NR1

Monday, May 19, 9:00 a.m.-10:30 a.m.

Does the Presence of Mental Disorders in Patients With AIDS Affect Time to Initiation of Antiretroviral Therapy Duration of Treatment?

Seth S. Himelhoch, M.D., Department of Psychiatry, Johns Hopkins, 600 North Wolfe Street, Carnegie 295, Baltimore, MD 21287; Kelly Gebo, M.D., Lars Ellison, M.D., Richard Moore, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the importance of offering antiretroviral therapy to those individuals with mental disorders and AIDS.

Summary:

Background: Despite the benefits of highly active antiretroviral therapy (HAART), physicians may be less likely to offer HAART to HIV+ individuals with mental disorders. The goal of this study was to investigate, among a group of individuals diagnosed with AIDS, whether or not a diagnosis of a mental disorder (1) affected the time to initiation of HAART; (2) predicted the likelihood of remaining on HAART for at least six months, and (3) affected survival time.

Methods: A retrospective cohort study of individuals enrolled in an urban HIV clinic between January 1996-January 2002. Individuals with baseline CD4 count<200 mm$^3$ or history of an opportunistic infection and no prior history of HAART were stratified based on the presence of a mental disorder. Cox proportional hazards regression models were used to estimate relative risk of receiving HAART and survival; multivariate logistic regression models were used to estimate relative odds of remaining on HAART for at least six months.

Results: Of the 315 individuals that met inclusion criteria, 100 (32%) individuals met criteria for a mental disorder. Compared with those without a mental disorder, those with a mental disorder were significantly more likely to be younger, white, female, and IDU (p<.01). Individuals with a mental disorder were also 50% more likely to receive HAART (Cox adjusted hazard ratio [95% CI]: 1.5 [1.1-2.1]), nearly 2.5 times more likely to remain on HAART for at least six months (adjusted odds ratio [95% CI]: 2.3 [1.3-3.9]), and 40% more likely to survive (Cox adjusted hazard ratio [95% CI]: 0.6[0.4-1.0]) through the study period.

Conclusions: These surprising findings suggest that individuals with mental disorders are receiving HAART and are able to reap the survival benefit by remaining on it.

References:


NR2

Monday, May 19, 9:00 a.m.-10:30 a.m.

Impact of Neuropsychiatric Illness on Quality of Life of HIV/AIDS Patients

Rupang Pandya, M.D., Department of Psychiatry, University of Calgary, 132 Christie Knoll Heights S.W., Calgary, AB T3H 2R9, Canada; Hartmut Krentz, Ph.D., M. John Gill, M.B., Christopher Power, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to (1) appreciate the impact of neuropsychiatric involvement on health-related quality of life in HIV positive patients; (2) understand the relationship between illnesses such as HIV-associated dementia and HIV sensory neuropathy on parameters such as mental health, cognitive functioning, level of pain, and overall perception of health.

Summary:

Objective: To examine the relationship between HIV-related neuropsychiatric illnesses including HIV-associated dementia (HAD) and sensory neuropathy (HIV-SN), and health-related quality of life (HRQOL).

Methods: HRQOL was evaluated cross-sectionally using Medical Outcomes Study HIV Health Survey (MOS-HIV) administered to 291 HIV-infected patients with or without a neurological diagnosis at 16-week intervals between 1999 and 2002.

Results: Seventy-nine (27%) patients met clinical criteria for a neurological condition (e.g., HAD, HIV-SN). Patients with neurological conditions had significantly lower mean HRQOL scores (i.e., lower functioning) at baseline than controls (p<0.01) for all dimensions. The mean MOS-HIV overall health (25.0), mental health (44.4), and cognitive functioning (54.5) scores were significantly lower (p<0.001) than controls (58.6, 70.3, 81.5, respectively). The mean MOS-HIV overall health (40.1) and level of pain (57.7) scores for neuropathy group were significantly lower (p<0.001) than controls (58.6, 81.4, respectively). Prospctive analysis demonstrated a decline in HRQOL scores prior to a neurological diagnosis but increased by 32 weeks after treatment.

Conclusions: This is the first report of an association of lower HRQOL scores in HIV-positive patients with neuropsychiatric syndromes. Although antiretroviral agents may have immuno-reconstitutive and neuroprotective features, a global approach towards patient care including enhanced neuropsychiatric management may have a positive impact on patients' overall well-being.

References:


NR3

Monday, May 19, 9:00 a.m.-10:30 a.m.

Do High-Risk Neuropsychological Differences Predict Alcoholism at Age 30?

Savia A. Coutinho, M.A., Department of Psychiatry, Kansas University Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160; Elizabeth C. Penick, Ph.D., Joachim Knop, M.D., Elizabeth J. Nickel, M.A., Per Jensen, M.D., William F. Gabrielli, Jr., M.D., Fini Schulsinger, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize certain limitations of the high-risk paradigm in predicting drinking outcomes when premorbid neuropsychological tests are utilized.

Summary:

Objective: To determine whether premorbid neuropsychological test differences between a group of high-risk sons of alcoholic fathers and a group of low-risk sons of non alcoholic fathers predicted alcohol dependence at age 30.

Method: In this prospective study, a Danish cohort of 9,182 children born between 1959 and 1961 was used to identify a group of 220 high-risk sons of alcoholic fathers and a matched control group of 110 low-risk sons of non alcoholic fathers from the na-
ional archival Psychiatric Register. Neuropsychological assessments were performed on 134 of the high-risk and 70 of the low-risk subjects when they were approximately aged 19, before any of them had started drinking alcoholically. Ten years later, the drinking status of 169 of these subjects was reevaluated extensively.

Results: At age 19, the sons of alcoholic fathers performed significantly less well on the WAIS Vocabulary subtest, Halstead Category test and Porteus Mazes test. Subjects who would become alcohol dependent performed significantly less well on a different set of neuropsychological tests. Unexpectedly, the premorbid neuropsychological tests that distinguished the high and low-risk groups did not predict later alcohol dependence.

Conclusion: The high-risk, prospective, research paradigm applied premorbidly to a neuropsychological test battery failed to discriminate those subjects who would develop alcohol dependence at age 30.

References:

NR4 Monday, May 19, 9:00 a.m.-10:30 a.m.
Validity of the Tri-Level Method of Defining Familial Alcoholism
Sreeelatha Spieker, M.D., Psychiatry Department, Kansas University Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160; Bjorn Ebdrup, M.D., Joachim Knop, M.D., Elizabeth J. Nickel, M.S., Elizabeth C. Penick, Ph.D., Per Jensen, M.D., William F. Gabrielli, Jr., M.D., Fini Schulsinger, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to learn about the pre- and post-dictive validity of the Tri-Level definition of familial alcoholism in a 30-year prospective study of the antecedents of alcohol dependence.

Summary:
Objective: At the previous APA meeting, we used 16 measures, collected over a period of 30 years, to compare the pre and post-dictive validity of nine different ways of defining familial alcoholism. The nine methods varied greatly in sophistication and ease of application. The present poster will focus on the predictive validity of the Tri-Level method of defining familial alcoholism, which proved to be most valid. The three levels of the Tri-level method are: 1) No first- or second-degree relative positive for abusive drinking. 2) Only one first- or second-degree relative positive for abusive drinking. 3) Two or more first- or second-degree relatives positive for abusive drinking.

Method: In this prospective study, a Danish birth cohort of 9,182 children born between 1959 and 1961 was used to identify a group of 220 high-risk sons of alcoholic fathers and a matched control group of 110 low-risk sons of non-alcoholic fathers from the national archival Psychiatric Register. At age 30, 241 subjects were extensively studied with interviews and psychometric tests.

Results: As expected, the Tri-Level method correlated strongly (p<.001) with the original high versus low-risk designation obtained from the national Psychiatric Register. Nevertheless, the Tri-Level method, based upon the subjects' report, was found to more accurately predict a variety of outcome measures at age 30 such as substance abuse, alcoholism severity, social functioning, and psychopathology.

Conclusion: The Tri-Level approach to defining familial alcoholism, unlike the archival method and other genetically more complex methods, is a very user-friendly, easily applied, accurate predictor of drinking outcomes that could easily be used in busy clinical settings.

References:

NR5 Monday, May 19, 9:00 a.m.-10:30 a.m.
Effect of Administration Rate on Response to IV Cocaine in Humans
Susan J. Boyd, M.D., IRP, NIDA, 5500 Nathan Shock Drive, Baltimore, MD 21224; Richard A. Nelson, M.D., Roy Ziegelstein, M.D., David A. Gorelick, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the rate hypothesis of psychoactive drug administration as it applies to human cocaine use.

Summary:
Objective: The “Rate Hypothesis” holds that the faster a drug exerts its positive psychoactive effects, the more it is rewarding. Evidence for this hypothesis in humans and animals is limited. This study directly investigated the rate hypothesis for IV cocaine in humans.

Method: Seventeen adult cocaine users (94% male, 82% African American, average age 35.1 years) received up to 10 double-blind sessions of saline placebo or cocaine at 8 different infusion rates (.17–5.0 mg/sec) based on three different doses (10, 25, 50 mg) and infusion durations (10, 30, 60 seconds). Heart rate, blood pressure, and psychological effects (100 mm visual analog scales) were recorded for one hour after infusion. Changes from baseline were analyzed by linear regression.

Result: Rate of cocaine administration significantly increased maximum feelings of “Rush”, “High”, “Strong”, “Good”, “Like Drug”, and “Stimulated” by about 1–3 mm for each 1g/sec increase in infusion rate (all p <.01). Rate of cocaine infusion significantly increased peak response for all cardiovascular variables: systolic blood pressure (p<.05), diastolic blood pressure (p<.01), and heart rate (p<.01).

Conclusions: These findings support the rate hypothesis for intravenous cocaine.

References:
NR6 Monday, May 19, 9:00 a.m.-10:30 a.m.
Dropout From 12-Step Self-Help Groups: Prevalence, Predictors, and Treatment-Related Influences
Department of Veteran Affairs
John F. Kelly, Ph.D., Department of Research, VA Palo Alto MPD152, 795 Willow Road, Menlo Park, CA 94025; Rudolf H. Moos, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should (1) gain greater knowledge regarding rates of drop out from 12-step groups, such as AA; (2) become more aware of the factors associated with such dropout; and, (3) recognize what modifiable treatment factors may contribute to a lower likelihood of dropout.

Summary:
Introduction: Attendance at 12-step, self-help groups is associated with improved substance-related outcomes and is thus frequently recommended as an adjunct to professional substance use disorder (SUD) treatment. Nevertheless, a substantial proportion of patients recommended to join self-help groups drop out. This study assessed the prevalence, predictors, and treatment-related factors affecting dropout in the first year following intensive SUD treatment.

