density in Male Schizophrenic Patients with Exposure to Antipsychotics

Hsieh-Jane Chiu, M.D., M.P.H. Yu-Li Hospital, DOH, Psychiatry, 448 Chung-Hwa Road, Hualien, 961, 5830, Tsu Hung Lan, M.D., Tsong-Ming Hwu, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to recognize the possible genetic variations may case impacts on the bone density change from a long-term antipsychotics exposure among people with schizophrenia.

**Summary:**

**Objective:** A lower bone density is suspected prevalent among schizophrenia patients while compared to the general population. This study is to explore the gene-gene interaction on bone density in male schizophrenic patients from ADRA2A gene and ADRB3 gene.

**Method:** This is a multi-center, investigator-initiated, naturalistic study project. Here we enrolled 119 male inpatients meeting DSM-IV criteria for schizophrenia or schizoaffective disorder from two psychiatric hospitals in Taiwan. Bone density indicated in BUA from baseline to final measurement in 80 genotyped, OFC-treated bipolar I depressed patients in a 6-month, randomized, double-blind study comparing OFC (6/25, 6/50, 12/25, or 12/50 mg/day) with lamotrigine. Single nucleotide polymorphisms (SNPs) were genotyped in candidate genes corresponding to reported and suspected predictors of hyperprolactinemia for antipsychotics and known sites of activity for olanzapine and fluoxetine. Primary outcome measure was increase from baseline to last observed measurement in the log of the serum prolactin concentration as assessed by the interaction of allele/gene by ANOVA with gender and baseline prolactin concentration as covariates. Outcomes for SNPs occurring in 3 or more patients per each genotypic group were assessed.

**Results:** Four tightly linked candidate SNPs within the pre-prioritized dopamine-2 receptor were associated with differences in mean log prolactin increases with OFC, corresponding to prolactin concentration increases of 213.3% for the SNP homozygote (N=7) vs. 53.5-55.2% and 33.7-34.6% for the heterozygote (N=29-30) and other homozygote (N=42-43) respectively (uncorrected p<.003). Significant uncorrected p values for serotonin-2C SNPs (p<.0004) also suggested a possible association with hyperprolactinemia. Associated clinical adverse events were not reported.

**Conclusions:** SNPs in the dopamine-2 receptor candidate gene differentially predicted prolactin increase in OFC-treated patients with bipolar I depression. Replication in other datasets is needed.

**References:**


Results: After controlling for gender, age, previous antipsychotics treatment, and BMI, the absolute regression coefficient of BUA of an interaction term between ADRA2A gene and ADRB3 gene for an individual male is -21.0±10.0 (p-value =0.03). Conclusion: It is suggested that the interaction between ADRA2A gene and ADRB3 gene indeed modified the bone density effect in our male schizophrenic patients significantly.

References:

NR780 Wednesday, May 23, 3:00 PM - 5:00 PM
Depot Haloperidol Treatment in Out-patients with Schizophrenia on Monotherapy: Impact of CYP2D6 Polymorphism on Pharmacokinetics and Treatment Outcome
Holger W. Arthur, M.D. Department of Clinical Neuroscience, Karolinska Institute, Stockholm, Sweden, Hasselsten 29, Alvsjö, SE-125 53, 4010, Georgios Panagiotidis, M.D.

Educational Objectives:
This poster addresses the importance of optimal dosing strategies for antipsychotics. Here a substantial metabolic variability between individuals is shown in the treatment with a depot antipsychotic. As the first pass metabolism of depot drugs are circumvented, genetic variability of drug metabolism can partially explain this variability.

Summary:
Introduction: Haloperidol and several other antipsychotic drugs are at least partially metabolised by the polymorphic cytochrome P450 2D6 (CYP2D6). The interindividual variation in metabolic capacity of CYP 2D6 might be of importance when dosing since some of these drugs are associated with dose dependent side effects such as Parkinsonian symptoms and tardive dyskinesia.

The major aim of this study was to assess the importance of the CYP2D6 polymorphism on treatment outcome and on steady state plasma concentrations in patients with schizophrenia treated with intramuscular haloperidol decanoate in monotherapy. Another aim was to use the collected data to establish a model for predicting steady state plasma concentration from dose and genotype.

Methods: 26 patients with schizophrenia were treated with depot haloperidol as monotherapy, which ascertains good compliance with intramuscular haloperidol decanoate in monotherapy. Another aim was to use the collected data to establish a model for predicting steady state plasma concentration from dose and genotype.

Results: We found a clear correlation between haloperidol plasma concentration and number of active CYP2D6 alleles but no correlation to treatment outcome or side effects. A model to predict plasma concentration from dose and number of active CYP2D6 alleles was formed from the obtained data. The model for prediction of haloperidol trough concentration explained 95% of the total variance.

References:

NR781 Wednesday, May 23, 3:00 PM - 5:00 PM
BDNF(Brain-Derived Neurotropic Factor) Gene Polymorphism of Late-Onset Depression in Korean Population and antidepressant Responsiveness
Kyu-Hyung Yu, M.S. Samsung Biomedical Research Institute, Dep. of Psychiatry, B215 #50 ilwon-dong kangnam-gu, Seoul, 135-710, 5800, Shinn-Won Lim, M.S., Tae-Young Hwnag, M.D., Boram Cha, Doh Kwan Kim, Ph.D.

Educational Objectives:
Brain-derived neurotropic factor(BDNF) has been studied, related to the neurogenesis of hippocampus after antidepressant administration in several studies using animal depression models. Also, the polymorphisms of BDNE gene was reported related to depression and antidepressant responsiveness, but these results controversial.

Our purpose is to evaluate whether the functional polymorphism of exon2 is associated to fluoxetine responsiveness in late-onset depressed patients.

Summary:
Introduction: Brain-derived neurotropic factor(BDNF) has been studied, related to the neurogenesis of hippocampus after antidepressant administration in several studies using animal depression models. Also, the Val66Met polymorphism of BDNE gene was reported related to depression and antidepressant responsiveness, but these results controversial.

Our purpose is to evaluate whether the polymorphism is associated to fluoxetine responsiveness in late-onset depressed patients.

Methods: Fifty-six patients with late-onset depression and 34 normal volunteers were classified from genomic DNA for Val66Met polymorphism of the BDNE gene, using primer flanking exon 2 region. Patients then entered a 6 week clinical trial with an Serotonin selective reuptake inhibitor(SSRI), fluoxetine, with documentation of plasma drug concentrations. Responder was defined as the decrease of HAM-D score (%) > 50 at 6 week after antidepressant treatment.

Results: No differences were any characteristics of subjects such as age, gender, age of onset, duration of illness between responder and non-responder group. Between normal volunteer and late-onset depressed patients were not differ, but was tendency existed (p=0.082, by Fisher exact test). A tendency of association existed for Val66Met polymorphism of BDNE gene, using primer flanking exon 2 region. Patients then entered a 6 week clinical trial with an Serotonin selective reuptake inhibitor(SSRI), fluoxetine, with documentation of plasma drug concentrations. Responder was defined as the decrease of HAM-D score (%) > 50 at 6 week after antidepressant treatment.

Conclusions: We found a clear correlation between haloperidol plasma concentration and number of active CYP2D6 alleles but no correlation to treatment outcome or side effects. A model to predict plasma concentration from dose and number of active CYP2D6 alleles was formed from the obtained data. The model for prediction of haloperidol trough concentration explained 95% of the total variance.

References:
NR782  Wednesday, May 23, 3:00 PM - 5:00 PM
Efficacy Of Duloxetine In The Treatment Of Unspecified Pain Associated With Depression
Stephan Brecht, M.D.  Boehringer Ingelheim GmbH, CDep.  Medical Affairs, Ingelheim am Rhein, 55216, 4280, Christine Courteel, M.D., Catherine Debeuvrie, M.D., Jens Croenlein, M.D., Durisala Desaiah, Ph.D., Joel Raskin, M.D., Koen Demyttenaere, M.D.

Educational Objectives:
At the end of this presentation, the participant should be able to understand the treatment effects of duloxetine of both emotional and painful physical symptoms in patients with moderate pain associated with major depressive disorder.

Summary:
Objective: Painful physical symptoms (PPS) in major depressive disorder (MDD) can obscure the diagnosis and impair treatment outcome. Antidepressants inhibiting serotonin and norepinephrine reuptake (SNRI) can be effective in the treatment of both emotional and PPS in MDD. This study evaluated efficacy and safety of duloxetine, an SNRI, in the treatment of patients with moderate pain associated with depression.

Methods: In this double-blind, placebo-controlled, European, 8-week study sponsored by Boehringer Ingelheim and Eli Lilly and Company, outpatients ≥18 years of age, presenting with major depression [Montgomery-Asberg Depression Rating Scale (MADRS) ≥20 and Clinical Global Impression-Severity (CGI-S) ≥4] and moderate pain (brief pain inventory [BPI] average pain score ≥3) not attributable to a diagnosed pain syndrome were randomized to either placebo (N=165) or duloxetine 60 mg (N=162) once daily. Primary outcome measure was the BPI average pain score at endpoint. Secondary measures were MADRS total score, CGI-S, PGI-I, SCL-90 R, response and remission in MDD, response on pain (> 30% decrease), safety and tolerability.

Results: Duloxetine compared with placebo significantly (P<0.01) improved the mean change of both BPI average pain (-2.57 ± -1.64) and MADRS total scores (-16.69 vs -11.31) with significant separation after 1 or 2 weeks. Remission in MDD (53% vs 29%) and response rates in pain (60% vs 44%) and MDD (55% vs 35%) were significantly higher in duloxetine-treated patients as compared with placebo. Duloxetine separated on most secondary outcome measures from placebo including the response rates in pain (60% duloxetine vs 44% placebo) and the BPI interference scores with daily functioning. Treatment-emergent adverse events (>10%) observed in duloxetine-treated patients were nausea, hyperhidrosis, and dry mouth. Discontinuation rates due to adverse events were 10.5% (duloxetine) vs 5.5% (placebo).

Conclusion: These results demonstrate duloxetine’s efficacy and tolerability in the treatment of patients with moderate pain associated with depression.

References:

NR783  Wednesday, May 23, 3:00 PM - 5:00 PM
Predictors of High Costs for Generalized Anxiety Disorder With or Without Pain
Baojin Zhu  Eli Lilly and Company, Information Science, Lilly Corporate Center, Indianapolis, IN, 46285, 9000, Zhongyun Zhao, Wenyu Ye, Ralph W. Swindle

Educational Objectives:
At the end of this presentation, the participant should be able to understand the presence of painful physical symptoms (PPS) in selective serotonin reuptake inhibitor non- or partial responders, and what is the impact of a switch to duloxetine (60-120 mg/day) on these PPS.

NR784  Wednesday, May 23, 3:00 PM - 5:00 PM
Switch To Duloxetine In SSRI Non- And Partial Responders: Effects On Painful Physical Symptoms Of Depression
David Peraiali, M.D.  Lilly Research Centre, Duloxetine, Lilly Research Center, Sunninghill Road, Windlesham, GU20 6PH, 4120, Deborah Quail, Ph.D., Durisala Desaiah, Ph.D., Angel-Luis Montejo, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand some key factors that predict high healthcare costs of managed care patients with generalized anxiety disorder (GAD).

Summary:
Purpose: To identify predictors for high treatment costs in individuals diagnosed with Generalized Anxiety Disorder (GAD) with or without pain.

Method: This analysis was conducted using the PharMetrics Integrated Outcomes Database. Individuals aged 18-64 diagnosed with GAD (ICD9-CM: 300.02) between 1/2003 and 6/2004 who had continuous eligibility 6-month prior and 1-year following GAD diagnosis were identified. Annual treatment costs during the year after GAD diagnosis were examined. The highest spenders (top 10%) of patients were compared with the rest on demographics, medication use and costs. Logistic regressions were used to identify predictors for high treatment costs. Patients with pain or without pain were examined separately.

Results: A total of 36,435 patients (67% female, mean age 41.5 years) were included in this analysis. The mean treatment costs were $48,248 for the top 10% spenders and $3,836 for the rest. The top 10% spenders accounted for 58.8% of the total costs. Patients with pain (N=22,133) were associated with higher costs than those without pain (N=14,302) ($11,445 vs. $3,639, p<.001).