Method: Participants were 2,778 male patients (Mage = 43 [9.6]; 47% African American), of whom, 91% (2,518) were identified as having attended 12-step self-help groups either in the 90 days prior to, or during, treatment. Results: At one-year follow up 40% had dropped out. A number of baseline demographic, clinical, and social factors predicted dropout. Importantly, patients who initiated 12-step behaviors during treatment were less likely to drop out. Further findings suggest patients at highest risk for dropout may be at lower risk if treated in a more supportive environment.

Conclusions: Clinicians may decrease the likelihood of dropout both directly, by screening for risk factors and focusing facilitation efforts accordingly, and indirectly, by increasing the supportiveness of the treatment environment, and facilitating active 12-step involvement during treatment.

References:

NR8 Monday, May 19, 9:00 a.m.-10:30 a.m.
Bupropion Sustained Release In Adolescents Nicotine Dependence: A Pilot Study Supported by GlaxoSmithKline
Himanshu P. Upadhyaya, M.D., Psychiatry, Medical University of South Carolina, 1159 Sea Eagle Watch, Charleston, SC 29412; Kathleen T. Brady, M.D., Wei Wang, M.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize and treat nicotine dependence in adolescents.

Summary:
Objective: Bupropion SR has been shown to be effective for treatment of nicotine dependence in adults. This pilot study was designed to examine the efficacy of bupropion SR in adolescents with nicotine dependence.

Method: Sixteen adolescents between ages 12 and 19 were enrolled in the study. Eleven of the 16 participants also had comorbid attention deficit hyperactivity, disorder (ADHD). Participants were titrated over one week to bupropion SR 150mg BID and maintained for six weeks. Participants also received two brief counseling sessions on smoking cessation.

Results: Nine participants received at least four weeks of medication. There was a significant decrease in average number of cigarettes smoked (p=0.001). Carbon monoxide levels also decreased on the medication (p=0.035). Participants’ weight was unchanged during the study (p=0.549). Intent to treat analysis showed that 31.25% of the adolescents were completely abstinent (5/16) at the end of the study. There was no significant improvement in ADHD symptoms during the study.

Conclusions: Bupropion SR may be an efficacious medication for adolescents with nicotine dependence. Smoking cessation trials in adolescents need to focus on strategies to increase retention for optimal effect.

References:
NR9  Monday, May 19, 9:00 a.m.-10:30 a.m.
Psychosocial and Work Impairment in Primary Care Patients With GAD
Supported by Pfizer Inc.
Kristin Maki, B.A., Department of Psychiatry, Brown University, Box G-BH, Duncan Building, Providence, RI 02912; Risa B. Weisberg, Ph.D., Martin B. Keller, M.D., Michael J. Spencer, Ph.D., Larry Culppepper, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the debilitating impact of GAD on primary care patients and the need for increased attention to the disorder in the primary care setting.

Summary:
Objective: The purpose of this investigation is to report on the psychosocial and occupational impairment of primary care patients with GAD.

Method: Data are obtained from 142 participants with GAD enrolled in the Primary Care Anxiety Project (PCAP), the only existing prospective, naturalistic, longitudinal study of primary care patients with anxiety disorders. Multiple indicators of psychosocial and occupational impairment are examined.

Results: Data from the LIFE-Base and Dartmouth COOP Charts identify significant deficits in emotional and social well-being. The RAND 36-Item Health Survey data indicate that primary care patients with GAD demonstrate physical and psychosocial impairment that is worse than or comparable to subjects in the Medical Outcomes Study (MOS) who had severe medical conditions such as diabetes, hypertension, and recent myocardial infarction. With respect to occupational impairment, substantial percentages of GAD participants were unemployed or employed part time. Those who were employed missed more partial and full days of work due to impairment than individuals from the National Comorbidity Study. They also reported a substantial number of workdays with diminished productivity due to their difficulties.

Conclusion: These findings highlight the pervasive and debilitating impact of GAD on primary care patients and the need for dissemination of diagnostic/treatment information to primary care providers.

References:

NR10  Monday, May 19, 9:00 a.m.-10:30 a.m.
Impairment in Primary Care Patients With Social Anxiety Disorder
Supported by Pfizer Inc.
Kristin Maki, B.A., Department of Psychiatry, Brown University, Box G-BH, Duncan Building, Providence, RI 02912; Risa B. Weisberg, Ph.D., Martin B. Keller, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the impairment in functioning associated with SAD in the primary care setting.

Summary:
Objective: This investigation reports on the functioning and well-being of individuals with social anxiety disorder (SAD) using data from the Primary Care Anxiety Project (PCAP), a naturalistic, longitudinal study of anxiety disorders in primary care patients.

Method: Functional impairment of 179 subjects with SAD is measured using the RAND 36-item Health Survey. These scores are compared with those of subjects in the Medical Outcomes Study (MOS) who had general medical and psychiatric conditions including hypertension, recent myocardial infarction, diabetes, and depression, as well as a general population sample. Data on suicide rates are also presented.

Results: RAND data indicate that subjects with SAD reported functioning that was worse or comparable to MOS subjects with several of the serious medical conditions across both physical and socio-emotional functioning subscales. Those with SAD and comorbid MDD reported impairment that was comparable to the inpatient depressed sample from the MOS study. Even individuals with SAD without comorbid MDD evidenced suicide rates that were four times that of the general public.

Conclusions: SAD is associated with poor functioning and well-being across a wide spectrum of domains. Results point to the importance of education of both the public and primary care providers to aid in the early identification and treatment of this disabling condition.

References:

NR11  Monday, May 19, 9:00 a.m.-10:30 a.m.
Trauma and PTSD in an Urban Xhosa Primary Care Population in Khayelitsha, South Africa: Epidemiology, Comorbidity, and Service Use Patterns
Supported by the MRC Research Unit on Anxiety and Stress Disorders
Paul D. Carey, M.B., Department of Psychiatry, University Stellenbosch, Francie Van Zyl Drive, Parow 7505, South Africa; Dan J. Stein, M.D., Soraya Seedat, M.D., Mpumi Zungu Dirwayi

Educational Objectives:
At the conclusion of this session, the participant should have a greater appreciation of the magnitude of challenge in a developing country of identifying and treating trauma and related psychiatric sequelae.

Summary:
Objective: To assess the prevalence of trauma, PTSD, associated demographic factors, comorbidity, service use, service satisfaction, and quality of life were assessed in a South African clinic.

Methods: Randomly selected participants were directly interviewed using standard, translated and locally validated instruments. Retrospective chart analysis assessed clinician case identification and psychotropic drug prescribing habits.

Results: Of the 201 participants, 94% reported exposure to traumatic events (mean 3.8). Trauma was associated with single status (p=0.01) and PTSD with poverty and single status (p=0.04). Both sexes were equally likely to develop PTSD. PTSD (current) (19.9%, mean duration 4.9 years), depression (37%) and somatisation disorder (18.4%) were the most common diagnoses. Comorbidity with PTSD included depression (75%), somatisation (35%) and panic disorder (25%). Levels of functional impairment were higher for subjects with PTSD, depression and somatisation than for those without (p<0.05). PTSD comorbid with depression compounded impairment (p=0.04). Levels of trauma, PTSD, and depression did not increase service use or dissatisfaction with services. Clinicians did not identify trauma (0%) or psychopathol-
ogy (0%) and psychotropic medication was prescribed in only 1% of participants.

Conclusions: In this population, trauma and PTSD was highly prevalent, associated with significant unidentified morbidity and co-morbidity remaining untreated for years.

References:

NR12 Monday, May 19, 9:00 a.m.-10:30 a.m.
Childhood and Adulthood Separation Anxiety Symptoms in Patients With Anxiety and Mood Disorders
Stefano Pini, M.D., Department of Psychiatry, University of Pisa, Via Roma 67, Pisa 56100, Italy; Mauro Mauri, M.D., Marianna Abelli, M.D., Susanna Banti, M.D., Paolo Iazzetta, M.D., Giovanni B. Cassano, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be aware of frequency of separation anxiety symptoms in adult patients with mood and anxiety disorders and have greater awareness of their clinical implications.

Summary:
Background: This study aimed to evaluate the frequency of childhood and adulthood separation anxiety symptoms in a cohort of patients with mood and anxiety disorders.

Methods: Twenty-four outpatients with panic disorder without comorbid major depression (PD), 20 with major depression (MDD), 19 with MDD comorbid with panic disorder (MDD+PD), 20 with obsessive-compulsive disorder (OCD), 37 with bipolar I disorder (BD), and 15 healthy controls (CC) have been recruited consecutively and assessed with the SCID-I, the Structured Clinical Interview for Separation Anxiety Symptoms (SCI-SAS), the Separation Anxiety Symptoms Inventory (SASI), and the Adult Separation Anxiety Checklist (ASA-CL).

Results: Regarding childhood separation anxiety, post-hoc comparisons showed that patients with BD had higher total scores than the PD group and CC and the group with MDD+PD had higher score than CC. As to adult separation anxiety, all clinical groups, with exception of MDD group, had significant higher scores than CC. The MDD+DP group had higher score than the DP, MDD and CC groups.

Conclusions: The present study suggests that both childhood and adult separation anxiety symptoms are frequent in patients with panic disorder with comorbid depression and in patients with bipolar disorder. Separation anxiety may warrant greater recognition as an anxiety dimension in adulthood.

References:
Summary:

Objective: To assess the utility of open adjunctive zonisamide (ZNS) for obesity in patients with bipolar disorders (BD).

Method: Six euthymic BD with obesity (baseline mean ± SD body-mass index [BMI] 34.5 ± 4.5) received ZNS starting with 100 mg at bedtime and increasing weekly by 100 mg/day as necessary and tolerated (final dose 467 ± 197 mg/day, range 100–600 mg/day). At baseline there were five patients on mood stabilizers, five on antidepressants, and three on atypical antipsychotics.

Results: Weight and BMI decreased at a rate of 0.4 ± 0.3 % per week during the first two months. Mood remained euthymic with no patient developing a major depressive, hypomanic, or manic episode. One patient (who was losing weight) discontinued ZNS 100 mg/day after six weeks due to cognitive problems. Otherwise ZNS was well tolerated.

Conclusion: Open adjunctive ZNS may yield weight loss in obese patients with BD. These preliminary data need to be considered with caution due to the small sample size and brief duration (only two months in a six-month trial) of this ongoing study.