Logistic regressions revealed significant risk factors for high costs including diagnoses of schizophrenia (odds ratio (OR)=2.03, p<.001), diabetes (OR=1.61, p<.001), asthma (OR=1.55, p<0.001), neuro-pain (OR=1.48, p<.001), musculoskeletal pain (OR=1.46, p<.001), depression (OR=1.31, p<.01), and alcohol abuse (OR=1.66, p<.001); prior utilization of narcotics (OR=1.62, p<.001), emergence services (OR=1.57, p<.001), hospitalizations (OR=1.56, p<.001). Similar predictors were obtained for GAD with pain but fewer predictors for GAD without pain.

Conclusions: This analysis showed that the top 10% spenders of GAD patients consumed nearly 60% of the total costs. GAD patients with pain incurred nearly 3 times as much cost as GAD patients without pain. The presence of prior pain, depression, other comorbidities, and prior resource utilization were significant predictors for high treatment costs. Special attention should be paid to those high costly patients in management of GAD.

References:
NR785  Wednesday, May 23, 3:00 PM - 5:00 PM  
An Open-Label Study of Levopromazine (Methotrimeprazine) As Add-On Therapy in Fibromyalgia Management  
Fernando Rico-Villademoros, M.D. Universidad de Granada, Instituto de Neurociencias, Ferraz 13, 1-7, Madrid, 28008, 4700, Piedad Morillas-Arques, M.D., Carmen M Rodriguez-Lopez, M.D., Juan S. Vilchez, Javier Hidalgo, M.D., Elena P. Calandre, M.D.  

Educational Objectives:  
At the end of this presentation, the participant should be able to:  
1. Learn about fibromyalgia and its management  

Summary:  
Background: Some second generation antipsychotics, namely olanzapine and especially quetiapine, have shown to improve fibromyalgia symptomatology. However, the acquisition cost of these drugs is much higher than that of first generation antipsychotics. The aim of this exploratory study was to assess the potential effectiveness and tolerability of levopromazine in the treatment of fibromyalgia.  

Methods: This was a uninecst, open-label study conducted in thirty-five outpatients, 18 years or older, meeting the ACR criteria for fibromyalgia who had not satisfiedfully responded to their previous fibromyalgia treatment. Levopromazine, flexibly dosed (6.25-100 mg/d) was added to their original treatment regimen for 12 weeks. The primary outcome measure was the mean change from baseline to endpoint in the Fibromyalgia Impact Questionnaire total score. Secondary efficacy measures included mean changes from baseline to endpoint in the scores of the Clinical Global Impression of Severity scale (CGI), Pittsburgh Sleep Quality Index (PSQI), Beck Depression Inventory (BDI), State-Trait Anxiety Inventory (STAI), 12-Item Short Form Health Survey (SF-12), and a patients' Global Impression Improvement scale (PGI).  

Results: Thirty one (88.6%) patients (mean age 46±8, 90.3% females) had a postbaseline evaluation and constituted the intent-to-treat efficacy sample. Mean FIO total score did not decreased statistically at the study endpoint (63.37±11.32 vs 61.19±9.32). A statistically significant reduction was observed in PSQI scores (15.65±3.33 vs 12.23±3.79, P<0.0001, effect size: 1.03) and the CGI scores (4.71±0.64 vs 4.03±1.01, P=0.0015, effect size: 1.06). No relevant changes were seen in BDI, STAI nor SF-12 scores after treatment. Four (12.9%) patients reported to be much improved and 14 (45%) reported to be slightly improved after treatment. Most frequent side effects were dry mouth (12.9%), xerostomia (12.9%) and somnolence (9.8%).  

Conclusions: Despite its efficacy in improving sleep quality, levopromazine does not seem a useful alternative for the treatment of fibromyalgia.  

References:  
fewer early opioid prescription fills than veterans without opioid. 240mL of 40% alcohol resulted in “dose-dumping,” dangerous diagnoses and a co-occurring opioid use disorder had significantly compared to those with no SUD. On average, veterans with pain diagnoses and a co-occurring opioid use disorder had significantly fewer early opioid prescription fills than veterans without opioid use disorder over the previous 1 year (2.6 v. 5.3 days, p < 0.01) and 3 years (6.1 v. 13.4 days, p < 0.001).

Conclusions: Pain and SUD diagnoses were common among HCV+ patients and opioids were frequently prescribed. However, SUD was not a predictor of opioid prescription misuse. Further research examining the characteristics and correlates of pain in patients with HCV is indicated.

References:


NR787 Wednesday, May 23, 3:00 PM - 5:00 PM
Effect of Alcohol on the Release Profile of Polymer-Coated Extended-Release Morphine Sulfate Capsules
Franklin Johnson, M.S. Alpharma Branded Products Division Inc, Medical Affairs, 1 New England Avenue, Piscataway, NJ, 08854, 9000, Stephen Sun, M.D., George Wagner, B.S., Joseph Stauffer, D.O.

Educational Objectives:
At the conclusion of this presentation, participants will be able to explain the recent concern over “dose-dumping” when extended-release products are taken with alcohol and to identify one product that continues to display an extended-release profile when consumed with study doses of alcohol.

Summary:
Introduction: Extended-release opioid formulations offer appropriately-selected patients with chronic, moderate-to-severe pain a long duration of analgesia without the rapid rise and decline in serum levels characteristic of short-acting opioids. In 2005, hydromorphone hydrochloride extended-release capsules (Palladone™) were removed from the market because ingestion with 240mL of 40% alcohol resulted in “dose-dumping,” dangerous increases in peak plasma hydromorphone concentrations (average 6X greater than when taken with water). In certain subjects, an amount of alcohol less than a typical serving of beer resulted in almost double the concentration than when taken with water. This has prompted studies of interactions of other extended-release products with alcohol. This study assessed the effect of alcohol on bioavailability of polymer-coated extended-release morphine sulfate (P-ERMS) capsules taken with alcohol vs water.

Methods: In this open-label, randomized, single-dose, 3-way crossover study, 32 opioid-naive, healthy men, aged 21-40y, moderate drinkers (>7-21 drinks/week) took 100mg P-ERMS capsule with 240mL of 40% alcohol (4 shots [101mL] 190-proof Everclear®, 139mL water, consumed within 20min of dosing) fasted and fed, and with 240mL water (fasted). Naltrexone was administered 12h and 2h prior to treatment to counter morphine effects.

Results: Twenty-seven subjects completed ≥1 study arm. Eleven vomited after taking P-ERMS+alcohol; none vomited after P-ERMS+water. Median T_max (time of maximum morphine concentration) in subjects taking P-ERMS with alcohol fasted and fed, and with water fasted was 6.0, 8.0, and 8.0h, respectively, consistent with an extended-release profile. Excluding subjects who vomited during the 12h-dosing interval, C_max (maximum morphine concentration, mean of log-transformed values) was similar: 16.7, 16.0, and 15.6ng/mL. Overall morphine exposure (AUC) was also similar among groups.

Conclusions: Results indicated that, in subjects who consumed 240mL of 40% alcohol, P-ERMS maintained its extended-release profile. 

References:

NR788 Wednesday, May 23, 3:00 PM - 5:00 PM
Pregabalin Monotherapy for Relief and Management of Fibromyalgia: A 14-Week, Randomized, Double-Blind, Placebo-Controlled Trial (A0081077)
Lesley M. Arnold, M.D. University of Cincinnati College of Medicine, Psychiatry, 222 Piedmont Ave., Ste 8200, Cincinnati, OH, 45219, 9000, I. Jon Russell, M.D., Ph.D., W. Rachel Duan, M.D., Ph.D., Erdal Diri, M.D., James P. Young, M.S., Susan Martin, M.P.H., Teresa Griesing, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize that pregabalin demonstrates robust efficacy at all dosages tested for the management of fibromyalgia.

Summary:
Introduction/hypothesis: Previous trials provided evidence in pregabalin’s effectiveness in treating pain of fibromyalgia. This study was designed to provide more evidence supporting pregabalin’s efficacy/safety in this setting.

Methods: Randomized, double-blind, placebo-controlled with 1-week single-blind placebo run-in. Patients meeting ACR fibromyalgia criteria (widespread pain for ≥3 months and pain in ≥11 of 18 tender points) with pain VAS score ≥40 mm (0-100-mm scale) and <30% reduction in pain VAS score during placebo run-in were eligible for randomization to pregabalin 300, 450, or 600 mg/d (BID) or placebo for 14 weeks (2-week dosage escalation; 12-week fixed-dosage). Primary efficacy parameter was endpoint mean pain score. If met, additional primary efficacy parameters included endpoint Patient Global Impression of Change (PGIC) and the total score on the Fibromyalgia Impact Questionnaire (FIQ).

Results: 745 patients were randomized: 95% female, mean age=50 years, median fibromyalgia duration=8 years, baseline mean pain score=6.7. Differences from placebo in mean change from baseline to endpoint in pain score were: 300 mg/d, -0.71 (P=.0009); 450 mg/d, -0.98; 600 mg/d, -1.00 (each P<0001). There was a statistically significant improvement in PGIC scores. A greater proportion of patients reported at least minimal improvement on the PGIC with pregabalin: 68% of 300 mg/d, 78% of 450...
mg/d, and 66% of 600 mg/d vs 48% of placebo. Pregabalin 450 and 600 mg/d were associated with statistically significant improvements in total FIQ score: mean differences from placebo at endpoint were: 450 mg/d (P=0.0041); 600 mg/d (P=0.0034). Incidence of AEs increased with dosage; most common AEs: dizziness (all pregabalin, 35.8% vs placebo, 7.6%); somnolence (18.0% vs 3.8%).

Conclusions/discussion: Pregabalin (all dosages) demonstrated robust efficacy in managing fibromyalgia. Efficacy in endpoint mean pain score PGIC (all dosages) and total FIQ (450 and 600 mg/d) confirmed the clinical relevance of these findings.

Study funded by Pfizer, Inc.

References:

NR790 Wednesday, May 23, 3:00 PM - 5:00 PM
Evaluation of the Effects of Divalproex Sodium on Body Weight and Energy Balance in Healthy Volunteers

cory K. Martin, Ph.D. Pennington Biomedical Research Center, Health Behavior, 6400 Perkins Rd., Baton Rouge, LA, 70808, 9000, Hongmei Han, M.S., Donald Williamson, Ph.D., Stephen Anton, Ph.D., Frank Greenway, M.D., Steven Smith, M.D.

Educational Objectives:

Educational Objectives: At the conclusion of this presentation, the participant should be able to understand the reasons that weight gain occurs with Depakote treatment. The participant should understand that weight gain associated with Depakote treatment appears to be due to an increased drive to eat food and subsequent eating behavior. Finally, the participant should understand concrete interventions that will help reduce weight gain associated with Depakote treatment, including: 1) reduce disinhibited eating, hunger, food cravings, and binge eating, and 2) increase dietary restraint and volitional exercise. Stemming weight gain should improve the acceptability of Depakote treatment.

Summary:
Depakote® (divalproex sodium) is an anti-convulsant medication associated with weight gain, which negatively affects treatment acceptability. The purpose of this study was to identify the causes of this weight gain. Fifty-two healthy lean and overweight participants were randomized to Depakote or placebo (1:1 ratio). Energy intake at lunch and dinner was measured in the laboratory, and free-living energy expenditure was measured with accelerometry over two days. Hormones/peptides that regulate food intake (Peptide YY3-36 or PYY3-36, glucagon-like peptide-1 or GLP-1, leptin, and ghrelin) were measured 2 hours before and one hour after the start of a test meal to measure hormone/peptide response to a test meal. Self-report measures assessed eating attitudes and behaviors. Measurements occurred at baseline and day 21. Change from baseline was evaluated between groups with mixed models. A marginally significant group effect (p=0.06) was found for change in body weight. Only the Depakote group significantly increased body weight, but change in energy intake and expenditure did not differ between the groups. The Depakote group experienced a significant (p<0.05) increase in disinhibition (the tendency to overeat), hunger, cravings for fast foods (e.g., pizza, chips), binge eating, depression, and fear of fatness (the placebo group did not experience significant changes on these variables). Cholesterol (total, LDL, HDL) and glucose decreased significantly in the Depakote group. Change in hormones/peptides did not differ between the groups. The results indicate that Depakote associated weight gain is likely due to an increased drive to eat and tendency to overeat. This study identifies targets to prevent weight gain associated with Depakote, including: 1) reduce disinhibited eating, hunger, food cravings, and binge eating, and 2) increase dietary restraint and volitional exercise. Additional research is
needed with more accurate measures of energy expenditure (doubly labeled water) and mitochondrial function.