References:

NR15  Monday, May 19, 9:00 a.m.-10:30 a.m.  Defense Mechanisms in Panic Disorder Patients Before and After Treatment

Giselle G. Manfro, M.D., Department of Psychiatry, HCPA, Luiz Manoel Gonzaga 630/11, Porto Alegre, RS 90470-280, Brazil; Leticia C. Kipper, M.D., Carolina Bleya, M.D., Luciano Isolan, M.D., Betina Teruchkin, M.D., Elizabeth Heldt, R.N., Kelin M. Mezzomo

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the defense mechanisms used by symptomatic patients with panic disorder and recognize what are the possible modifications in defense mechanism style after treatment remission.

Summary:

The aim of this study is to evaluate the defense mechanisms used by patients with acute panic disorder compared with a control group and to verify if they changed with treatment remission.

Methods: Twenty-eight patients with symptomatic panic disorder and 33 controls participated in the study. The MINI was used to confirm the diagnosis and exclude patients with comorbid conditions. Severity was assessed by CGI and defense mechanisms were evaluated by DSQ-40 at the baseline and 16 weeks after pharmacological treatment with sertraline.

Results: Patients used more neurotic (4.6 vs. 3.6; p=0.007) defenses as compared with controls at baseline. There is no difference in the use of mature defenses (5.6 vs. 5.1; p=0.12) and a trend toward a higher use of immature defense (3.5 vs. 3.0; p=0.06) by patients compared with the control group. After treatment, although most patients remitted, the neurotic defense mechanisms used by panic patients do not change (4.6 vs. 4.2; p=0.13) and there was a trend toward a lower use of immature defense compared with baseline evaluation (3.5 vs. 3.3; p=0.09).

Conclusion: Panic patients used neurotic defense mechanisms that are not dependent on the state of the illness. It is suggested that the immature defense style is not characteristic of panic patients and seems to change with treatment.

References:

NR16  Monday, May 19, 9:00 a.m.-10:30 a.m.  Social Phobia and Anxiety Inventory for Children (SPAI-C) Validation in a Brazilian Children Sample

Gabriel J.C. Gauer, M.D., Department of Psychiatry, PUCRS University, Rua Felicissimo de Azevedo 1455-406, Porto Alegre, RS 90640-110, Brazil; Patricia Picon, M.D., Samuel M. Turner, Ph.D., Deborah C. Beidel, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that the SPAI-C is a reliable instrument to be used in USA as well as in Brazil.

Summary:

Objectives: The main objective of this study is to examine the factor structure and psychometric properties of SPAI-C in a school student sample of Brazilian children.

Method: The study was performed in a cross-sectional design and the SPAI-C Portuguese version was applied to the sample. It consisted of 1,952 children between the third and eighth grades, attending two private and 11 public schools. Two weeks after the initial administration, the SPAI-C was readministered to 440 children of the original sample.

Results: As seventy-nine subjects were excluded due to incomplete questionnaire, the final sample was 1,873 children. Using the Pearson product moment correlation, the two-week test-retest reliability coefficient was r=0.780 and Cronbach’s alpha was 0.946. The factor structure was almost similar to that reported in previous studies.

Conclusion: The results regarding the internal consistency, the test-retest reliability and the factor structure were similar to the findings in studies performed with children where English is the spoken language. The present study has shown that the Portuguese version of SPAI-C is a reliable and valid measure of social anxiety for Brazilian children.

References:
Summary:

Introduction: Studies suggest that 28% to 35% of people exposed to terrorist attacks may develop post-traumatic stress disorder (PTSD), with preexisting psychopathology being a risk factor. We studied the psychiatric effects of 9/11 on Manhattan adolescents with preexisting mental illness.

Methods: The PTSD Reaction Index (PTSI-R) was completed during a semi-structured interview in a Manhattan Adolescent Day Hospital population. Data were collected 7 days (Time1), and four to six weeks after the attack (Time2).

Results: Subjects were 17 patients, 13–18 years of age. Prior psychiatric disorders included anxiety (12%), depression (47%), PTSD (6%), psychotic (46%), and bipolar (12%) disorders. At Time1 43.7% had mild, 31.25% moderate, and 25% severe symptoms. At Time2 42.8% had mild, 35.7% moderate, 14% severe, and 7% very severe symptoms. PTSD-RS scores tended to increase over time, without reaching statistical significance. Preexisting diagnoses of depression and psychosis significantly predicted higher PTSD-RS scores at Time1. PTSD-RS scores at Time1 and 2 were significantly correlated. Only Time1 scores were predictive of more severe Time2 outcome.

Conclusions: This study demonstrates that preexisting psychopathology is a risk factor for developing post-disaster traumatic symptomatology in adolescents. Patients with more severe PTSD symptoms initially remained symptomatic after one month, suggesting that identifying and treating this group is indicated.

References:


NR18 Monday, May 19, 9:00 a.m.-10:30 a.m.
Illness Characteristics in Rapid-Cycling Bipolar Patients
Michelle M. Wankmuller, B.S., Department of Psychiatry, Weill Medical College Cornell, 525 East 68th Street, Box 140, New York, NY 10021; Kari H. Sutherland, B.A., Joseph F. Goldberg, M.D.; Laura E. Oakley, B.A.

Educational Objectives:
At the conclusion of this session, the participant should gain familiarity with the clinical-psychopathologic features that differentiate bipolar patients with versus without rapid cycling.

Summary:
Background: The nosologic importance of rapid cycling as a distinct bipolar subtype remains controversial. In particular, the extent to which depression predominates the illness course of rapid cycling has been an area of growing interest. We examined clinical features in a cohort of rapid cycling and nonrapid cycling bipolar patients who sought treatment in an academic research center.

Method: 39 consecutive DSM-IV bipolar adult outpatients with past year rapid cycling (RC) and 24 nonrapid cycling (NRC) subjects were assessed for symptoms and related illness characteristics.

Results: (1) 17% of rapid cyclers sought treatment during pure manic/hypomanic illness phases, as did 31% during pure depressed phases, and 53% during mixed manichypomanic phases; (2) RC patients were significantly more likely than NRC patients to have a bipolar first degree relative (p=0.01) and to manifest lifetime comorbid substance abuse (p<.01); lifetime suicide attempt rates were comparable in RC and NRC subjects; (3) Among RC patients, 54% of past year episodes were manic/hypomanic, although over half took antidepressants during that time.

Conclusions: Depression with concurrent mania or hypomania—rather than pure depression—may typify illness presentations in RC bipolar patients. RC illness may be a unique illness subtype for which treatments that target mixed affective features may be more crucial than those with sheer antidepressant or antimanic properties.

References:


NR19 Monday, May 19, 9:00 a.m.-10:30 a.m.
Tamoxifen Treatment and New-Onset Depression In Breast Cancer Patients
Kaiser Permanente
Kelly C. Lee, Pharm.D., Department of Clinical Pharm, UC San Francisco, 521 Parnassus Avenue, C-152, San Francisco, CA 94143-0622; Patrick R. Finley, Pharm.D., Thomas Ray, M.B.A., Enid M. Hunkeler, M.A.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that patients who receive tamoxifen for breast cancer may be at increased risk for developing depression.

Summary:
Objectives: Clinical observations suggest that breast cancer (BRCA) patients who receive tamoxifen may be at increased risk for developing depression. The current study investigated the association of new-onset depression and tamoxifen treatment in BRCA patients.

Methods: We conducted a retrospective cohort study of female patients diagnosed with BRCA between 1/1/97 and 12/31/00, using an HMO electronic database. Patients treated with tamoxifen were compared with breast cancer patients not treated with tamoxifen. The primary outcome was the rate of new-onset depression after one year from BRCA diagnosis. Depression was defined as either (1) ICD-9 for depression, (2) initiation of antidepressant or (3) both.

Results: A cohort of 2439 patients was identified (tamoxifen = 1930, no tamoxifen = 509). Approximately 60% of patients were <65 yo and 83% of the patients were Caucasians. The total rate of new-onset depression was 17.82% in the tamoxifen group compared with 14.34% in the no-tamoxifen group (p=0.0641). In a secondary analysis using variable follow-up period, the rate of depression was 27.31% and 21.99% in the tamoxifen group and no-tamoxifen group, respectively (p=0.0076).

Conclusion: Additional analysis is necessary to allow for variability in duration of time between tamoxifen initiation and cancer diagnosis.

References:

NR20  Monday, May 19, 9:00 a.m.-10:30 a.m.
5HT Transporter Polymorphisms and Adverse Effects With Fluoxetine Treatment
Roy H. Perlis, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACO-812, Boston, MA 02114; David Mischoulon, M.D., Keh-Ming Lin, M.D., Jordan W. Smoller, M.D., Jerrold F. Rosenbaum, M.D., Yu-Jui Y. Wan, Ph.D., Maurizio Fava, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the possible role of genetic polymorphisms in predicting treatment-emergent adverse effects.

Summary:
Background: Homozygosity for the "short" (s) rather than "long" (l) allele of the serotonin transporter gene-length polymorphic region (5HTTLPR) has been associated with poorer antidepressant response in major depressive disorder (MDD) as well as SSRI-induced switch into mania, but its impact on treatment-emergent adverse effects has not been studied. The objective of this study was to investigate a possible association with SSRI-induced insomnia and agitation.

Methods: 38 outpatients with MDD (mean age 36.3 +/-11.3 years; 53% female; all Caucasian) were treated openly with fluoxetine up to 60mg/d for 12 weeks and genotyped at the 5HTTLPR locus. Treatment-emergent adverse effects were assessed at each weekly or biweekly study visit.

Results: seven of nine subjects homozygotic for the 's' allele (78%) developed new or worsening insomnia, versus nine of 29 subjects who were not homozygotic (31%); Fisher's exact p=.02. Similarly, six of nine subjects homozygotic for the 's' allele (66%) developed agitation or akathisia, versus 8 of 29 subjects who were not homozygotic (28%); Fisher's exact p=.05. 's' homozygous subjects reported a mean of 1.52 (SD 0.83) adverse effects, compared to 1.67 (SD 1.23) among all other subjects (p=0.67).

Conclusion: The 'short' allele of the 5HTTLPR may identify patients at risk for developing insomnia and agitation or akathisia with SSRI treatment. This preliminary result will require confirmation in a larger sample.

References:

NR21  Monday, May 19, 9:00 a.m.-10:30 a.m.
Ten-Year Outcome in Patients With Bipolar Disorder Supported by APIRE and Janssen Pharmaceuticals
Gonzalo Laje, M.D., Department of Psychiatry, New York University, 67 Fox Run Drive, Englewood, NJ 07631; Eric D. Peselow, M.D., Scott Soloway, M.D., Ronald R. Fieve, M.D.