References:


**NR791 Wednesday, May 23, 3:00 PM - 5:00 PM
Assessing Persistence on Antipsychotics in the Treatment of Schizophrenia: Using Medicaid Data to Understand the Challenges**

Baojin Zhu, Ph.D. Eli Lilly and Company, US Outcomes Research, Lilly Research Laboratories, DC 4133, Indianapolis, IN, 46285, 9000, Daniel E. Ball, D.Phil., Glenn A. Phillips, Ph.D., Douglas E. Faries, Ph.D., Zhongyun Zhao, Ph.D., Haya Ascher-Svanum, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that in claims database studies, the approaches used to define persistence and treatment episodes affect the persistence of individual medications. A careful consideration of the analysis criteria along with the use of sensitivity analysis with multiple data-cutting scenarios is important in the medication persistence study.

Summary:

Objectives: Among the challenges in assessing persistence with data are the potential variations in persistence definitions and data-cutting criteria. This study compared persistence on atypical antipsychotics (olanzapine, risperidone, quetiapine, and ziprasidone) using different definitions of persistence and data-cutting criteria to assess their impact on the results and conclusions.

Methods: Using the Pennsylvania Medicaid database (1/1999 - 6/2003), patients diagnosed with schizophrenia, aged 18-64 who initiated an antipsychotic of interest after a 3-month period without the index drug were identified. A treatment episode was defined as the period from the initiation date of index medication to the first medication gap. To assess the effect of methodological changes on study outcomes, three methodologies were implemented:
1. 30- vs. 90-day gap definition of treatment discontinuation.
2. Multi-episode vs. first- or last-episode.
3. 1-year fixed study duration.

Results: Using a 30-day gap to define treatment discontinuation, 43,491 treatment episodes were identified (olanzapine=16,709, risperidone=14,847, quetiapine=8,648, ziprasidone=3,287) for 24,365 patients. Average duration of these episodes was 211, 197, 180, 130 days, respectively for olanzapine, risperidone, quetiapine, and ziprasidone and increased to 253, 236, 201, and 144 days respectively using the last episode approach. Imposing a fixed 1-year study duration effectively truncated the longer treatment episodes and had a different impact on the persistence of olanzapine (190 days), risperidone (183 days), quetiapine (170 days), and ziprasidone (143 days). Similar patterns were observed using a 90-day gap criteria.

Summary: In claims database studies, the approaches used to define persistence and treatment episodes affect the persistence of individual medications and may impact the outcomes and conclusions of a persistence study. It is critical, therefore, to carefully consider the analysis criteria and the use of sensitivity analysis with multiple data-cutting scenarios in order to provide a better understanding of the data.

References:

1. Caetano PA, Lam JMC, and Morgan SG: Towards a standard definition and measurement of persistence with drug therapy: Example from research on statin and antihypertensive utilization. Clinical Therapeutics.

**NR792 Wednesday, May 23, 3:00 PM - 5:00 PM
Impact of Juvenile Abuse on Treatment Outcome in Depression**

Gahan J. Pandina, M.D. Medical Affairs, Janssen Pharmaceutica, Inc., Medical Affairs, 1125 Trenton-Harbourton Road, Titusville, NJ, 08560, 9000, Cynthia Bossie, Mary Kujawa, M.D., Colette Kosik-Gonzalez, M.D., Ibrahim Turkoz, Ph.D., Ramy A. Mahmoud, M.D., Charles B. Nemeroff, M.D.

Educational Objectives:

At the conclusion of the presentation, the participant should be aware that juvenile abuse is associated with more severe illness in patients with MDD who are suboptimally responsive to standard antidepressants. They should recognize that a history of juvenile abuse may be a marker for non-response to standard antidepressants, but not necessarily a marker for non-response to augmentation strategies. Finally they should recognize that these patients may be less like to experience or report adverse events.

Summary:

Background: Vulnerability to depression and poor treatment response are associated with early life traumatic experiences including juvenile abuse. This post-hoc analysis assessed the impact of juvenile abuse on response to risperidone or placebo augmentation in patients with major depressive disorder (MDD) suboptimally responsive to antidepressant therapy.

Methods: Patients with MDD, a Clinical Global Impressions of Severity (CGI-S) score >/=4, and >/=4 weeks of antidepressant treatment, continued their antidepressant at an optimized dose during a 4-week open-label phase. Those with persistent depression were randomized to 6-weeks of double-blind risperidone or placebo augmentation. The Hamilton Rating Scale for Depression (HRSD-17) measured depressive symptomatology.

Results: Juvenile abuse was reported by 52.6% (141/268) of patients (risperidone n=73, placebo n=68). Baseline data showed greater years since first episode (p=0.009) and higher HRSD-17 anxiety/somatization (p=0.048) and Maier-Phillip severity (p=0.019) scores in patients with vs. without abuse. HRSD-17 total score improvement at endpoint with risperidone vs. placebo augmentation was -9.8±7.5 vs. -7.6±6.9 (p=0.039) in patients with abuse, and -10.2±6.4 vs. -8.3±7.4 (p=0.084) in those without abuse. Responder rate at endpoint (>/=50% HRSD-17 reduction) with risperidone vs. placebo was 40.8% vs. 23.1% (p=0.028) in those with abuse, and 41.0% vs. 34.4% (p=0.457) in those without abuse. Substantially fewer patients reported adverse events among those with (risperidone 16.4% and placebo 20.6%) vs. without abuse (71.9% and 65.1%).

Conclusions: Baseline differences suggest more severe illness among patients with a history of abuse. In contrast to prior reports, abuse status did not seemingly impact response. Confounding factors may include a differential in impact of type of abuse or placebo response. Abuse may also be a marker for non-response to standard antidepressants vs. augmentation strategies. Adverse event data suggest that patients with abuse may be less likely to experience or report adverse events.


References:


NR793 Wednesday, May 23, 3:00 PM - 5:00 PM

Content Validity and Inter-Rater Reliability of the Medication Adherence Assessment Tool

Jean-Pierre Lindenmayer, M.D. New York University School of Medicine, Dept of Psychiatry, Manhattan Psychiatric Center, Wards Island, New York, NY, 10035, 9000, Mary J. Kujawa, M.D., Kenneth A. Koback, Ph.D., R. Bruce Simonson, B.S., Lucy Mahalchick, B.S., Ramy Mahmoud, M.D., John M. Kane, M.D.

Educational Objectives:

- At the conclusion of this presentation, the participant should be able to recognize the psychometric properties of the Medication Adherence Assessment Tool, understand the population for which this scale is intended, and understand the methodology by which the content and the reliability of the scale were determined.

Summary:

Introduction: Partial- or non-adherence to medication regimens among patients with psychotic disorders is difficult to recognize in clinical practice. The Medication Adherence Assessment Tool is a brief 12-item clinician-administered scale developed to assess treatment adherence.

Methods: The tool content was based on input from 18 investigators, using predictors of partial adherence identified through literature research. The group provided input on item selection, wording, Likert-type assessment scales, and overall item order. Consequently, a study was designed to examine the inter-rater reliability of the scale, on both an item level and total score. Four videotapes were made by two expert clinicians administering the scale to 4 different outpatients with a diagnosed psychotic disorder and varying levels of medication adherence. These 4 videotapes were rated by 12 trained clinicians with expertise in assessing psychotic patients. Ten of the 12 raters observed all four tapes, and two of the raters observed three of the four tapes, resulting in a total of 46 observations. All tapes were rated independently, i.e., alone, with no discussion between the raters. Raters received no prior training or orientation to the scale prior to the reliability study.

Results: The tool demonstrated very high inter-rater reliability on both item level and total score. Intra-class correlation coefficient (ICC) for the total scale score was r=0.960. The majority of the individual item ICC's were greater than 0.6, which is considered significant. The four tapes represented a wide range of medication adherence, with mean total scores of 13.42, 19.6, 23.4, and 30.4, respectively (possible range: 12-48).

Conclusion: This tool demonstrates significant inter-rater reliability on both item level and total score, providing a useful tool for assessing medication regimen adherence. Additional studies for content and predictive validity are planned.

References:


NR794 Wednesday, May 23, 3:00 PM - 5:00 PM

Long-Term Remission In Schizophrenia With Long-Acting Risperidone: 18 Months Open-Label Study

Pierre-Michel Llorca Centre Hospitalier Universitaire, Centre Medico-Psychologique B, BP69 Cedex, Clermont-Ferrand, 63003, 4279, Emilio Sacchetti, Keith Lloyd, Werner Kissling, Rossella Medori

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that in stable schizophrenic patients whose antipsychotic drug therapy is not sufficiently effective there is a well established, well tolerated long-term alternative. By switching to risperidone long-acting injectable treatment it has been established that this treatment in the long term provides various advantages over previous antipsychotic therapies by achieving and maintaining higher levels of remission.

Summary:

Objective: To monitor long-term symptomatic remission and tolerability of risperidone long-acting injectable (RLAI) in clinically stable adults with schizophrenia who required treatment change.

Method: This subgroup analysis of the European Switch to Risperidone Microspheres (StoRMI) trial followed symptomatically stable patients taking stable doses of one or more antipsychotic drugs for at least 4 weeks prior to study assessment (Möller et al., 2005). Patients were converted to RLAI for a period of 18 months or until RLAI became commercially available in their respective country. The primary efficacy endpoint was achieving and maintaining (≥ 6 months) symptom remission (defined as ≤3 on all 8 key PANSS items [Andreasen et al., 2005]). Patients were monitored for the development of adverse events (AEs). Discontinuation rates were calculated based on Kaplan-Meyer estimates, where patients switching to commercial RLAI were used as censored observations.

Results: 529 patients were followed for up to 18 months, with 211 (40%) completing. At 18 months, the discontinuation rate was 55.7% based on Kaplan-Meyer estimates. The median time to discontinuation was 15.7 months (95% CI [14.0; 17.5]). Among patients not meeting severity remission criteria at baseline, 44.8% were in remission at endpoint. Among patients meeting severity criteria for remission at baseline, 84.2% had a sustained remission at endpoint. 93.7% of the patients who achieved or maintained remission at 6 months experienced sustained remission at endpoint. RLAI was generally well tolerated, with most AEs mild to moderate in severity. Thirteen percent of patients discontinued treatment due to an AE.

Conclusions: Most patients achieved and maintained a sustained remission after conversion to RLAI. RLAI is effective and safe in long-term treatment up to 18 months in clinically stable adults with schizophrenia.

References:


NR795 Wednesday, May 23, 3:00 PM - 5:00 PM

Impact of Drug Side Effects on Treatment Satisfaction in Antidepressant Users

Marc VanAudenrode, Ph.D. Analysis Group Inc., Healthcare Research, 1080 Beaver Hall Hill, Suite 1810, Montreal, PQ, H2Z 158, 1220, Jane Chang, M.P.H., Érick Moyneur, M.A.
NR796 Wednesday, May 23, 3:00 PM - 5:00 PM
Pharmacologic Treatment of Generalized Anxiety Disorder with Comorbid Depression and Pain Conditions
Wenyu Ye 
Eli Lilly and Company, Information Science, Lilly Corporate Center, Indianapolis, IN, 46285, 9000, Zhao, Baojin Zhu, Ralph W. Swindle

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe the classes of medications associated with treatment of generalized anxiety disorder (GAD) and describe the extent to which comorbid depression and pain is associated with these treatment patterns.

Summary:

Objective: To examine pharmacologic treatment patterns for individuals diagnosed with Generalized Anxiety Disorder (GAD) with comorbid depression and/or pain. 

Method: Data were from PharnMetrics Integrated Outcomes Database. Patients aged 18-64 were selected if they had a diagnosis of GAD (ICD9-CM: 300.02) between 1/2002 and 6/2004, preceded by 6 months without GAD diagnosis, and continuous enrollment during 6-month prior and 12-month after GAD diagnosis. Treatment regimens during the year after GAD diagnosis were examined for six-classes of psychotropics (anxiolytics, antidepressants, anticonvulsants, noradrenergic agents, atypical antipsychotics, and hypnotics). Comparisons were made for patients with GAD only versus those with comorbid depression and/or pain conditions. Poisson regressions controlling patient demographic and clinical characteristics (including provider specialty and other comorbidities), were used to evaluate the impact of depression and pain on GAD treatment patterns.

Results: Of 36,435 patients (mean age 41.5 years, 67% female) included in this analysis, 23.8% had GAD only, 15.5% GAD/depression, 32.8% GAD/pain, and 28.0% GAD/depression/pain. For patients with GAD/depression/pain, 48.5% received anxiolytics, 15.7% anticonvulsants, and 15.4% hypnotics. Patients reporting all three conditions received significantly more antidepressants (46.2% vs. 21.3%, p<0.001) and muscle relaxants (14.5% vs. 3.2%, p<0.001), and less anticonvulsants (44.8% vs. 71.5%, p<0.001). Regression results from Poisson model revealed that patients with GAD/depression/pain received 0.67 more classes of anxiolytics and 1.28 more number of psychotropic drugs (p<0.001 for both) when compared to GAD only. Similar results were also observed for patients with GAD/depression and for those with GAD/pain though to a lesser extent.