Educational Objectives:
At the end of this session, the participant should be able to recognize long-term predictors of outcome in bipolar disorder patients.

Summary:
Introduction: The purpose of this study was to investigate the course and 10-year naturalistic outcome of a sample after being euthymic for at least six months on a treatment regimen. Additionally, we attempted to identify other characteristics as predictors of outcome.

Methods: Data on 367 patients from the Foundation for Depression/Manic Depression were analyzed at two specific points, July 1, 1989, and August 1, 1994. Patients who were included in this analysis all met Feighner criteria for primary affective disorder, and RDC as well as DSM-III criteria for recurrent bipolar illness. To be included in the study, the patients had to be evaluated by a psychiatrist and rated as having a euthymic mood for six months on their treatment regimen. Once stable on their treatment regimen (single medication n=167, or combination n=200) for 6 consecutive months the patients were then followed until one of two possible outcomes: termination well or failure.

Results: Using a survival analysis comparing the two samples (one drug vs. combination) no significant differences between the two samples (z=-.899, p>.37) were noted. The overall probability of remaining stable for the entire group of 367 patients at one year, two years, three years, four years, five years, and 10 years was 91.23%, 80.66%, 65.94%, 56.56%, 47.97% and 31.72%, respectively. There was no difference in survival rates between males & females (z= -.347 p>.7). There was a significant correlation between length of time stable and average number of depressive symptoms in the prophylactic period (r= -.148 p<.004). There was also a statistically significant correlation between length of time stable and average number of manic symptoms in the prophylactic period (r= -.148 p= .209 p<.001). There was no correlation between length of time stable & age (r= -.011 p>.8) or age of onset (r= -.071 p>.8).

Conclusion: These findings suggest the existence of poor outcome, in patients with subsyndromal manic/hypomanic or depressive symptoms. Patients that remained stable after six months on a medication regimen (with one or more drugs) have a probability of remaining stable over the course of ten years of 31.72% regardless of sex, age, and age of onset.

References:

NR22  Monday, May 19, 9:00 a.m.-10:30 a.m.
Patient Versus Physician Factors Used in Selecting Antidepressants
Nova Scotia Health Research Fund
David M. Gardner, Pharm.D., Department of Psychiatry, Dalhousie University, 5909 Jubilee Road, Halifax, NS B3J 2E2, Canada;

Educational Objectives:
At the conclusion of this session, the participant should be able to (1) identify and differentiate among the factors that patients and physicians give high priority to when selecting an antidepressant, and (2) involve patients in selecting antidepressants giving greater credence to their informational needs.

Summary:
Introduction: In making collaborative treatment decisions with patients about antidepressant choice, it is necessary to know what information they value and how this may differ from physicians. This study compared the priorities attributed to the various antidepressant selection factors by patients and physicians.

Methods: Focus groups and surveys were used to identify selection factors and quantify their values. 20 factors were identified, 12 of which were considered to differentiate antidepressants. The
physician survey was mailed to randomly selected general practitioners (GPs) in Nova Scotia. The patient survey was conducted at 4 GP sites selected purposefully to enroll a broad representation of the GP population.

Results: 110 physicians and 126 patients participated. The five most highly ranked antidepressant selection factors by patients included (1) common side effects, (2) prescriber experience, (3) precautions, (4) serious adverse reactions, and (5) discontinuation reactions. For physicians, common side effects were ranked first but two different factors were in the top 5 (cost and dosing frequency). The ranking distributions were significantly different for 8/12 differentiating factors. Twenty-five percent of patients were taking antidepressants, however this did not change how factors were rated.

Conclusions: These data demonstrate that patients and physicians value antidepressant selection factors dissimilarly.

References:

NR23 Monday, May 19, 9:00 a.m.-10:30 a.m.
Quality of Life in Patients With Bipolar Disorder: Does Group Psychoeducation Have an Impact?
Supported by Wyeth Research

Erin E. Michalak, Ph.D., Department of Psychiatry, University of British Columbia, 2255 Wesbrook Mall, Vancouver, BC VGT 2A1, Canada; Lakshmi N. Yatham, M.B., Geoffrey G. Ineson, B.A., Raymond W. Lam, M.D.

Educational Objectives:
At the conclusion of this session, the participant should have an overview of previous research examining QoL in BD and the use of PE as a treatment intervention in bipolar populations.

Summary:
Objectives: A large body of research has now accumulated concerning quality of life (QoL) in patients with major depressive disorder. However, there is a paucity of information concerning QoL in bipolar disorder (BD), and there is little published evidence concerning the effectiveness of psychological interventions for BD. We aimed to assess the impact of a psychoeducation (PE) group upon QoL in patients with BD.

Method: Participants were euthymic patients (N=57) with BD type I or II attending a mood disorders program in Canada. Treatment intervention was a standardized eight-week group PE course. QoL was assessed at baseline and eight weeks via the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q).

Results: Mean baseline Q-LES-Q scores were 56%, representing moderate impairment in QoL. Group PE resulted in a five-point improvement in Q-LES-Q scores. Two Q-LES-Q domains (physical functioning and general satisfaction) improved significantly following PE. Multivariate analysis indicated that only one factor, having had a recent episode of depression, significantly predicted pre and post treatment Q-LES-Q scores.

Conclusion: Patients with BD continue to show impairment in QoL even when euthymic. Although preliminary, our results indicate that group PE significantly improves QoL in this population. The use of PE as an adjunct to pharmacotherapy in BD should be further studied, with a particular emphasis upon characterizing the effects of treatment intervention upon perceived QoL.

References:

NR24 Monday, May 19, 09:00 a.m.-10:30 a.m.
Quality of Life in Bipolar Disorder: A Review of the Literature
Supported by Wyeth Research

Erin E. Michalak, Ph.D., Department of Psychiatry, University of British Columbia, 2255 Wesbrook Mall, Vancouver, BC VGT 2A1, Canada; Lakshmi N. Yatham, M.B., Geoffrey G. Ineson, B.A., Raymond W. Lam, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the importance of assessing QoL as well as symptomatic outcomes in BD, have an overview of previous research in this field and insight into important avenues of future research.

Summary:
Objectives: Growing emphasis is being placed upon patient-centered assessment of health status, with one burgeoning area of research addressing quality of life (QoL). Uptake of QoL research in relation to bipolar disorder (BD) has been slow, but increasing numbers of QoL studies are now being conducted in bipolar populations. We performed a review of all peer-reviewed literature addressing the assessment of QoL in BD.

Method: A literature search was conducted in a comprehensive selection of databases including MEDLINE. Articles were included if they were published in English and reported on a QoL assessment in patients with BD but were excluded if they assessed fewer than 10 patients or did not use instruments that assessed multiple QoL dimensions.

Results: The literature search initially yielded 648 articles or abstracts. Of these, 627 did not meet our inclusion criteria, leaving a final total of 21 articles.

Conclusions: There is growing interest in QoL research in BD populations. The scientific quality of this research is variable, but increasing numbers of studies of good design are being conducted. Most studies indicate that QoL is markedly impaired in BD patients, even when clinically euthymic. Future research should include more assessments of QoL in acutely manic patients, more longitudinal research and the development of a disease-specific measure of QoL for BD patients.

References:

NR25 Monday, May 19, 09:00 a.m.-10:30 a.m.
Effect of Antidepressant Use on Admissions to Hospital Among Elderly Bipolar Patients

Ayal Schaffer, M.D., Department of Psychiatry, Sunnybrook and WCHSC, 2075 Bayview Avenue, Toronto, ON M4N 3M5, Canada; Muhammad Mamdani, M.P.H., Anthony J. Levitt, M.D., Nathan Herrmann, M.D.
NR26
Monday, May 19, 9:00 a.m.-10:30 a.m.

Naturalistic Outcome of Bipolar Disorder in a Community-Based Cohort

Mohit P. Chopra, M.D., Department of Psychiatry, University of Pennsylvania, 2535 Market Street, 2nd floor, Philadelphia, PA 19104; K.V. Kishore Kumar, D.P.M., Sanjeev Jain, M.D., D.K. Subbakrishna, Ph.D., R. Srivinsava Murthy, M.D., Anthony L. Rostain, M.D., Jay D. Amsterdam, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the outcome of bipolar disorder varies in different settings and locations, and appreciate the methodology involved in performing longitudinal community-based follow-up.

Summary:
Background: Recent studies on patients with bipolar disorder in specialist report poor outcome.
Aims: To study the outcome of a community-based cohort of bipolar patients.
Method: All patients diagnosed with bipolar disorder during an epidemiological survey in a fixed geographical area in southern India (n = 34) were followed longitudinally. Psychiatric status and psychosocial functioning on multiple domains was assessed using the SADS-L and the LIFE after varying durations of illness. Detailed direct evaluation could be carried out in 27 patients who could be traced. Predictors of outcome were examined using linear and logistic regression models.
Results: Twenty patients (74%) showed good overall functioning at the time of follow-up, with no patient subjectively reporting more than slight impairment. Patients were most impaired in their interpersonal relationships with relatives and friends, and in their recreational ability, with only 28%, 37%, and 22% of patients experiencing moderate to severe impairment in these areas. All patients, except one, had been married, although separation/divorce was twice as likely for females. Alcohol dependence syndrome was the commonest co-morbid condition, affecting females three times as often. None of the putative variables examined appeared to predict outcome in any way.

Conclusions: The proportion of patients with favorable outcomes and the pattern of impairment differed from other reports. This has implications for the outcome of bipolar disorder in non-clinic settings.

References:

NR27
Monday, May 19, 9:00 a.m.-10:30 a.m.

Clinical Features Related to Age at Onset in Bipolar Disorder

Carrie L. Ernst, M.D., Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02138; Joseph F. Goldberg, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be informed about the impact of early age at onset relative to clinical outcome states in bipolar disorder.

Summary:
Background: Early age at illness onset has been associated with poor functional and syndromal outcome in bipolar disorder, although debate remains about the likely robustness of this variable, especially while controlling for other illness parameters.
Method: 56 consecutive bipolar outpatients underwent semi-structured interviews to assess varied dimensions of clinical psychopathology and outcome. We hypothesized that early age at onset would be linked with more prevalent rapid cycling, psychosis, comorbid substance abuse, and lifetime suicide attempts.
Results: Illness onset before age 19 (seen in 46% of subjects) was associated with an increased likelihood for lifetime rapid cycling (P < .05) and for comorbid substance abuse/dependence (P < .05), each maintained while controlling for current age or depressive symptom severity. First episodes among early-onset patients were more likely to be insidious rather than acute (p = .025). No significant associations were observed between age at onset and bipolar family history, lifetime suicide attempts, lifetime psychosis, or illness duration.

Conclusions: Early onset of bipolar illness appears related to the development of rapid cycling and comorbid substance use disorders, unconfounded by the potential effects of chronicity or state-dependent illness severity. The findings raise developmental implications for the pathogenesis of these outcome states.

References:
NR28  Monday, May 19, 9:00 a.m.-10:30 a.m.
Effects of Anxiety Symptoms on Bipolar I Disorder Maintenance Treatment
Supported by GlaxoSmithKline
Weizhang, M.D., Department of Psychiatry, Duke University Medical Center, Box 3812, Durham, NC 27710; Robert A. Leadbetter, M.D., Ted Spaulding, Ph.D., Zoran Antonijevic, Ph.D., Jonathan R.T. Davidson, M.D., Alan Metz, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the significance of anxiety symptoms during bipolar I disorder treatment.

Summary:
Objective: To examine the predictive value of anxiety symptoms for response in the maintenance treatment of bipolar I disorder.
Methods: 638 currently or recently symptomatic bipolar I patients (DSM-IV) were stabilized and randomized to 18 months of double-blind monotherapy with lamotrigine, lithium, or placebo. The effects of anxiety symptoms as measured by the baseline psychic anxiety score (BPAS) and baseline somatic anxiety score (BSAS) on the Hamilton Depression Rating Scale (HAM-D) were examined against time to intervention for a mood episode (TIME) using a Cox Proportional Hazard Model.
Results: BPAS=0 was predictive of overall response when analyses were controlled by index mood (mania or depression) and treatment (p<0.002). BPAS=0 was predictive of a treatment response within lamotrigine (p=0.04) or lithium (p=0.04) but not placebo (p=0.05) group. When compared with placebo, lamotrigine (p=0.003) and lithium (p=0.001) delayed TIME significantly among patients with BPAS=0 or BSAS=0.
Conclusions: Absence of baseline anxiety symptoms predicted the most favorable response in the lamotrigine and lithium maintenance treatment of bipolar I disorder, consistent with previous reports for the acute treatment of bipolar I disorder.

References:

NR30  Monday, May 19, 9:00 a.m.-10:30 a.m.
Patterns of Antidepressant Use in Patients With Hepatitis-C and Comorbid Depression in Mental Health Setting
Janardhana R, Jonnalagadda, M.D., 604 Summer Place, Flowood, MS 38632; Dinesh Mittal, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the pattern of antidepressant use in mental health setting in this cohort group.

Summary:
Objective: To examine the patterns of antidepressant use in Hepatitis C patients with depression in the mental health setting.
Methods: Retrospective study of 154 patients.
Results: Mean age: 51.2 years: Males: 95.4%, Females: 4.6%; Caucasians: 52.6%, African Americans: 47.8%, 94.2% were recruited to gastroenterology but only 8.4% received rebetron. 82% patients received antidepressants. Lag time between HCV diagnosis and antidepressant trial was 12-13 weeks. SSRIs were used in 90.6% and tricyclics in 9.4%. First antidepressant was continued in 76%, while 24% required other trial. Reasons for change were intolerance (7%) or poor response (10.7%). Frequency of antidepressants used: sertraline 33% > fluoxetine 15.5% > paroxetine 13% > TCA 8.1%, Trazodone was used in 16.8%. Longest duration of antidepressant trial in weeks: fluoxetine 32 > sertraline 28 > paroxetine 29.8 > TCA 22.7 > citalopram 28.5. Frequency of longest duration of trial with each antidepressant: sertraline 33.3% > fluoxetine 16.3% >, paroxetine in 10%, TCA in 8.1%, citalopram...
in 7.3%. Other psychotropics: antipsychotics: 26.6%; mood stabilizers: 14.3%; benzodiazepines: 11.7%.

Conclusions: (1) Most patients receive antidepressant treatment. SSRI's are used most commonly. (2) Only 8.4% patients receive antiviral medication. (3) While patients stayed longest on fluoxetine compared to other antidepressants, more patients who received sertraline stayed on it for a longer duration in that group.

References:

NR31 Monday, May 19, 9:00 a.m.-10:30 a.m.
An Open-Label Study of Adjunctive Oxcarbazepine in the Treatment of Refractory Bipolar Disorder Supported by Novartis Pharmaceuticals Corporation
Charles R. Conway, M.D., Psychiatry, Saint Louis University, 1221 South Grand, Saint Louis, MO 63104; Leigh A. Nelson, Pharm.D., Jerry M. McGuire, Pharm.D., Katherine E. Bonan, M.A., Praveen F. Abraham, D.O., Vadim Y. Baram, M.D., John Chimbah, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to demonstrate an understanding of the potential role of oxcarbazepine in the treatment of bipolar disorder.

Summary:
Objective: To investigate the efficacy of oxcarbazepine as adjunctive therapy for bipolar I disorder refractory to standard mood stabilizer treatment.
Method: Fourteen bipolar I patients (at baseline: 10 depressed, 4 manic at baseline) were enrolled in a prospective, open-label, 24-week trial. All received oxcarbazepine adjunctive to current mood stabilizers. Dose was titrated over eight weeks to 2400mg/day or maximum tolerated dose. Measures of efficacy included Hamilton Depression Rating Scale (HAM-D), Montgomery Asberg Depression Rating Scale (MADRS), Young Mania Rating Scale (YMRS), and Clinical Global Impression of Change (CGIC).
Results: For patients depressed at baseline, data available at week 12 showed improvement from baseline on the HAM-D (mean difference = 12.1, SD = 8.2, p = 0.06), the MADRS (mean difference = 7.0, SD = 5.8, p = 0.10), and the CGIC (mean difference = 0.0, SD = 0.8, p = 0.09). Among patients manic at baseline, significant change at week 12 was noted for the YMRS (mean difference = 15.1, SD = 3.6, p < 0.05) and the CGIC (mean difference = 1.7, SD = 0.6, p < 0.05).
Conclusion: Oxcarbazepine supports the use of oxcarbazepine as an adjunctive therapy for mood stabilization in refractory bipolar I disorder.

References:

NR32 Monday, May 19, 9:00 a.m.-10:30 a.m.
Effects of Newer and Older Antidepressants in Bipolar Depression
Klara J. Rosenquist, B.S., Department of Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139; S. Nassir Ghaemi, M.D., James Y. Ko, A.B., Frederick K. Goodwin, M.D., Ross J. Baldessarini, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to evaluate relative risks of unfavorable responses to modern vs. older antidepressants in bipolar depression, including early and late nonresponse, manic-switching, and rapid-cycling.

Summary:
Objective: To compare risks of unfavorable responses in depressed DSM-IV bipolar disorder patients treated with older vs. modern antidepressants.
Methods: We analyzed 155 trials (in 41 patients) involving tricyclic (N=23), serotonin-reuptake-inhibitor (N=82), buproprion (N=29) or other modern antidepressants (N=21 trials).
Results: There were no significant risk-differences among the four classes of agents (df=3) for: [1] nonresponse (in 39.2% of trials; x² = 5.18, p=0.16); [2] manic-switching (in 18.7%; x² = 2.29, p=0.13); [3] rapid-cycling (9.8%; x² = 3.36, p=0.34); and [4] late loss of antidepressant-effect (tolerance: 26.6%; x² = 3.26, p=0.35). No difference between specific agents was significant for any outcome except tolerance (x² = 15.6, p=0.004), ranking: fluoxetine (11/16; 68.8%) => venlafaxine (2/7; 28.6%) > bupropion (5/23; 21.7%) > sertraline (3/15; 20.0%) > paroxetine (1/12; 8.3%). Mania was the only unfavorable outcome affected by mood-stabilizer co-treatment (10/29 [34.5%] with, vs. 19/29 [65.5%] without mood stabilizer; x² = 4.41, p=0.04).
Conclusion: Risks of unfavorable responses of bipolar-depressed patients to modern and older antidepressants were remarkably similar, with no advantage of any specific modern agent, and tolerance seeming especially frequent with fluoxetine.

References:

NR33 Monday, May 19, 9:00 a.m.-10:30 a.m.
Cognitive Impairment in Acute and Remitted Bipolar Patients
Stanley Medical Research Institute
Anabel Martinez-Aran, Ph.D., Department of Psychiatry, Hospital Clinic, Villarreal 170, Barcelona 08036, Spain; Eduard Vieta, M.D., Francesc Colom, Ph.D., Maria Reinares, Ph.D., Carla Torrent, Ph.D., Jose Sanchez-Moreno, Ph.D., Manel Salmero, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the neuropsychological differences between bipolar patients and healthy controls.
Summary:
Objective: Cognitive impairment has been reported more consistently in acute than in euthymic bipolar patients. The aim of the study was to ascertain whether bipolar patients showed cognitive dysfunctions, regardless of clinical state as well as the weight of clinical features and cognitive function in psychosocial functioning.
Methods: 30 depressed bipolar patients (DSM-IV criteria for major depression, HDRS≥17), 34 manic or hypomanic bipolar patients (DSM-IV criteria for manic or hypomanic episode, YMRS≥12), 44 euthymic bipolar patients (at least six months of remission, HDRS<3 and YMRS<6) were assessed in several cog-
nitive domains, such as executive function, attention and memory. The control group consisted of 30 healthy subjects without history of neurologic or psychiatric disorders.

Results: All patient groups showed dysfunctions in verbal memory (California Verbal Learning Test) and in executive function (Wisconsin Card Sorting Test, Backward Digit Span and Stroop Color and Word Test) compared with the control group. Low neuropsychological performance was associated to a severe course of illness and a poor functional outcome.

Conclusion: A poorer performance was observed in all bipolar groups regarding verbal memory and executive function compared with healthy controls. Cognitive dysfunctions were associated to worse functional outcome. Further research should study whether optimizing prophylactic pharmacological treatment and psychological might reduce cognitive impairment.

References:

NR35 Monday, May 19, 9:00 a.m.-10:30 a.m.
Quantification of Alcohol Use in Bipolar Disorder
Stanley Medical Research Institute: Abbott Laboratories
Alexander H. Fan, M.D., Department of Psychiatry, UCLA, 300 Medical Plaza #1544, Los Angeles, CA 90095; Lori L. Alshuler, M.D., James W. Mckowen, B.S., Michael J. Gillin, M.D., Rosanne C. State, M.D., Mark A. Frye, M.D.