Conclusions: The findings suggest that there is a high comorbidity prevalence of depression and pain with GAD.1,2 Associated with this high comorbidity, complex patterns of polypharmacy are common in the treatment of GAD.

References:


NR797 Wednesday, May 23, 3:00 PM - 5:00 PM
A Case-Controlled Study of Atypical Antipsychotic Use in Adolescent Psychiatric Inpatients
David L. Pogge, Ph.D. Four Winds Hospital, Psychology, 800 Cross River Road, Katonah, NY, 10536, 9000, Kevin Young, B.A., Philip D. Harvey, Ph.D.

Educational Objectives:

At the close of this presentation, the attendee will have an increased understanding of:

1) The diagnoses of adolescent psychiatric inpatients who do and do not receive antipsychotics during their inpatient stay;
2) The pattern of symptoms in adolescent psychiatric inpatients who do and do not receive atypical antipsychotic medications;
3) The medications received by adolescent inpatients who do not receive atypical antipsychotic medications
The samples were compared on demographic factors, clinical comparisons and their diagnoses to a sample also suggest an urgent need to study the safety and efficacy of antipsychotics. Adolescents who were treated with atypical antipsychotic medications had diagnoses consistent with either adult indications who were treated with atypical antipsychotic medications during their hospitalization.

Methods: One hundred and fifty consenting consecutive admissions who were treated with atypical antipsychotic medications were compared to 150 consecutive cases who were admitted during the same time period and not treated with antipsychotics. The samples were compared on demographic factors, clinical diagnoses, clinical symptoms at admission, and other medications received during their inpatient stay.

Results: Sex and ethnicity did not differ significantly as a function of antipsychotic medication status. Significantly fewer of the cases with a diagnosis of major depression received antipsychotic medications and significantly more of the cases with diagnosis of bipolar and or conduct disorder were treated with antipsychotic medications. Clinical symptom differences and additional medications received were consistent with the diagnostic differences. Despite the fact that significantly fewer cases with major depression had been treated with antipsychotic medications, 47% of the cases who did receive antipsychotic medications in this study had a diagnosis of major depression.

Implications: While there are several differences between these inpatient data and previous studies of outpatient claims databases, the majority of adolescent inpatient cases treated with antipsychotic medications had diagnoses consistent with either adult indications or previous research with adolescent patients. These data also suggest an urgent need to study the safety and efficacy of atypical antipsychotic medications on aspects of depression in adolescents.

References:

Method: Atypical antipsychotic dosage data was obtained from 44,989 schizophrenia episodes and 100,144 bipolar treatment episodes over a five year period (2001-2005) from Commercial, Medicare and Medicaid databases (obtained via MarketScan®). Patients ≥18 years with an atypical antipsychotic claim during the study period who were continuously enrolled were included. Daily dose was measured as initial, maximum and mean daily dose. Dose trends were analyzed using autoregression, time-series models in SAS.

Results: Significant trends in mean dose were found for newer atypical antipsychotic agents in the schizophrenia and bipolar episodes assessed. Ziprasidone doses in schizophrenia episodes increased significantly in Commercial (98.6 to 130.1 mg/d, p < .05) and Medicaid (107.7 to 126.1 mg/d, p < .01), but not Medicare populations, with similar trends observed for bipolar episodes. Aripiprazole doses in schizophrenia episodes declined significantly in Medicaid (19.8 to 17.7 mg/d, p < .01) and Medicare (19.1 to 14.2 mg/d, p < .05), but not in Commercial populations (18.9 to 16.5 mg/d, p < .06), with similar trends observed for bipolar episodes. No dosage trends for older atypical antipsychotics (olanzapine, risperidone, and quetiapine) were observed.

Conclusions: Doses of ziprasidone in schizophrenia and bipolar disorder have steadily increased over the past 5 years, while aripiprazole doses have decreased. Ziprasidone doses appear to be approaching the optimally effective range established in fixed dose trials.

References:

NR799 Wednesday, May 23, 3:00 PM - 5:00 PM
Predictors of High Dose Ziprasidone Use in Routine Clinical Practice
Christopher Reist, M.D. University of California, Irvine, Department of Psychiatry and Human Behavior, 5901 East 7th St, Research Service (151), Long Beach, CA, 90822, 9000, Lisa M. Mucha, Ph.D., Leslie B. Montejano, B.A., Brian J. Cuffel, Ph.D., Hiep P. Nguyen, M.P.H., Antony D. Loebel, M.D.

Educational Objectives:
At the end of this presentation, the participant should be able to describe evidence for use of ziprasidone above 160 mg/d and patient characteristics predictive of such use.

Summary:
Introduction: Fixed dose clinical trials of ziprasidone indicate a dose-response relationship with maximal efficacy observed in the range of 120-160 mg/d when taken with food.[1-2] The present study estimates the proportion of ziprasidone treatment episodes that exceed 160 mg/d and the patient and clinician factors that predict high dose treatment.

Method: Data from the MarketScan® claims database yielded 79,713 ziprasidone treatment episodes between 2001 and 2005 that exceeded 160 mg/d for the initial or later prescription. Logistic regression estimated the likelihood of above 160 mg/d treatment as a function of age, sex, diagnosis, payer-type (Commercial, Medicaid, and Medicare) and prior psychotropic use.

Results: Results indicate that 19.9% of ziprasidone episodes started with a prescription above 160 mg/d, 13.7% of episodes received a prescription above 160 mg/d later in the treatment episode, and 4.4% of episodes averaged more than 160 mg/d for the entire episode. There was no trend in overall proportion of episodes over time above 160 mg/d although initial prescriptions
above this dose gradually increased over the study period. Younger, male, Medicaid patients with a diagnosis of schizophrenia or bipolar disorder were significantly more likely to receive doses above 160 mg/d (p < .05). In a separate analysis, psychiatrists were more likely to exceed 160 mg/d than PCPs/GPs’ internists, and “other” specialties (p < .01). Finally, use of other antidepressants in the 3-months prior to starting zonisamide increased the likelihood of initiating treatment above 160 mg/d.

Conclusions: Up to one third of zonisamide-treated schizophrenic or bipolar patients, particularly those involving younger, male patients on Medicaid, receive doses above 160 mg/d. Initial use above 160 mg/d appears to be increasing. In most cases these doses are not sustained over the entire episode.

References:

NR801 Wednesday, May 23, 3:00 PM - 5:00 PM
Pharmacotherapy of the Catatonic Syndrome: Literature Review and Analysis of Treatments used in 151 Episodes
Joseph W. Lee, M.D. Graylands Hospital & University of Western Australia, Department of Psychiatry, Brockway Road Mt. Claremont, Perth, 6010, 6021

Educational Objectives:
At the conclusion of the session, the participant should be able to demonstrate knowledge of the pathophysiology of the catatonic syndrome and the various medications used in its treatment.

Summary:
Objective: To review the pharmacotherapy of the catatonic syndrome

Methods: (a) A literature review of the pharmacotherapy and pathophysiology of catatonia was conducted. (b) The treatments used in 151 episodes of catatonia (134 acute, 17 chronic) were examined. The catatonic episodes were first treated with benzodiazepines. Failing benzodiazepines, they received other treatments for their catatonic symptoms.

Results: (a) The efficacy of benzodiazepines in acute catatonia is well documented, supported by case reports and open studies. A double-blind placebo-controlled study shows that benzodiazepines are ineffective for chronic catatonia. There have been case reports supporting the use of dopaminergic agents (L-dopa, bocarizine), glutamate NMDA antagonists (amantadine, memantine), dopamine D₂ antagonists (zolpidem), anticholinergics (benztropine, biperiden), antiepileptics (carbamazepine, phenytoin, valproate, topiramate), atypical antipsychotics (risperidone, olanzapine, quetiapine), amisulpride and aripiprazole), dantrolene (for malignant catatonia) and lithium for acute catatonia, and atypical antipsychotics (risperidone, olanzapine). Selegiline (MAO-B inhibitor), amantadine and memantine for chronic catatonia. The place of conventional antipsychotics is unclear. There is evidence suggesting that antipsychotics may exacerbate catatonia in some cases. GABA A hypoactivity, dopamine D₂ hypoactivity, glutamate NMDA hyperactivity, 5-HT₂ hyperactivity, and cholinergic hyperactivity have been proposed in the pathophysiology of catatonia.

(b) 90 (67%) of the acute episodes and only 1 (5.9%) of chronic catatonia showed full responses to benzodiazepines. In the remaining acute episodes, 17 responded to electroconvulsive therapy, 7 to lithium (with antipsychotics), and 3 (with neuroleptic-induced catatonia) to amantadine. In the chronic episodes, 3 showed good responses to amantadine, 2 selegeline, 3 lithium and 4 atypical antipsychotics (2 risperidone, 2 olanzapine); electroconvulsive therapy was used in 5 without significant responses.

Conclusions: Diverse medications have been used in the treatment of the catatonic syndrome with variable success, suggesting
that catatonia is a heterogeneous condition with subtypes different in treatment responses and pathophysiology.

References:

NR802 Wednesday, May 23, 3:00 PM - 5:00 PM
Effect of Metabolic Risk Status on Atypical Antipsychotic Treatment Choice
Elaine Morrato University of Colorado Health Science Center, Children’s Outcomes Research Center, 12477 East 19th Avenue, F443, Denver, CO, 80045, 9000, Brian Cuffel, John W. Newcomer, Ilise Lombardo, Siddhesh Kamat, John Barron

Educational Objectives:
At the conclusion of this presentation, the reader should be able to discuss (1) the effect of baseline laboratory values on treatment choice of atypical antipsychotic medications, and (2) the relationship of subsequent laboratory-based metabolic risk assessments to changes in choice of antipsychotic medications

Summary:
Introduction: Antipsychotic treatment guidelines recommend routine metabolic screening and consideration of patient metabolic status in choice of medication.\(^1\)\(^2\) This study evaluated the effect of patients’ metabolic status on clinician choice of antipsychotic and likelihood of medication changes associated with laboratory values indicating metabolic risk.

Methods: Laboratory assessments (1999-2004) were retrospectively examined in 1,162 adult patients in the 6-months prior to initiation of atypical antipsychotic (olanzapine, risperidone, quetiapine, ziprasidone, or aripiprazole) and 982 patients in the three months following initiation of treatment using a commercial US health plan database. LDL, HDL, total cholesterol (TC), triglycerides (TG), and fasting blood glucose (FBG) values were analyzed individually to assess the association with choice of antipsychotic.

Results: Increased baseline metabolic risk as measured by LDL \(\geq\)130mg/dL, HDL <40 mg/dL, TC \(\geq\)200 mg/dL, TG \(\geq\)200 mg/dL, and FBG \(\geq\)126 mg/dL was unrelated to choice of initial antipsychotic medication (p > 0.10) with comparable proportions of patients with increased risk found to be treated with each agent. Subsequent metabolic status of the patient did not change the overall likelihood of switching antipsychotic medications. However, patients with TG \(\geq\)200 mg/dL were twice as likely to switch to ziprasidone (OR = 2.27, p =0.022) than olanzapine, risperidone, or quetiapine after adjusting for age, gender, presence of schizophrenia and bipolar disorder in patients with a laboratory assessment prior to the switch. Similarly, a higher percentage of patients with TC \(\geq\)200 mg/dL switched to ziprasidone than olanzapine, risperidone, or quetiapine but this difference was not statistically significant (OR= 1.97, p=0.052).

Conclusions: In this pharmacoepidemiological sample, patient’s metabolic status appears to have little effect on initial choice of atypical antipsychotic and subsequent antipsychotic prescription switching decisions. These results suggest that psychiatric prescribing patterns are not commonly associated with recommended responses to available clinical laboratory assessments.\(^2\)

References:

NR803 Wednesday, May 23, 3:00 PM - 5:00 PM
Improving Antipsychotic Adherence in Schizophrenia: A Randomized Pilot Study of a Brief CBT Intervention

Peter J. Weiden, M.D. SUNY Downstate Medical Center, Psychiatry, 450 Clarkson Avenue, Box 1203, Brooklyn, NY, 11203, 9000, Page Burkholder, Nina R. Schoeler, Ph.D., Jeremy Weeden, Ph.D., Sarah Uzenoff, B.S., Douglas Turkington

Educational Objectives:
The participant will learn new approaches to psychosocial interventions to prevent medication nonadherence in schizophrenia.

Summary:
Background: Most medication adherence strategies assume that patients will agree with their given diagnoses. This assumption is not true for schizophrenia, and many patients may reject diagnostic-based psychoeducation programs out of hand. A Cognitive Behavior Therapy (CBT) uses a symptom-based rather than diagnosis-based approach and therefore may be an appropriate platform for an adherence intervention.

Methods: Recently relapsed and stabilized schizophrenia patients currently taking an oral antipsychotic were screened for a pilot study of a CBT-based adherence intervention (CBT-AI) in a public mental health outpatient setting. After baseline evaluations, patients were randomized to either treatment as usual (TAU), or to a 12-session course of CBT-AI given over the next 4 months. Major outcome measures were changes in adherence attitude (ROMI scale), and nonadherence behavior defined by time until first episode of nonadherence.

Results: Between 10/2004-3/2005, 41 patients were screened, 19 consented and 16 randomized to CBT-AI (n=9) or TAU (n=7). The mean number of CBT-AI sessions was 7 (SD 4.8) with 44% (n=4) completing all sessions. Therapists employed CBT principles based on audiotaped fidelity review.

Adherence attitude outcome: the CBT-AI group was significantly more likely to endorse reasons for both adherence and nonadherence on the ROMI, a finding that was consistent with the a priori hypothesis.

Adherence behavior outcome: At the 4 month assessment, 33% of CBT-AI subjects had discontinued antipsychotic medication vs. 83% of TAU (p = .07).

Discussion: This pilot study shows that CBT principles can be used to address medication adherence in schizophrenia patients at very high risk of imminent nonadherence. The changes in adherence attitudes as well as a trend in improved adherence behavior in the CBT-AI group compared to TAU support the hypothesis that a CBT platform can be adapted to improve medication adherence.

References:
NR804 Wednesday, May 23, 3:00 PM - 5:00 PM

Group Cognitive Behavior Therapy Versus Selective Serotonin Reuptake Inhibitors for OCD patients: An Open Trial

Juliana B. Diniz, M.D., Ph.D. University of São Paulo, Psychiatry Department, R Dr Ovidio Fores Campos 785, Sao Paulo, 05403-010, 3510, Cristina B. Silva, Ph.D., Roseli G. Shavitt, Marcia M. Motta, Psy.D., Andre A. Seixas, M.D., Raquel Chilvarquer, M.D., Eurípedes C. Miguel, Jr., M.D., Ph.D.

Educational Objectives:

To know the results of an open trial that compared the results of group cognitive behavior therapy and selective serotonin reuptake inhibitors and that found that both therapies are equally effective for OCD treatment in accordance with previous studies.

Summary:

Objective: to evaluate the clinical efficacy for OCD patients of group cognitive behavior therapy (GCBT) and selective serotonin reuptake inhibitors (SSRIs).

Methods: This project was approved by the ethics committee of the University of São Paulo Medical School. One hundred consecutive OCD outpatients that sought treatment in an OCD research program from a tertiary hospital were recruited after informed consent. A minimum initial YBOCS score of 16 was required. CGBT consisted of 12 sessions based on a semi-structured protocol with groups of 8 or 9 patients. SSRIs treatment consisted of four consultations (one every four weeks) with SSRI maximum recommended dosage aimed at week four. Fluoxetine was preferred over other SSRIs. Initial and 12 weeks’ evaluations included YBOCS score and CGI. The last evaluation was performed by a researcher blinded to the treatment received by the patient. Statistical analysis were performed on an intention to treat, last observation carried forward methodology. The percentage of YBOCS score reduction was calculated. Patients were classified as responders when YBOCS score reduction was > 35% and CGI scores of improvement were 1 (very much improved) or 2 (improved).

Results: Twenty-five patients were excluded (6 for missing the first consultation). Sixty percent (N=45) of the final sample had never received previous adequate treatment and 78% reached maximum recommended dosage. After treatment, the ISRS group had a mean YBOCS reduction of 23% (SD=28) and the GCBT of 26% (SD=27). The frequency of responders was 26% in the SSRI group and 30% in the GCBT. Drop out rate was 31% in the SSRI group and 16% in the GCBT. No differences between groups were statistically significant for a p value 0.05.

Conclusion: SSRIs and GCBT are both effective treatments for OCD patients. However, using strict response criteria only 30% present an adequate response after 12 weeks.

References:

NR805 Wednesday, May 23, 3:00 PM - 5:00 PM

Findings of a National Metabolic Screening Program for Psychiatric Outpatients in Public and Private Settings

Benjamin G. Druss, M.D. Emory University, Health Policy and Management, 1518 Clifton Road, NE, Atlanta, GA, 30322, 9000, Christoph U. Correll, M.D., Brian J. Cuffel, Ph.D., Manny Garcia, M.D., Suzanne Giordano, Ph.D., Cynthia O. Siu, Ph.D.

Educational Objectives:

At the end of this presentation the participant should be able to understand the high prevalence of weight and metabolic impairments in patients with severe mental illness and the need for increased attention to improving these health parameters.

Summary:

Introduction: A variety of barriers appear to limit the ability of clinicians to routinely obtain lipid and glucose assessments in patients with severe mental illness consistent with published treatment guidelines. To assist in addressing this problem, a national comprehensive metabolic screening program for patients in a variety of public and private mental health facilities, group practices, and behavioral health clinics, was funded by Pfizer beginning in 2005.

Method: A 1 day, voluntary metabolic health fair offered patients free metabolic screening and same-day feedback from a HIPAA-compliant biometrics testing third party.

Results: The first 10,111 patients and 299 sites were included in the analysis with the majority having a self-reported schizophrenia or bipolar disorder diagnosis (75%). Participant characteristics were: 57% female; 65% under 51 yrs; 55% Caucasian, 19% African American and 6% Hispanic. Screening results indicated substantial elevations in metabolic risks: 54% were obese (BMI >30), 81% were overweight/obese (BMI >25), 33.4% had elevated total cholesterol (TC >200mg/dl), 43% had elevated HDL (<40 mg/dl), 32.7% had elevated triglycerides (TG >200 mg/dl), 44.9% had an elevated TC/HDL ratio (>4.5), 33% had elevated glucose (>100 mg/dl) [fasting glucose, n=2671] and 30.7% were hypertensive (>140/90 mmHg). Up to 64% of patients with abnormal lipid values were untreated and up to 46% of those treated remained hyperlipidemic.

Conclusions: The prevalence of weight, lipid and glucose disturbances was substantial and frequently untreated, in this national health screening program. Further research is needed to assess the effects of screening in improving health outcomes for people with severe mental illness.

References:
between countries with different socioeconomic and cultural development levels.

**Summary:**

**Introduction:** The definition of a psychiatrist is frequently challenged by scientific, social and economic factors, reason why it is important to comprehend which skills and knowledge are required for the psychiatric practice in a given country and between different countries.

**Objective:** To compare results on 48 skills and 51 knowledge required for the professional practice between American and Brazilian psychiatrists.

**Method:** The American questionnaires from 1987 were translated, adapted and applied to Brazilian psychiatrists in 2000. The responses, transformed into percentages, were classified in decreasing order, based on results obtained in 1987 and compared from the qualitative and quantitative standpoint.

**Results:** Two invariance cores were identified, one of 27 skills and another of 45 knowledge. Items of psychosocial content seemed to be less valorized than items of the medical practice itself.

**Discussion:** American and Brazilian psychiatrists are quite similar in relation to their responses to questionnaires on skills and knowledge required for the psychiatric practice in both countries. This similarity is more evident for knowledge at the proportion of 45/51 and less evident for skills at the proportion of 27/48. This may be an actual trend even between countries with different socioeconomic and cultural development levels. The increasing unit on skills and knowledge required for the psychiatric practice is another evidence of the modern psychiatric practice globalization.

**Conclusions:** American and Brazilian psychiatrists tend to valorize items of the Medical Practice and Biological Psychiatry in their responses with more emphasis in Psychopharmacotherapy and less in Social Psychiatry and Psychotherapy.

**Keywords:** psychiatry; training; residency; continued medical education; skills; knowledge; questionnaires.

**References:**


**NR807**

Wednesday, May 23, 3:00 PM - 5:00 PM

**Cell Phones and Clinical Lectures: An Educational Convergence**

Seth M. Powsner, M.D. Yale University, Psychiatry & Emergency Medicine, 20 York Street, Room 2039 CB, New Haven, CT, 06510-3202, 9000

**Educational Objectives:**

After reviewing this presentation, viewers should be able to describe the basic steps for producing cell phone presentations, basic data requirements, and approximate costs. They should also recognize those types of educational presentations and material, which are suitable for personal cell phone viewing, and those which are not.

**Summary:**

**Purpose:** To develop and test a method for delivering educational video on cell phones.

**Methodology:** The most efficient strategy found was: digitally record a traditional lecture (one hour review of suicide prevention), transfer the recording to the cell phone (LG VX8300), note playback quality and recording data rate (megabytes/minute). Lecture slides were also converted to cell phone format; visual quality was noted.

Original recording was made from a web cam on a laptop computer as it was being used for lecture slide presentation (iSight, MacBook). Automatic compression during recording yielded MPEG-4 format, 320x240 pixels, 30 frames/second.

**Results:** Adequate renditions of both lecturer and slides were obtained, but only with further compression: Smooth video playback requires data reduction to match a phone's smaller display and bandwidth (3gp format, 176x144 pixels). Without additional compression, video playback is jerky. Data rates were 2.6 megabytes/minute for the laptop and 0.66 megabytes/minute for the cell phone version. This means that a one-gigabyte micro SD memory card ($50) can hold over 20 hours of video.

Computer slides using only large type fonts can be read on a cell phone screen (7-9 lines per slide, 24 characters across). Small type fonts, fine detail, and some background patterns do not play well.

Good audio playback did not require extra compression. The cell phone market demands quality MP3 music playback, far exceeding lecture requirements.

**Significance:** Didactic lectures can be presented on modern cell phones. A trainee on rotation can carry a whole set of lectures. And, the low video data rate for a phone could allow lectures to be downloaded as needed via WIFI or other Internet connections. Modern cell phones have become an effective way to provide education-on-demand for just-in-time-learning.

**References:**


**NR808**

Wednesday, May 23, 3:00 PM - 5:00 PM

**Teaching to Teach: The Evaluation of a Full Day Curriculum Aimed at Residents on Teaching Medical Students**

Kien T. Dang, F.R.C.P.C. St. Michael's Hospital, Psychiatry, 30 Bond St., 17 Floor CC, Toronto, ON, MSB 1W8, 1220, Andrea E. Waddell, M.D., Lana M. Benedek, M.D., Jodi S. Lotchy, F.R.C.P.C.

**Educational Objectives:**

1) Describe a full day curriculum for residents on teaching medical students
2) Examine/evaluate the perceptions residents have about their teaching skills after experiencing this full day curriculum.
3) Demonstrate which teaching set of teaching skills are most valued by residents.

**Summary:**

There is an expectation that residents be involved in the teaching of medical students during their residency. However, upon entrance into a residency program, junior residents will have had no formal instruction or training on how to teach effectively.

In a needs assessment of junior residents, we found that 73% of residents wanted to devote at least 7 hours of their educational curricula (approximately 5% of structured educational time) to improving teaching skills.

In January 2007 at the University of Toronto, we have implemented a full day compulsory curriculum/workshop aimed at psychiatric residents to teach skills, improve their comfort level, and promote the importance of good teaching skills when teaching medical students. This curriculum comprises a number of modules
including teaching medical students one-to-one, teaching medical students in small groups, providing appropriate feedback, and teaching the challenging student. Each of the modules is evaluated by the residents as to their effectiveness and importance. Our curriculum that will be outlined, and the analysis of the evaluations can help other educators in the design of their own resident teaching curriculum.

References:

NR809 Wednesday, May 23, 3:00 PM - 5:00 PM
Mindfulness Based Cognitive Therapy and Possible Cognitive and Biological Mechanisms
Guido BONDOLFI University of Geneva, Psychiatry, 16-18 Bd St Georges, GENEVA, 1225, 4419

Educational Objectives:
- Presentation of the results of a randomised controlled study aiming to examine the efficacy of MBCT as compared with treatment as usual (TAU) in the prevention of depressive relapse and to investigate MBCT effects on cognitive and on biological mechanisms (hypothalamic-pituitary-adrenal (HPA) system regulation).