Educational Objectives:

NR34 Monday, May 19, 9:00 a.m.-10:30 a.m.
Seasonality of Mood in African and African-American Students
Department of Mental Health
Samina M. Yousufi, M.D., Department of Psychopharmacology, St. Elizabeths Hospital, 2700 Martin Luther King Jr. Avenue, Washington, DC 20032; Kelly J. Rohan, Ph.D., Charles O. Agumadu, M.D., Michael A. Jackson, B.S.; Courtney M. Thrower, B.A., Mariana J. Niemtzoff, M.D., Teodor T. Postolache, M.D.

Educational Objectives:

NR35 Monday, May 19, 9:00 a.m.-10:30 a.m.
Quantification of Alcohol Use in Bipolar Disorder
Stanley Medical Research Institute: Abbott Laboratories
Alexander H. Fan, M.D., Department of Psychiatry, UCLA, 300 Medical Plaza #1544, Los Angeles, CA 90095; Lori L. Alshuler, M.D., James W. Mckowen, B.S., Michael J. Gillin, M.D., Rosanne C. State, M.D., Mark A. Frye, M.D.

Educational Objectives:

Summary: At the conclusion of this presentation, the participant will have a greater appreciation of alcohol use in bipolar disorder.
Depressive Symptoms Among College Students as Assessed by the Symptom Questionnaire

Shamsah B. Sonawalla, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114; Yasmin Mahal, B.A., Ella L. Masson, B.A., Albert Yeung, M.D., David Mischoulon, M.D., Jonathan E. Alpert, M.D., Maurizio Fava, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize depression and its presentation among college students.

Summary:
Objective: To assess the prevalence and symptom patterns of depression among college students.
Method: 701 students at a college in the greater Boston area (mean age: 21 years ± 3.0 years; 54.3% women) were screened for depressive symptoms. After obtaining written, informed consent, the Beck Depression Inventory (BDI) and the Symptom Questionnaire (SQ) were distributed to all students. Students who scored greater than or equal to 16 on the BDI and consented to be interviewed were further assessed using the MDD module of the Structured Clinical Interview for DSM-IV (SCID-P). The Mann Whitney-U test, Spearman rank correlation and multiple linear regression were used for data analysis.

Results: 14.2% of the students scored ≥ 16 on the BDI and 16.4% of the students had suicidal ideation (score of ≥ 1 on BDI item #9). Students who scored ≥ 16 on the BDI also had significantly higher scores across all four SQ scales (depression, anxiety, somatization and anger-hostility), compared to those with BDI scores of less than 16 (p<0.0001). Students who had suicidal ideation also had significantly higher scores across all four SQ scales compared to those who did not have suicidal ideation (p<0.0001). Women scored significantly higher compared to men on SQ-anxiety and SQ-somatic symptom scales (7.5 ± 5.6 vs 5.8 ± 4.9; p<0.0001, and 7.2 ± 5.1 and 5.2 ± 4.8; p<0.0001 respectively).

Conclusion: A substantial percentage of students in this sample reported experiencing significant depressive symptoms. Women experienced greater anxiety and somatic symptoms compared to men. This study highlights the importance of screening of depressive symptoms in the college population, and suggests that depressive symptoms may vary with gender.

References:

NR36 Monday, May 19, 9:00 a.m.-10:30 a.m.
A Voxel-Based Morphometric MRI Study in Female Patients With BPD
Nicolas Rusch, M.D., Department of Psychiatry, University of Freiberg, Hauptstrasse 5, Freiberg 79104, Germany; Ludger Tebartz van Elst, M.D., Berno Hesslinger, M.D., Klaus Lieb, M.D., Martin Bohus, M.D., Marko Wilke, M.D., Dieter Ebert, M.D.

Educational Objectives:
At the conclusion of this session, the participant should better understand the neurobiological underpinnings of BPD, especially the role of the amygdala in affective dysregulation. Also, the participants should be able to critically discuss advantages and disadvantages of the structural imaging methodology employed.

Summary:
Objective: To further validate the previously reported findings and to more precisely describe the nature of the structural change, we performed a voxel-based morphometric (VBM) study in patients with BPD.
Method: 20 female patients with BPD and 21 female healthy controls were investigated. High resolution 3-D-data sets were acquired and analyzed following an adapted and updated version of the optimized VBM-protocol as described by Good and colleagues (2001) in the framework of statistical parametric mapping (SPM99).
Results: Gray matter volume loss was found in the left amygdala. No other significant differences in gray or white matter volume or density were found anywhere else in the brain.
Conclusions: Our findings support the hypothesis that temporal-lobar abnormalities and especially the amygdala play a role in the pathophysiology of BPD. Prefrontal structural alterations in BPD were not observed in this study. Larger sample sizes might be necessary to detect further changes described in the literature. Alternatively, VBM might not yet be sensitive enough to detect the subtle structural changes to be expected in BPD.

References:

NR39 Monday, May 19, 9:00 a.m.-10:30 a.m.
Backward Visual Masking and Transcranial Magnetic Stimulation-Induced Visual Suppression
Giulio Tononi, M.D., Department of Psychiatry, University of Wisconsin, 6001 Research Park Boulevard, Madison, WI 53719-1176; H. Magnus Haralosson, M.D., Fabio Ferrarelli, M.D., Ned H. Kalin, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize backward visual masking and visual cortex transcranial magnetic stimulation (TMS) as tools for investigating early visual processing. We introduce application of TMS induced visual suppression to study populations with impaired early visual processing, such as schizophrenia patients.

Summary:
Objective: In backward visual masking (BVM), the perception of a visual stimulus is reduced by a subsequently presented mask. Abnormalities in BVM are well established in schizophrenia. Visual perception can also be suppressed by Transcranial Magnetic Stimulation (TMS) of the visual cortex, possibly through similar mechanisms. In preparation for a study of TMS-induced visual suppression in schizophrenics, we examined BVM and TMS-induced visual suppression in normals.
Method: Eight healthy subjects were presented with visual stimuli (letters) at one of four screen locations. The stimuli were followed, at different inter-stimulus intervals (ISIs), either by a second visual stimulus (mask), or by single TMS pulses over the right occipital cortex.
Results: As expected, BVM was strong at ISIs under 40 milliseconds (ms) but performance returned to 90% of normal at ISI = 100 ms. TMS-induced visual suppression was strongest at ISIs between 65 and 95 ms. At those ISIs, error rate was 42–52% for stimuli presented in the left visual field vs. 10–18% in the right visual field.

Conclusions: In normal subjects, right occipital TMS induces left visual field suppression with a well-defined peak at 65–95 ms. Further studies will investigate whether schizophrenic subjects are abnormally sensitive to TMS-suppression as they are to BVM.

References:

NR39 Monday, May 19, 9:00 a.m.-10:30 a.m.
First-Episode Psychosis: Diagnostic Stability Over One Year
Stanley Foundation
Ulrik Haahr, M.D., Psychiatric Department, Fjorden Hospital, Smedegade 10–16, Roskilde DK-4000, Denmark; Erik Simonsen, M.D., Anne B. Dahl, M.D., Ingrid Meille, M.D., Tor K. Larsen, M.D., Per Vaglum, M.D., Thomas H. McGlashan, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the importance of early assessment of predictors for the course of early psychosis.

Summary:
Background: First-episode psychosis is heterogeneous and DSM-IV identifies seven varieties. This study addresses the question whether and how these types evolve over the first year of treatment.

Material and methods: This study includes 256 patients from the TIPS project from Jan 1997 to Dec 2000.

Assessment: SCID-1, GAF, PANSS. PAS and Duration of Untreated Psychosis (DUP) were made at baseline, SCID-1 again at one year follow-up.

Results: The diagnostic distribution at baseline/follow-up was: schizophrenia (S) 29%/46%, schizoaffective disorder (SA) 12%/15%, affective disorder with mood-incongruent psychotic symptoms (AD) 14%/14%, delusional disorder (DD) 6%/4%, brief psychosis (BP) 7%/6% other psychoses (OP) 11%/6%. Patients who kept their diagnosis: S 97%, SF 36%, SA 88%, AD 76%, DD 67%, BP 74% and OP 50%. Worse premorbid scores in early childhood and long DUP predicted change from SF to S.

Conclusion: There was high prospective consistency for most diagnostic groups, except SF, PAS seems to be an important predictor for changing diagnosis from SF to S. SF underwent the greatest change, mostly to S, and premorbid adjustment and long DUP predicted this change.

References:

NR40 Monday, May 19, 9:00 a.m.-10:30 a.m.
Shared Decision Making in Routine Care of Inpatients With Schizophrenia
German Ministry of Health
Johannes G. Hamann, M.D., Department of Psychiatry, Tu-Muenchen, Moehistrasse 26, Muenchen 81675, Germany; Carolin Mischo, Bernadette Langer, M.D., Werner Kissling, M.D.

Educational Objectives:
At the conclusion of the session, the participants should be familiar with the model of shared decision making, as well as with its prerequisites in schizophrenia treatment.

Summary:
In somatic medicine, “shared decision making” (a strategy for including patients to a greater extent in therapeutic decision processes), has already shown positive effects in studies on the patients’ knowledge about their illness and their treatment adherence. We studied two prerequisites of shared decision making in schizophrenia treatment: information exchange and participation of patients in therapeutic decisions. Semi-structured interviews were performed with hospital psychiatrists (N=50) and the next two patients of each of them to be discharged (N=100); answers as well as levels of agreement were analysed.

Results: Overall, patients had little knowledge about their treatment. Only 72% of the patients had accurate knowledge about which medication they were taking and only 29% knew their actual dosage. Agreement on the recommended duration of antipsychotic treatment was even lower. Only 24% of the patients had the same expectation as their physicians about the length of their treatment. Consequently, over 60% of the patients declared that their physicians more or less alone decide on their treatment.

Conclusion: Considering low treatment adherence in long term treatment of schizophrenia improvements in doctor patient relationships (towards more shared decision making) would be an important step forward.

References:

NR41 Monday, May 19, 9:00 a.m.-10:30 a.m.
Predictors of Short-Term Treatment Response to Risperidone in First-Episode Schizophrenia
Jang Won-Seok, M.D., Department of Psychiatry, Samsung Medical Center, Irwon-Dong 50, Kangnam-Ku, Seoul 125-710, South Korea; Kim Sang-Wook, Hong Kyung-Sue, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify the predictors of short-term treatment response to risperidone from first-episode schizophrenia.

Summary:
Objective: The purpose of this study is to identify the predictors of short-term treatment response to risperidone from first-episode schizophrenia.