Summary:
Mindfulness Based Cognitive Therapy (MBCT) is a psychological preventive approach whose efficacy has been demonstrated. Its theoretical foundation is derived from a model of cognitive vulnerability to depressive relapse: recovered depressed patients are vulnerable to relapse as transient mild dysphoric states may reactivate depressive cognitive-affective patterns analogous to those present during a depressive episode, these patterns tending to escalate to a clinical level of depression.

Objective: This randomised controlled study aims to examine the efficacy of MBCT as compared with treatment as usual (TAU) in the prevention of depressive relapse and to investigate MBCT effects on cognitive and on biological mechanisms (hypothalamic-pituitary-adrenal (HPA) system regulation).

Method: Sixty patients with recurrent depression (at least 3 prior episodes, 2 of which during the last 5 years), without pharmacological prophylactic treatment, were recruited and randomised, after a 12-week run-in phase to check stability of remission, into either MBCT+TAU or only TAU. MBCT consisted of intensive 8 weekly group sessions and 4 follow-up group sessions during the following year. Every three months during one year, patients were interviewed and they completed weekly and monthly self-evaluations.

Results: Based on preliminary findings collected to date (follow-up period ending in spring 07), it seems that MBCT halves the rate of relapses in the MBCT+TAU (N=4) versus the TAU group (N=8) and influences executive functioning, dysfunctional attitudes and ruminate behaviours but not the specificity of the autobiographical memories recall. Finally, MBCT does not seem to attenuate or normalize the salivary cortisol (HPA axis).

Conclusions: This study allows to confirm the efficacy of a group-based training program for the prevention of depressive relapse and to validate MBCT in a non-English language context using second generation instructors. Further data on the mechanisms of action of MBCT and its effect on relapse-related biological variables need though to be collected.

References:

NR810 Wednesday, May 23, 3:00 PM - 5:00 PM
Reliability and Validity of the Obsessive-Compulsive Inventory - OCI and Obsessive-Compulsive Inventory- Revised - OCI-R Versions: Preliminary Results
Fernanda P. de Souza UFRGS, Psychiatry, Avenida Neusa Goulart Brizola, 500/304, Porto Alegre, 90460-230, 3510, Elisabeth Meyer da Silva, Andrea Lilvin Raffin, Aristides Volpato Cordioli

Educational Objectives:
At the conclusion of this presentation, the participant should be able to examine the test-retest reliability, sensitivity, internal consistency and construct validity of the OCI and OCI-R Brazilian version.

Summary:
Introduction: Obsessive-Compulsive Inventory (OCI) and Obsessive-Compulsive Inventory- Revised (OCI-R) are a self-report instruments designed to assesses distress associated with common obsessive-compulsive disorder (OCD) symptoms.

Objectives: The present study examined the test-retest reliability, sensitivity, internal consistency and construct validity of the OCI and OCI-R Brazilian version using a clinical and non-clinical sample.

Method: After translation, back translation and cultural adaptation the scales were applied in 33 patients with OCD, 66 patients with other anxiety disorders, and 97 nonanxious individuals, in order to assess convergent and divergent validity, reliability and construct validity. OCD patients did a Group Cognitive Behavioral Therapy. (GCBT) The applicability and sensitivity of the instruments to measure changes was evaluate and compared with the Y-BOCS and CGI.

Results: Preliminary results suggest that the OCI-R had no significant differences in the test-retest reliability and presented strong association with the Y-BOCS. When the focus was the sensitivity to change both OCI and OCI-R showed reduction of the symptoms of OCD after the GCBT and agreement with Y-BOCS and CGI.

Conclusions: The OCI and OCI-R Brazilian version differentiated well between individuals with and without anxious. The instruments evidenced good convergent validity, and performed well in discriminating OCD from other anxiety disorders.

References:

NR811 Wednesday, May 23, 3:00 PM - 5:00 PM
Awareness of Metabolic Syndrome in Patients with Bipolar Disorder: A Comparison of US and European Psychiatrists
Trisha Suppes, M.D., Ph.D. University of Texas Southwestern, Psychiatry, 5323 Harry Hines Boulevard, Dallas, TX, 75390-
the US than in the EU (94% versus 72%). They also reported that EU psychiatrists monitored metabolic parameters significantly more often than US psychiatrists (48% versus 40%, \( p < .05 \)) but had similar proportions who monitored BMI, waist circumference, triglycerides, and low HDL. Patients in US and EU countries were more likely to stop/switch treatments “often” or “very often” (25% versus 8% for EU, \( p < .05 \)). Significantly more US than EU psychiatrists reported being extremely or very concerned about weight gain as an AE (78% versus 51%, \( p < .05 \)). In each country olanzapine was the BD medication most often associated with metabolic AEs. US psychiatrists were more likely to monitor metabolic health and adjust treatment if abnormalities emerge, but practice habits differ across EU countries.

References:
of Atherosclerosis 2) Differences of the risk of Atherosclerosis between Coping strategies for Stress.

Methods: Cardiologist has examined 24 female patients (50.5±10.58 years) who visited Hwa-byung Clinic voluntarily for treatment, using echocardiography, carotid internal media thickness measurement, electrocardiogram and laboratory test. Thereafter, all patients have been undergone psychiatric interview by psychiatrist for evaluating psychiatric symptoms and family background.

All subjects completed the Korean version of the ways of coping checklists.

Results: In terms of psychiatric diagnosis, 85% of patients have met the diagnostic criteria of undifferentiated somatoform disorder. 67% of patients suffered from familial conflicts and difficulties to express their anger.

All subjects have shown negative findings in cardiologic evaluation. However, in partial correlation, wishful thinking was inversely related to ankle brachial pressure index (ABPI) (left: r=0.510, right: r=0.672, p<0.05). Moreover, in Multiple regression analysis, wishful thinking could amount 53% of ABPI-Right and 42% of ABPI-Left significantly after controlling age and BMI.

Conclusion: Hwa-byung would not increase the risk of definite atherosclerosis. But, more usage of passive coping strategies was significantly related to risky factors of atherosclerosis. This result suggested the inefficient coping strategies might trigger the actual physical problem as well as psychological difficulties.

References:

NR814 Wednesday, May 23, 3:00 PM - 5:00 PM
Plasma Brain-Derived Neurotrophic Factor Levels in Patients with Somatization Disorder before and after Pharmacotherapy
Jong-Chul Yang, M.D. Chonnam National University Hospital, Psychiatry, 8 Hak-dong, Dong-gu, Gwangju, 501-757, 5800, Yong-Ku Kim, M.D., Moo-Suk Lee, M.D., Jin-Sang Yoon, M.D., Il-Seon Shin, M.D., Jae-Min Kim, M.D., Sung-Jong Eun, B.A.

Educational Objectives:
1. At the conclusion of the presentation, the participant should be able to recognize that alteration of brain-derived neurotrophic factor (BDNF) may be associated with the development and pathophysiology of somatization disorder.

Summary:
Objective: Brain-derived neurotrophic factor (BDNF) is known to be involved in the plasticity of neurons and pathophysiology of several psychiatric illnesses. The purpose of this study was to determine whether there is an abnormality of plasma BDNF levels in patients with somatization disorder, and the alteration after pharmacotherapy.

Methods: The 27 patients with somatization disorder (mean age: 46.33±9.73 years, 12 males, 15 females) who fulfilled the DSM-IV criteria for somatization disorder and 27 healthy controls (mean age: 46.81±6.81 years, 12 males, 15 females) were enrolled in the study. The clinical assessment of the somatization disorder was measured by Korean version of Wahler physical symptom inventory (K-WPSI), Beck Depression Inventory (BDI), Hamilton Depression Rating Scale (HAMD), Hamilton Anxiety Rating Scale (HAM-A). BDNF was assayed using the DuoSet ELISA Development System (R&D Systems. DY248). The difference in the plasma BDNF levels between patients and healthy controls was analyzed using non-parametric Mann-Whitney test by the SPSS 12.0 (p<0.05). Moreover, we assessed the alteration of plasma BDNF levels after treatment using Wilcoxon Signed Ranks test. 22 among 27 patients with somatization disorder took the antidepressant medication, mainly selective serotonin reuptake inhibitors, for 9 to 16 weeks. And the correlations between the BDNF level and the clinical assessment scale scores were examined using Spearman correlation coefficient.

Results: The mean plasma BDNF levels of 27 patients with somatization disorder were significantly lower compared with those of controls (83.61±89.97 pg/ml vs. 771.36±562.14 pg/ml, Z=-5.735, p<0.001). In 22 patients after the antidepressant treatment, the plasma BDNF levels were significantly increased (118.13±91.45 pg/ml vs. 72.92±88.21 pg/ml, Z=-2.029, p=0.042). However, clinical assessment scales did not reveal any significant correlations with BDNF levels.

Conclusions: These results suggest that BDNF may play a role in the pathophysiology of somatization disorder.

References:

NR815 Wednesday, May 23, 3:00 PM - 5:00 PM
Integrative Multidisciplinary Treatment for Borderline Personality Disorder and Other Treatment-Refractory Conditions
Catherine Romero, Ph.D. Baylor College of Medicine, Dept. of Psychiatry and Behavioral Sciences, One Baylor Plaza, Houston, TX, 77030, 9000, Elizabeth F. Weinberg, M.D.

Educational Objectives:
1. Describe Integrative Multidisciplinary Treatment (IMT) and the principles that underlie the treatment.
2. Explain how IMT has been initiated in a public sector clinic.
3. Identify who is appropriate for IMT.
4. Discuss the treatment outcomes associated with IMT.

Summary:
Introduction: Borderline personality disorder (BPD) is associated with high rates of healthcare utilization and suicide (Linehan & Heard, 1999; Stone, 1990). Although well-validated treatment models exist (e.g., DBT, Linehan, 1993; MBT, Bateman & Fonagy, 1999), pragmatic issues may prevent clinicians in public sector settings from using these longer-term models. We hypothesized that short-term integrative, multidisciplinary treatment (IMT), incorporating common factors across established treatments, would be easily integrated into a publicly-funded psychiatry clinic. We further hypothesized that patients receiving IMT would have decreased symptoms and healthcare utilization, and increased quality of life.

Methods: The study employed a naturalistic, pre-post design. The 10-12 week IMT program comprises 13 hours per week of groups, individual therapy, and medication management. The program is staffed by a multidisciplinary team (psychiatry, psychology, social work, etc.) within a publicly-funded outpatient clinic. Of 133 patients admitted, 84 completed pre- and post-treatment measures including the Brief Psychiatric Rating Scale, Hamilton De-
pression Rating Scale, Beck Scale for Suicide Ideation, and measures of healthcare utilization and quality of life.

Results: Prior to IMT, 33% of treatment-completers had received outpatient treatment for ≥ 1 year; 68% had at least one hospitalization and 38% had two or more. 41% of the sample had BPD. Despite their previous treatment-refractory status, by the end of IMT, treatment-completers improved significantly (p < .05) on measures of general psychiatric disturbance, depression, suicidality, frequency of hospitalizations and emergency room visits, and quality of life outcomes.

Conclusion: IMT was easily integrated into a publicly-funded clinic and was acceptable to clinicians of varying theoretical orientations. Upon completing treatment, patients improved significantly in multiple areas, including symptoms, healthcare utilization, and quality of life. IMT appears to hold promise as a shorter treatment for BPD and other treatment-refractory conditions.

References:

NR816 Wednesday, May 23, 3:00 PM - 5:00 PM
Evaluation of the Results of a Protocol to Treat Traumatized Women With Severe Depression in a Rural General Hospital in Chile
Verónica E. Vitriol Hospital Curico, Mental Health Service, vvvitriol@hospitalcurico.cl, verovitriol@gmail.com, curico, oo, 3370, Ramon N. Florenzano, Soledad Ballesteros, Ignacio A. Iturria, Ana Calderon, Andrea Vacarezza, Kristina Weil

Educational Objectives:
At the conclusion of this presentation the participant should be able to demonstrate that a brief structured protocol is more effective that treatment as usual in women with diagnosis of severe depression and antecedents of childhood politrauma. However, a significant score remains symptomatic and dysfunctional. We conclude there is a need to develop longer term follow-up of patients and develop lengthier interventions for this population.

Summary:
This study aims to determine the effectiveness of a protocol to treat women with severe depression and antecedents of childhood politrauma, compared to treatment as usual. The protocol is designed to treat during three months, linking the chief complaint with the traumatic episode.