Method: Eighteen schizophrenic patients in their first episodes were recruited and received treatment with risperidone for eight weeks. Clinical response was measured using Positive and Negative Syndrome Scale (PANSS) and Clinical Global Impression (CGI) scale. Demographic (age, sex), clinical (family history, age at onset, premorbid and baseline levels of functioning, premorbid
tested. Stepwise multiple regression was performed to identify the predictors for each treatment response index. Extrapyramidal symptoms after one week treatment was also related with poor treatment response. According to the regression analysis, duration of illness strongly predicts all response indices ($\Delta R^2 = 0.42 - 0.79$), and the highest functioning level in the past predicts the improvement rate in general psychopathology.

Conclusion: These results suggest that early diagnosis and intervention could increase the rate of short-term treatment response to risperidone. In addition to the duration of illness, extrapyramidal symptoms of early treatment phase and level of premorbid functioning also predict certain aspects of treatment response.

References:

NR42 Monday, May 19, 9:00 a.m.-10:30 a.m.
The Effects of Galantamine in Patients With Schizophrenia Receiving Risperidone
Supported by Janssen Pharmaceutica Products, L.P.
Trina B. Allen, M.D., Department of DBPS, Duke University School of Medicine, 1003 12th Street, Building 32, Butner, NC 27509; Joseph P. McEvoy, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to assess the effects of galantamine on behavior and cognition in patients with schizophrenia treated with risperidone.

Summary:
Objective: To investigate the effects of galantamine in patients with schizophrenia receiving risperidone.
Methods: All patients were treated with a fixed dose of risperidone (1–8 mg daily) throughout the four-week study. All patients smoked at least 10 cigarettes per day. Patients were randomly assigned in three sequential blocks of eight subjects each (first eight, placebo [n = 2] or galantamine 16 mg/day [n = 6]; next eight, placebo [2] or galantamine 24 mg/day [6]; final eight, placebo [2] or galantamine 32 mg/day [6]). Psychopathology (Brief Psychiatric Rating Scale and Clinical Global Impression) and cognitive psychomotor performance (computerized test battery and Brief Assessment of Cognition in Schizophrenia) were the primary outcome measures.
Results: After four weeks, patients treated with galantamine demonstrated superior cognitive and behavioral effects compared with placebo-treated patients. A statistically significant difference ($p < 0.05$) favoring galantamine was shown for the delayed matching to sample, CPT errors of commission, and verbal fluency tests.

Conclusions: Galantamine provides cognitive and behavioral benefits in patients with schizophrenia treated with risperidone. These results and subsequent studies may aid in establishing a therapeutic use for galantamine in this patient population.

References:

NR43 Monday, May 19, 9:00 a.m.-10:30 a.m.
Aggression in Asian Patients With First-Episode Psychosis
Swapna K. Verma, M.B.B.S., EPIP, Institute of Mental Health, 10 Bangkok View, Singapore 539747, Singapore; Lye Yin Poon, B.S., Mythily Subramaniam, M.B.B.S., Siow A. Chong, M.B.B.S.

Educational Objectives:
At the end of the session, participants will be able to appreciate the risk factor of aggressive behavior in first-episode psychosis.

Summary:
Objectives: To examine the prevalence and correlates of aggressive behavior in patients with first-episode psychosis.
Methods: A total of 146 consecutive subjects aged 15–40 years admitted to the Early Psychosis Intervention Program of Singapore were evaluated for history of aggressive behavior. Subjects with psychosis secondary to substance use or general medical condition were excluded. Diagnosis was established using Structured Clinical Interview for DSM-IV (SCID). Psychopathology was assessed using Positive and Negative Scale for Schizophrenia (PANSS). Severity of aggression was rated on a two-point scale where level 2 or serious aggression was defined as weapon use, sexual assault, or victim injury. Level 1 or lesser aggression was all other acts of aggression against others or damage to property.
Results: 23.3% of subjects demonstrated level 1 aggression and 13.7% had level 2 aggression. There were no significant age or gender differences between subjects with and without aggressive behavior. Subjects with serious aggression had significantly longer duration of untreated psychosis (DUP) than subjects with no or lesser aggression ($p < 0.05$). There were no significant differences between subjects with or without aggression on PANSS total scores, however subjects with aggression had significantly elevated general psychopathology scores as well as hostility and poor impulse control scores.
Conclusion: There is high prevalence of aggression among Asian patients with first-episode psychosis. The association between serious aggression and longer DUP highlights the need for early intervention in psychosis.

References:

NR44 Monday, May 19, 9:00 a.m.-10:30 a.m.
Sexual Life in Schizophrenic Patients
Supported by Janssen Pharmaceutica Products, L.P.
Meltem Efe Sevim, M.D., Bakirkoy Mental Hospital, 2Uhruratbaba Mah-Bakir Sok 11/3, Istanbul-Bakirkoy 34711, Turkey; Salih Yasar Ozoen, M.D., Ferah Veli, M.D.
that the psychiatrists should absolutely give information to male
patients. 70% of these patients have complained compared with females. The rate of having out of wedlock children by schizophrenic women in European countries has been 10 times more as compared with schizophrenic women in our country. 

Conclusion: It has been concluded that the schizophrenics are not asexual but they have insufficient knowledge about sexuality; that the psychiatrists should absolutely give information to male and female schizophrenics whom they follow up about sexuality and contraception; that the sufficient knowledge on this subject may affect positively the treatment, prognosis, and quality of life, and that there is need for further studies on this subject. 

References:

NR45 Monday, May 19, 9:00 a.m.-10:30 a.m.
Atypical Antipsychotics Attenuate the Neurotoxicity of H2O2 and A-Beta in PC12 Cells
AstraZeneca Pharmaceuticals, L.P.
Xin-Min Li, M.D., Department of Neuropsychiatry, University of Saskatchewan, 103 Wiggins Road/A4 Med Res Bldg, Saskatoon, SK, S7N 5E4, Canada; Zelian Wei, Ph.D., Zhong-Jun Shao, M.D., Darrell Mousseau, M.D., Lillian Dyck, M.D., Steve Richardson, M.D.

Educational Objectives:
At the conclusion of this presentation, participants should realize that in addition to being effective in the treatment of behavioral disturbances and psychotic symptoms, the atypical antipsychotics quetiapine and olanzapine may slow down the process of neurodegeneration in patients with Alzheimer’s disease or other neurodegenerative disorders.

Summary:
Objective: To investigate the ability of quetiapine and olanzapine to prevent H2O2- and A-beta (25–35) induced cell death in PC12 cells.
Methods: Cell viability was measured using the MTT reduction assay. 
Results: After exposure to increasing concentrations of H2O2 (100, 200, and 400 μM), or A-beta (25–35) (1, 10, and 25 μM), cell viability decreased; pretreatment with quetiapine and olanzapine attenuated the decrease in cell viability accordingly.

Conclusions: Our data suggest that these atypical antipsychotics may have neuroprotective potential to slow down the process of neurodegeneration in patients with Alzheimer’s disease or other neurodegenerative disorders.

References:

NR46 Monday, May 19, 9:00 a.m.-10:30 a.m.
Quality of Life in First-Episode Psychosis With Comorbid Depression
Sim Kang, Department of General Psychiatry, Institute of Mental Health, 10 Buangkok View, Singapore 539747, Singapore; Swapna K. Verma, M.B.B.S., Rathi Mahenoran, M.B.B.S., Siow A. Chong, M.B.B.S.

Educational Objectives:
At the conclusion of this session, the participant should recognize the high prevalence of comorbid depression in patients with first-episode psychosis and treat it in a timely way in light of the associated poorer subjective quality of life.

Summary:
Objective: Previous studies have reported high prevalence rates of depressive symptoms/depression in patients with first-episode psychosis, but data are lacking on the quality of life (QOL) in these patients. This study seeks to compare the QOL of first-episode psychosis patients with comorbid depression, other comorbidities, as well as those without any psychiatric comorbidity in the island state of Singapore.

Methods: One hundred and thirty-one consecutive patients in our Early Psychosis Intervention Program (EPIP) were included in the study. The SCID, SUMD, PANSS, WHOQOL-Bref were administered to determine psychiatric diagnoses, insight, severity of psychopathology, and quality of life respectively. Sociodemographic and clinical data were also collected.

Results: Patients with first-episode psychosis and depression had a shorter duration of hospitalisation (p<0.05), greater insight (lower scores on SUMD item 1,2,3) (p<0.05) but poorer quality of life in the physical health domain (p<0.05) compared with patients without psychiatric comorbidity.

Conclusions: The poorer subjective quality of life in patients with first-episode psychosis and depression may be explained by the greater degree of insight in these patients and their attributing to poor health.

References:

NR47-Monday, May 19, 9:00 a.m.-10:30 a.m.
Shape of the Cingulate and Outcome in Schizophrenia
Serge A. Mitelman, M.D., Department of Psychiatry, Mount Sinai School of Medicine, One Gustave Levy Place, Box 1505,
Summary:
We obtained high-resolution T1-weighted 1.2-mm-thick MR images of 37 patients with schizophrenia and 37 age- and sex-matched controls. The images were reoriented to standard position, segmented into CSF/gray/white tissue types with circulate cortex assigned to Brodmann’s areas using the Perry post-mortem histological atlas. Patients were subdivided into poor-outcome (n=13) and good-outcome (n=24) subgroups. Schizophrenia patients as a group had significant gray matter reductions in anterior perigenual cingulate (BA 24). White matter deficits were observed in right BA 24, whereas white matter volumes were increased in BA 31. Schizophrenia patients showed abnormal white matter lateralization in posteroventral area 30. Poor-outcome subgroup, in addition to these changes, exhibited significant gray matter deficits in posterior areas 29 and 31. Abnormalities in volumetric lateralization in poor-outcome group were found in BA 31 for gray matter and subcallosal area 25 for white matter volumes. Thus, poor outcome in schizophrenia may be associated with gray matter deficits in posterior cingulate/retrosplenial cortex (areas 31/29). This is in concert with our previous finding of a general tendency of schizophrenia.

References:

NR49 Monday, May 19, 9:00 a.m.–10:30 a.m.
Effectiveness of Zaleplon Versus Trazodone for the Treatment of Insomnia in Psychiatrically-Treated Inpatients: A Pilot Study
Subhdeep Virk, M.D., Department of Psychiatry, SUNY Upstate Medical University, 750 East Adams Street, Syracuse, NY 13210; Nikhil D. Nihalani, M.D., Shefali Jindal, M.D., Thomas L. Schwartz, M.D., Anne Costello, M.D., Ray Muldoon, R.N., Nouman Azhar, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be better able to treat insomnia in psychiatric inpatients.