87 women diagnosed with severe depression according ICD 10, with antecedents of childhood trauma (69% sexual abuse), consulting for the first time at the Psychiatry Unit Curicó Hospital, were randomly assigned to the experimental protocol (TP, n=44), and treatment as usual ( TC n = 43). Evaluated at intake, after one and three months, with Hamilton Depression Scale, Lambert's OQ 45.2 in its Chilean adaptation, and a scale to score presence of Post Traumatic Stress Disorder (TOP 8).

We present the three months pre-post evaluation. The TP group decreased in the HAM-D score from 34.46 to 20.92 (t =9.15 p < 0.001); the TOP 8 decreases from 18.11 to 13.81 (t = 3.96 p < 0.001); the OQ45 global score decreased from 113.1 to 91.3 (t = 14.4 p< 0.001). In the TC group, the HAM-D scored decreased from 35.3 to 27.9 (t = 4.62; p < 0.001); the TOP 8 scores decrease from 20.7 a 15.94 (t =3.613; p =0.001) ;the OQ45 global score decreases from 118 a 109.9 (2.82 p<0.04). There were statistically significant differences in the mean score changes between both group in the HAM-D (F=7,613 y p=0.007); OQ45.2 global score (F=4.950 y p=0.029). According to Jacobson and Truax Clinical significance criteria, in the TP group 25.6 % recovered and 30.77% improved. In the TC group 15 % recovered and 22.8% improved.

Conclusiones: This study demonstrates that a structured protocol is more effective that treatment as usual in women with diagnosis of severe depression and antecedents of childhood politrauma. However, a significant score remains symptomatic and dysfunctional.

References:

NR817 Wednesday, May 23, 3:00 PM - 5:00 PM
Is Pain Related to Under-diagnosis of Depression Among Primary Care Patients?
Kathryn Magruder Medical University of South Carolina, Psychiatry and Behavioral Sciences, 67 President Street, Post Office 250861, Charleston, SC, 29425, 9000, Derik Yeager, Rebecca G. Knapp, Rebecca Robinson

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the relationship between self-reported pain and the under-diagnosis of depression in primary care patients as measured by comparing depression detection through medical records and a structured clinical interview using the MINI. The association between the under-diagnosis and appropriate diagnosis of depression with self-reported pain, pain-related diagnoses, and patient demographic factors will also be addressed.

Summary:
Pain is a well known correlate of depression in medical patients. We examined if pain is also a factor in physicians' recognition of depression in primary care.

Methods: Subjects were 816 randomly selected primary care patients drawn from four VA hospitals in the Southeast who were administered a structured psychiatric assessment (Mini International Neuropsychiatric Interview - MINI) and the SF-36. MDD and dysthymia were assessed using the MINI; all medical and psychiatric ICD9 diagnoses (including MDD, depression NOS, and dysthymia) were taken from electronic medical records for a 24-month period (+/-12 months from the clinic interview); self-rated pain was assessed with the SF-36 bodily pain subscale. From those who were MINI positive for MDD or dysthymia (n=191), patients were classified into 2 categories based on congruence with ICD9 chart diagnoses: correctly diagnosed (n=100) (MINI positive, ICD9 positive) and under-diagnosed (n=91) (MINI positive, ICD9 negative). Analyses compared patients who were under-diagnosed with correctly diagnosed patients.

Results: Logistic regression analyses showed that after adjustment for age, race, and gender, higher self-reported pain was significantly related to correct recognition of depression (p=.008). Males (OR=2.6; CI's 1.2-5.7) and minorities (OR=2.2; CI's 1.1-4.3) were more likely to be under-diagnosed. Patients with >1 diagnoses related to chest pain (OR=3.0, 1.3-7.0) or neurological pain (OR=3.5, 1.1-11.6) were significantly more likely to be correctly diagnosed for depression; however, these relationships became nonsignificant in models where the presence of self-reported bodily pain was also included. Self-reported bodily pain remained significant in these expanded models. Back, muscle, and other
pain-related diagnoses were not significantly related to depression recognition.

**Conclusion:** Patients with pain were more apt to be correctly diagnosed as depressed. Self-reported pain was a more robust predictor than pain-related diagnoses. Providers should carefully evaluate patients for depression - especially males, minorities, and those who do not present with pain.

**References:**
2. Karlsson H, Joukamaa M, Lehtinen V. Differences between patients with identified and not identified psychiatric disorders in primary care.

**NR818 Wednesday, May 23, 3:00 PM - 5:00 PM**
Pharmacologic Management with Methylphenidate in Adults with Attention-Deficit/Hyperactivity Disorder: An Analysis of Safety, Efficacy, and Dosing
Timothy E. Wilens Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA, 02114, 9000, Anthony L. Rostain, M.D.

**Educational Objectives:**
Clinical study data have demonstrated the safety and efficacy of stimulant medications in the treatment of adults with ADHD, but treatment guidelines in adults are still lacking. At the conclusion of this presentation, the participant should be able to recognize that clinical studies in adults with ADHD demonstrate that both immediate-release and extended-release methylphenidate formulations are safe and effective in the management of ADHD in adults when used at equipotent daily doses to those used in pediatric studies in ADHD (~1.0 mg/kg/d).

**Summary:**

**Objective:** To evaluate methylphenidate (MPH) safety, efficacy, and dosing patterns in published clinical studies on the management of attention-deficit/hyperactivity disorder (ADHD) in adults to better understand optimal MPH dosing.

**Methods:** Available published scientific data regarding MPH for the management of adult ADHD were reviewed. The literature search included double-blind and open-label studies evaluating the management of ADHD in adults with immediate-release MPH and/or extended-release MPH.

**Results:** Nineteen published studies of MPH were identified in the scientific literature from 1976 through 2006. The average number of patients in the studies was 556 (range: 8-149), and the average age of the adults in the studies was 34.4 years (range: 18-65 years). Fifteen of the studies were double-blind, and four were open-label. The average length of the studies was 6 weeks (range: 2 weeks-9 months). Diagnosis of ADHD in these studies was not well defined, and there was a high rate of comorbidity seen in the adult patient population. The average dose of MPH was 0.8 mg/kg/d (range: 30 mg/d-100 mg/d). A dose-response relationship was demonstrated in some studies. The average treatment response was 62.5%, and the range of response was 25% to 90%. Overall, MPH treatment was well tolerated, with side effects reported in approximately 30% of patients treated.

**Conclusions:** Clinical studies demonstrate that when therapeutic doses of MPH are used in adults with ADHD, a robust clinical response is seen that is similar to that reported in clinical studies of children with the disorder.

**References:**
Adult ADHD and Stimulant Dosing in the Community Setting

Mark Olfson, M.D., M.P.H. New York State Psychiatric Institute, Department of Psychiatry, College of Physicians and Surgeons of Columbia Uni, 1051 Riverside Drive, New York, NY, 10032, 9000, Steven C. Marcus, Ph.D., Huabin F. Zhang, M.D., M.P.H., George J. Wan, Ph.D.

Educational Objectives:

- At the conclusion of this presentation, the participant will recognize that adults treated for ADHD in a community setting generally receive stimulant doses that are considerably lower than doses associated with optimal efficacy in adult clinical trials, and that stimulant dosing appears to be only modestly related to patient demographic and clinical characteristics.

Summary:

Objective: The purpose of this analysis was to be able to describe initial and maximum dosing patterns of commonly prescribed stimulants in the community treatment of adults with adult attention-deficit/hyperactivity disorder (ADHD).

Methods: Claims data from more than 75 US managed care plans (2000-2004) were analyzed focusing on stimulant treatment episodes of patients 18 to 64 years of age treated for ADHD who received OROS® methylphenidate (OROS MPH), mixed amphetamine salts extended-release (MAS XR), immediate-release methylphenidate (IR MPH), or immediate-release mixed amphetamine salts (IR MAS). A treatment episode was defined as the period of consecutive stimulant prescriptions with a gap of ≤ 30 days in the stimulant supply. For each stimulant group, mean initial and maximum daily stimulant doses are presented overall and stratified by patient age group, gender, physician specialty, ADHD subtype, and presence of other treated mental disorders. Multivariate models are also presented.

Results: Mean initial dose was 31.2 mg/day for OROS MPH, 26.8 mg/day for IR MPH, 20.3 mg/day for MAS XR, and 23.5 mg/day for IR MAS, and mean maximal dose was 39.9 mg/day for OROS MPH, 32.1 mg/day for IR MPH, 26.1 mg/day for MAS XR, and 30.0 mg/day for IR MAS. For each stimulant group, initial dosing was statistically significantly higher, although only modestly higher for male compared with female patients and for patients treated by psychiatrists compared with non-psychiatrists, except in the IR MPH group. Similar trends were observed for maximum dose. For all but the IR MPH group, older patient age was associated with higher maximum dose.

Conclusions: Stimulant dosing in the community treatment of adult ADHD falls well below doses associated with optimal efficacy in adult clinical trials. Patient demographic and clinical characteristics are only modestly related to stimulant dosing.

References:


Mindfulness-Based Cognitive Therapy for Treatment Resistant Depression

Stuart James Eisendrath, M.D. University of California San Francisco, Psychiatry, 401 Parnassus Avenue, San Francisco, CA, 94143-0984, 9000, Maura McLane, M.S., Kevin Delucchi, Ph.D., Paul Fenimore, M.A., Robin L. Blter, M.D., Martina Smit, M.D., Ellen Haller, M.D.

Educational Objectives:

- At the conclusion of this presentation, the participant should learn: 1) what Mindfulness-Based Cognitive Therapy (MBCT) entails, 2) that MBCT appears effective in the treatment of major depression that has failed to remit with antidepressant treatment, 3) that it is a feasible treatment intervention in this population, and 4) that further controlled trials are needed to more fully evaluate the efficacy of MBCT, particularly in treatment resistant patients.

Comparison of Bifrontal and Unilateral Ultra-Brief Pulse Electroconvulsive Therapy for Depression

Pascal Sienaert, M.D. University Psychiatric Center - Catholic University Leuven, ECT Dept & Dept Mood Disorders, Leuvensesteenweg 517, Kortenberg, 3070, 4231, Kristof vansteelandt, Ph.D., Koen Demyttenaere, Ph.D., Joseph Peuskens

Educational Objectives:

- At the conclusion of this presentation the participant should be aware of the fact that ultra-brief ECT is an affective and safe treatment for depressive disorder, and that both bifrontal and unilateral ECT produce high rates of remission without provoking immediate cognitive side-effects.

Summary:

Objective: The clinical and cognitive effects of bifrontal ultra-brief pulse (0.3 msec) electroconvulsive therapy (UBPECT) and right unilateral UBPECT were compared, in the treatment of patients with a depressive episode.

Method: Sixty four patients with a depressive episode that was highly medication refractory, and with a high degree of comorbidity were treated with a course of bifrontal UBPECT at 1.5 times seizure threshold (ST) or unilateral UBPECT at 6 times ST by random assignment. The Hamilton Rating Scale for Depression (HDRS) and the standardized Mini-Mental State (MMSE) were administered at baseline and repeated during and after the course of treatment, by a blinded rater.

Results: Of the 64 patients (22 male, 42 female) that were included in this ongoing study, 32 (50%) were treated with bifrontal ECT, 32 (50%) with unilateral ECT. At the end of the treatment course, 78.1% of the bifrontal group and 78.1% of the unilateral group responded (≥ 50% decrease HDRS-scores). 59.38% (N= 19) of the bifrontal group and 71.88% (N=23) of the unilateral group achieved remission (HDRS-score <=10). There were no significant differences between the patients given bifrontal ECT and those given unilateral ECT. MMSE scores registered one week after the final ECT treatment (27.67 in the bifrontal group, 27.81 in the unilateral group) were higher than baseline MMSE scores (26.72 in the bifrontal group, 27.17 in the unilateral group), and did not differ significantly between the two treatment groups.

Conclusions: Bifrontal UBPECT at 1.5 times ST was as efficacious as unilateral UBPECT at 6 times ST and neither of these treatment techniques resulted in cognitive impairment, as measured with the MMSE.

References:


Summary:

Purpose: Mindfulness-Based Cognitive Therapy (MBCT) for depression has been shown to prevent depression relapse in remitted individuals. The present study extends MBCT to treat individuals with current treatment resistant depression (TRD). Treatment resistance, defined here as an incomplete response to > 1 antidepressant trial of adequate duration, is suffered by a majority of patients.

Methods: This study is a nonrandomized cohort comparison of 2 groups of subjects with TRD. One group consisted of 53 TRD patients who received MBCT in a group format based on the manual developed by Segal, Williams, and Teasdale as an adjunct to treatment as usual (TAU). Their Beck Depression Inventory-II (BDI-II) scores were compared at the beginning and end of the 8 week MBCT course. The other group included 29 TRD patients who received TAU in a Depression Center Clinic where BDI-II scores are routinely obtained every 12 weeks. All had incomplete responses at week 12. Week 24 BDI-II scores were compared to week 12 scores.

Results: Within group comparisons indicated a significant (p < 0.01) decrease in BDI-II scores in the MBCT group from a mean of 24 to 12. Reduced depressive symptoms were associated with increased mindfulness skills as measured by the Freiburg Mindfulness Inventory. The TAU group had a nonsignificant BDI-II decrease from 24 to 22, despite a longer interval of treatment. The between group comparison indicated a significant difference between the MBCT and TAU groups of p < 0.001.

Conclusions: When used in TRD patients, MBCT appears effective in reducing depression levels compared to TAU. MBCT appears to offer a way for individuals to learn skills that allow them to “decenter” themselves from a depressive stream of cognitions with significant decreases in symptoms. This study needs to be expanded to a randomized clinical trial to more fully evaluate the efficacy of MBCT.

References:


of these classes, as were the expenditures (p < .001 for all comparisons). Total 12-month expenditures for prescription medications among fibromyalgia patients with use were $3,034.15 compared to $1,177.82 among controls with use (p < .001).

Conclusions: Higher utilization of pharmacologic interventions for fibromyalgia and its comorbidities results in significantly greater direct medical care expenditures among these patients and suggests the need for new interventions.

NR824 Wednesday, May 23, 3:00 PM - 5:00 PM
Trauma and PTSD Symptom Severity in Mandated COD Patients, Voluntary COD Patients, and Non-Substance Abusing Psychiatric Patients
Sonya B. Norman, Ph.D. UCSD, Psychiatry, 140 Arbor Drive, San Diego, CA, 92130, 9000, Richelle McGee, Chad Bousman, M.P.H., Joseph Obeji, Ph.D., Patricia Judd, Elizabeth Twamley, Ph.D., Robert Heaton, Ph.D., Ian Everall, M.D.

Educational Objectives:
At the conclusion of this presentation, participants will have learned about 1) the high prevalence of psychological trauma and PTSD symptoms in patients court-mandated to substance use treatment, 2) the validity of prison deferment programs for substance abusers with psychiatric comorbidity, and 3) the importance of including trauma focused treatments in clinical programs with mandated patients.

Summary:
A growing number of patients with co-occurring substance use disorders (SUD) and other mental disorders (COD) are mandated to treatment through prison deferment programs. However, most treatment programs have been developed for voluntary patients. Understanding differences between voluntary and court mandated patients with COD and non-substance abusing psychiatric patients has important clinical and public policy implications. Psychological trauma history and PTSD are frequently present in COD patients. Voluntary COD patients with PTSD tend to have greater symptom severity than psychiatric patients without SUD. Little is known about trauma and PTSD in mandated patients. We compared rates of trauma exposure and PTSD symptom severity between court-mandated patients (through California Prop-36, n=28) patients presenting voluntarily to COD treatment (n=14), and psychiatric patients without a SUD (n=23) in an outpatient psychiatric clinic.

Participants completed the Posttraumatic Stress Diagnostic Scale and a demographic questionnaire prior to entering treatment. Data collection is ongoing. Average age of participants was 41 (range = 18-63), 43% were female, 72% Caucasian, 15% African American, and 11% Hispanic. All patients were below the poverty line. The groups did not differ significantly on demographics.

Voluntary (100%) and court mandated COD patients (99%) were more likely to have experienced psychological trauma than patients without a SUD (67%). Among patients with trauma histories, mandated patients (m=2.17, s.d.=1.26) reported greater PTSD symptom severity than patients without SUD (m=1.29, s.d.=1.20; F(2,26)=3.44, p<.05). Voluntary COD patients (m=2.23, s.d.=.92) did not differ significantly from the other two groups.

Mandated COD patients report psychological trauma and resulting psychiatric distress at similar levels to voluntary COD patients and greater levels than psychiatric patients without SUD. These findings highlight the severity of illness in mandated patients, the validity of court ordered treatment and the importance of inclusion of trauma focused treatments in clinical programs with mandated patients.

References:

NR825 Wednesday, May 23, 3:00 PM - 5:00 PM
Characteristics of Repeatedly Aggressive Incidents In An Acute Psychiatric Unit in Taiwan
Cheng-Chen Chang, M.D. Changhua Christian Hospital, Department of Psychiatry, No.135 Nanhsiao Street , Changhua, Changhua city, 500, 5830, Shu-Kuei Chang

Educational Objectives:
Violence and aggression among patients in psychiatric units poses threats to ward staff, patients and families. The evaluation of a patient's potential for aggression presents an important issue in psychiatric care. Although studies have found a small proportion of inpatients are responsible for 50-70% of inpatient violence, the topic of repeated inpatient aggression was often overlooked. At UCSD, Psychiatry, 140 Arbor Drive, San Diego, CA, 92130, 9000, Richelle McGee, Chad Bousman, M.P.H., Joseph Obeji, Ph.D., Patricia Judd, Elizabeth Twamley, Ph.D., Robert Heaton, Ph.D., Ian Everall, M.D.

Summar...

**NR826 Wednesday, May 23, 3:00 PM - 5:00 PM**

**A Novel Method for the Assessment of Stress Levels in Disaster Victims**

Bhupendra K. Gupta, M.D. Private Practice, N/A, 133 Chenoweth Lane, Louisville, KY, 40207, 9000, Neil K. Gupta, David B. Moore, Ph.D.

**Educational Objectives:**

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

1. Recognize the potential to measure the stress levels of different populations facing Post-traumatic stress disorder (PTSD) and other symptoms of distress using GSR.
2. Demonstrate the usefulness of GSR in Gulf veterans, Olympic athletes, and other populations who are prone to high stress and anxiety levels, and other groups, without the intervention of any medications.
3. Understand the applicability of GSR in the diagnosis and treatment of stress-related disorders, including Post-Traumatic Stress Disorder.
4. Understand mind-body medicine in disaster victim populations.

**Summary:**

Hurricane Katrina was one of the worst natural disasters in recent times to strike the United States. The goal of these studies is to test the hypothesis that exposure to extreme environmental stressors can alter the galvanic skin response (GSR) through biofeedback. The GSR meter measures the electrical conductance in the skin. It measures changes in the sweat glands and enables one to assess stress levels and emotional arousal. Subjects were comprised of three groups: Hurricane Katrina victims, homeless population, and a control population. GSR measurements were recorded for three minute duration before treatment and during relaxation music, which was followed by two post-treatment phases of three minutes each. The Katrina victims showed a statistically significant increased GSR activity compared to the controls. Both the Katrina and the homeless groups showed a higher GSR at the beginning of music than the controls. The results showed a significantly higher GSR during the music period for the homeless group compared to the Katrina and control group. Toward the end of the music, the Katrina and the control group showed a decrease in GSR, while the homeless group showed an increase. In the post treatment phase, the GSR activity of Katrina victims returned to baseline levels, while the homeless group showed an increase in the first three minutes followed by a return to baseline in the last three minutes. The control group resumed baseline GSR rather immediately than the other two groups. These studies suggest the potential to measure the stress levels of different populations facing Post-traumatic stress disorder (PTSD) and other symptoms of distress using GSR. It can be a useful tool for the Gulf veterans, Olympic athletes who are prone to high stress and anxiety levels, and other groups, without the intervention of any medications.

**References:**


**NR827 Wednesday, May 23, 3:00 PM - 5:00 PM**

**Peritraumatic Tonic Immobility: A Predictor of Poor Response to Treatment of PTSD In Victims of Urban Violence**

Adriana Fiszman, M.D. Universidade Federal do Rio de Janeiro (UFRJ), Institute of Psychiatry (IPUEB), Avenida das Americas 3333 sala 1018, Barra da Tijuca, Rio de Janeiro - RJ, 22531-003, Carla Marques Portella, M.D., Mauro V. Mendlovicz, M.D., Ellane Volchan, M.D., Wanderson F. Souza, Ph.D., Jair J. Mari, M.D., Ivan Figueira, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to recognize that peritraumatic tonic immobility (PTI) is prevalent in PTSD and a potential predictor of a poor prognosis. PTI in humans comprises conversion symptoms: paralysis/freezeing and analgesia/anesthesia. Although conversion and dissociation are related, peritraumatic dissociation is the most studied predictor for PTSD whereas PTI remains understudied. PTI has only been reported in sexual abused women; our study showed its occurrence also in men with PTSD during non-sexual violence. Moreover, a significant relationship was found between PTI and poor response to the standard pharmacological treatment for PTSD.

**Summary:**

**Background:** Tonic immobility is the last defense against predation in animals, characterized by paralysis with rigidity and analgesia. Two studies in humans reported tonic immobility during the trauma (peritraumatic) in 37% and 52% of women victims of sexual abuse.

**Objectives:** We evaluated the prevalence of peritraumatic tonic immobility (PTI) in patients with Post-Traumatic Stress Disorder (PTSD) and its correlation with response to PTSD treatment.

**Patients and Methods:** Victims of urban violence were diagnosed with PTSD (n = 23, 14 males, 9 females) using the Structured Clinical Interview for DSM-IV (SCID-IV). Patients underwent a structured pharmacological treatment according to the recommended guidelines for PTSD. The Post-Traumatic Stress Disorder Checklist - Civilian Version (PCL-C) and the Clinical Global Impressions (CGI) Severity scores were applied at baseline and endpoint. PTI was probed using the Tonic Immobility Scale (TIS). Baseline and endpoint PCL-C and CGI scores data were compared among patients with and without PTI.

**Results:** PTI was reported by 43% of the sample, with a higher prevalence in men. Patients without PTI responded better to treatment: their PCL-C and CGI scores dropped significantly more in comparison to patients with PTI (p<.05 and p<.001, respectively). Moreover, at the endpoint, only 1 out of 10 patients with PTI presented their PCL-C scores below the cut-off for PTSD, as compared to 7 out of 13 patients without PTI.

**Conclusion:** Our study has expanded the scope of the two previous investigations on tonic immobility in victims of sexual abuse by showing its occurrence also in men and during traumatic events involving non-sexual violence. In addition, our finding of a significant relationship between PTI and poor response to the standard pharmacological treatment for PTSD suggests that PTI may carry a relevant prognostic value in this disorder.

**References:**

NR829        Wednesday, May 23, 3:00 PM - 5:00 PM
Generational exposure to war violence and how it is processed
David P. Law, M.D. Emory University, Psychiatry, 12574 Huntington Trace, Alpharetta, GA, 30005, 9000, Sun Young Yum, M.D.

Educational Objectives:

At the conclusion of the presentation, the participants will be able to recognize that (1) trauma processing is influenced by multiple factors, including socio-cultural systems, (2) characteristic coping behaviors may be associated with transgenerational victimization of war violence (3) little is known about how psychiatry can help. The participants will also be encouraged to discuss the boundaries of professional ethics and roles when social systems that cause mental disease are identified.

Summary:

Objective: To determine the psychological impact of generational civilian victimization in war zones, and to examine the integration of multiple factors in the processing of trauma, with an emphasis on the socio-cultural context in which violence is experienced.

Method: Field notes were taken while visiting ethnic minority villages at the Burma-Thai border. These villages have been constantly exposed to military violence for generations. Villagers were interviewed; the interviewees were encouraged to narrate their life experiences in response to some topics posed by the interviewer pertaining to 1. transgenerational history, 2. relations of power in the environment 3. influence of history and culture on individual lives, and 4. life expectations, future hopes. Qualitative analyses of field notes were performed, identifying recurrent themes and patterns of thoughts. The themes were further categorized into psychiatric symptoms that would warrant mental health intervention in the Western world.

Results:
1. During the course of the dialogues, recurrent themes of fear, anger, and despair frequently arose. Villagers were not only reliving traumatic events in their memory, but also in actual lives for generations.
2. Emotions were repressed as well as basic primitive urges by employing various defense systems.
3. Children were withdrawn, with diminished emotional responsiveness and no communicative gesture.

Discussions: These observations suggest that characteristic coping behaviors may be associated with transgenerational victimization of war violence. Much research has been done to help those who are reliving memories of trauma, but the basic premise of such treatment cannot be applied here: people cannot be told that memories are not dangerous, that they are actually quite safe. Nor can people be carelessly be empowered to seek to change their situations. Acceptance of what they cannot change, they have already achieved on their own without cognitive therapy.

References:
1. Law DP. Generational exposure to violence at the Karen and other ethnic groups of Burma. Paradigm 2007 Spring.
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