Summary:
Objective: To assess the effectiveness of two hypnotic agents on psychiatric inpatients with insomnia. trazodone (Desyrel), a sedating antidepressant used off-label, was compared with zaleplon(Sonata), an FDA-approved drug to treat insomnia, in order to see which is more effective and tolerable
Method: Fifteen patients were assigned openly and randomly to receive trazodone (50–100mg) or zaleplon (10–20mg). Analogue sleep scales, sleep logs, Eppworth Sleepiness Scales were completed daily.
Results: Seven subjects received zaleplon and eight received trazodone. One subject discontinued zaleplon due to headache and another discontinued trazodone due to postural hypotension. Five zaleplon subjects showed ESS improvement, three showed Analogue Sleep Scale improvement. The ESS improved only in two trazodone subjects and worsened in five patients due to morning residual sedation side effects. The Analogue Sleep Scale improved in six subjects. Trazodone patients were statistically more likely to sleep longer.
Conclusion: This pilot study suggests that trazodone may be a better agent to promote subjectively deeper, longer, sleep for psychiatric inpatients with insomnia. However, tolerability was better with zaleplon as daytime residual side effects were less. Trazodone’s residual daytime sedation may affect patients’ ability to wake up and participate fully in ward activities.

References:
NR50  Monday, May 19, 9:00 a.m.-10:30 a.m.
Towards a New Model of Sleep EEG Delta Activity Dynamics
Supported by Belgian National Scientific Research Funds
Xavier A. Preud'Homme, M.D., 1016 Sycamore Street, Durham, NC 27707-2136; Andrew D. Krystal, M.D., Jean-Pol Canquart, Ph.D., Philippe Bogaerts, Ph.D., Paul Linkowski, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand a new model of Delta power dynamics and its potential utility for studying sleep pathophysiology.

Summary:
Background: The standard for studying sleep is the polysomnogram (PSG), where physiologic time series (EEG/EOG/EMG) are used to partition the night into a sequence of stages. The criteria for staging have never been validated physiologically, which may explain the PSG’s limited utility. An advance occurred when Borbély quantified slow-wave activity (SWA) in PSG EEG data and incorporated these data into a model of sleep homeostasis. We now build on this work, presenting a model, which, unlike the Borbély model, does not involve PSG staging and includes some promising new mathematical features.

Methods: Delta (0.5-3 Hz) spectral power was computed in 5 second epochs from a vertex-to-mastoid EEG channel in 18 healthy men (21–29 years). The model was fit using iterative nonlinear regression (simplex algorithm) assuming that SWA is a sinusoid with period and amplitude that decreased over time. The sinusoid was raised to an exponent (>2) to better fit the proportion of REM to NREM duration across the night. Statistics reflecting model fit are detailed. The model particularly well characterizes SWA dynamics including oscillation, decreasing period and amplitude over time. Statistics reflecting model fit are detailed.

Conclusion: The model captures many aspects of SWA dynamics without staging and merits further study.

References:

NR51  Monday, May 19, 9:00 a.m.-10:30 a.m.
Seasonal Changes in Self-Reported Sleep Duration in Students
Supported by Pfizer Inc.
Janna Volkov, M.D., Department of Psychopharmacy, St. Elizabeth’s Hospital, 2700 Martin L. King Jr Avenue SE, Washington, DC 20032; Kelly J. Rohan, Ph.D., Samina M. Youssouf, M.D., Michael A. Jackson, B.S., Courtney M. Thrower, B.A., Charles O. Agumadu, M.D., Teodor T. Postolache, M.D.

Educational Objectives:
At the conclusion of this session, the participant will be able to recognize biological and social determinants of seasonal changes in sleep duration in students.

Summary:
Objectives: The biological (“internal”) night, determinant of sleep duration, is longer in winter than in summer in seasonal affective disorder (SAD) patients, but not in healthy controls. We thus hypothesized that seasonality will correlate positively with absolute difference between winter and summer sleep duration.

Methods: Participants were 820 students living in the Washington, DC metropolitan area who completed a Seasonal Pattern Assessment Questionnaire (SPAQ), which was used to calculate a global seasonality, score (GSS) and classify subjects in seasonal and nonseasonal. We performed simple correlations between GSS and the absolute difference between winter and summer sleep duration. Paired t-tests were also used to compare winter and summer sleep duration in the entire sample and separately in seasonal subjects.

Results: Winter-summer differences in sleep duration were significant and positively correlated with GSS (p<0.001), as hypothesized. Overall, students reported sleeping longer in the winter than in the summer (p < .001). Surprisingly, students with winter SAD slept less in winter than in summer (p < .001).

Conclusions: Although biological “internal” night may drive sleep duration, motivation and environmental demands could also play a significant role. A decreased efficiency of academic performance secondary to winter depression may result in a compensatory decrease in winter sleep duration to meet academic demands.

References:

NR52  Monday, May 19, 9:00 a.m.-10:30 a.m.
The Efficacy of Biofeedback Treatment in Patients With Chronic Headache
Yu Bum-Hee, Department of Psychiatry, Samsung Medical Center, 50 Ilwon, Kangnam-Ku, Seoul 135-710, South Korea; Kim Sang-Wook, Tang Myung-Sum, Kang Eun-Ho

Educational Objectives:
At the conclusion of this session, the participant should be able to assess the efficacy of biofeedback treatment in patients with chronic headache.

Summary:
Objectives: The purpose of this preliminary study is to assess the efficacy of biofeedback treatment in patients with chronic headache.

Method: Six patients with chronic tension type headache (TH) and five patients with migraine headache (MH) were recruited and received eight sessions of biofeedback treatment for four weeks. Biofeedback treatment for patients with TH consisted of EMG trainings with relaxation techniques. Biofeedback treatment for patients with MH consisted of temperature trainings with relaxation techniques. Headache severity was assessed using MPQ (McGill Pain Questionnaire). CGI (Clinical Global Impression) scale and
VAS (visual analogue scale) at the first 4th and final sessions. We also measured MIDAS (Migraine Disability Assessment Scale). STAIS & STAIT (Spielberger state & trait anxiety inventory). Hamilton depression rating scale (HAMD) and Hamilton anxiety rating scale (HAMA) in all subjects. Each of the subjects was asked to keep a headache diary during four weeks of biofeedback treatment.

Result: For patients with TH significant improvement was observed for sensory subscale of MPQ(t=4.66, p=0.006), VAS(t=4.54, p=0.007) and CGI(t=3.00, p=0.03) during eight sessions of biofeedback treatment. HAMD(t=4.64, p=0.006) and HAMA(t=6.08, p=0.002) scores were significantly reduced during biofeedback treatment in patients with TH. For patients with MH, significant improvement was observed for VAS(t=4.22, p=0.06) and CGI(t=4.64, p=0.013) during 8 sessions of biofeedback treatment. HAMD and HAMA scores did not show significant changes during biofeedback treatment.

Conclusion: These results suggest that biofeedback treatment with relaxation techniques could help to improve headache symptoms.

References:

NR53  Monday, May 19, 9:00 a.m.-10:30 a.m.
Self-Esteem in Patients With BDD
Supported by NIMH, Eli Lilly and Company, Forest Laboratories, Inc., and Gate Pharmaceuticals
Satyam Jain, M.D., Butler Hospital, Brown University, 345 Blackstone Boulevard, Providence, RI 02906; Katharine A. Phillips, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will be knowledgeable about the association between body dysmorphic disorder and self-esteem.

Summary:
Introduction: It has been hypothesized that patients with BDD have low self-esteem, but this hypothesis has been only minimally researched. The few studies done to date have found that BDD patients tend to have low self-esteem, but these studies had limitations such as a small sample size, use of nonclinical student samples, and diagnosis of BDD using self-report questionnaires.

Method: 93 consecutive participants in BDD pharmacotherapy studies (27 males and 66 females; mean age=32.1 ± 10.5) with current DSM-IV BDD (clinically diagnosed with a reliable measure) completed the Rosenberg Self-Esteem Scale (RSES). This is a reliable, valid, and widely used self-report measure of self-esteem; higher scores indicate more positive self-esteem. Reliable and valid scales assessed BDD severity, delusionality (how delusional appearance-related beliefs are), and depressive symptoms. Participants in a double-blind treatment study of fluoxetine vs placebo completed the RSES at study baseline and endpoint (n=54).

Results: The mean RSES score was 23.8 ± 5.4, which is approximately one and a half standard deviation units lower than commonly reported means for nonclinical samples. Poorer self-esteem was significantly associated with more severe BDD (r=−.39, p=.0001) and depressive (r=−.60, p=.0001) symptoms as well as greater delusionality (r=−.32, p=.003). Delusional patients had significantly poorer self-esteem than nondelusional patients (t=3.0, df=87, p=.003). Self-esteem did not improve significantly more with fluoxetine than placebo treatment (F(1,51)=1.06, p=.31), although there was a trend for treatment responders to have greater improvement in self-esteem than treatment nonresponders (F(1,51)=3.03, p=.09).

Conclusion: This study, the largest to assess self-esteem in BDD, found that these patients have poor self-esteem. Poorer self-esteem was associated with more severe BDD and depressive symptoms as well as greater delusionality.

References:

NR54  Monday, May 19, 9:00 a.m.-10:30 a.m.
Quetiapine Augmentation in Treatment-Resistant OCD
AstraZeneca Pharmaceuticals, L.P.
Ann M. Bogan, M.D., Psychiatry Department, Stanford University, 401 Quarry Road, Room 2142, Stanford, CA 94305; Helen W. Chuong, M.S., Lorrin M. Koran, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to discuss augmentation with atypical neuroleptics in treatment-resistant OCD.

Summary:
Objective: Many patients with obsessive-compulsive disorder (OCD) are treatment resistant to serotonin reuptake inhibitors (SRIs). In such cases, evidence supports augmentation with an atypical neuroleptic. We describe an open-label study of augmentation with the atypical neuroleptic quetiapine in treatment-resistant OCD.

Method: In an eight-week trial, 16 outpatient adults with a primary DSM-IV diagnosis of OCD treatment resistant to at least one adequate SRI trial received quetiapine augmentation. Fourteen subjects completed the trial; two withdrew due to adverse effects. Behavioral ratings including Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) were obtained.

Results: The subjects’ mean Y-BOCS score was 27.7 ± 7.0 (range, 13 [obsessions only] – 39) at baseline and 23.3 ± 8.4 (range, 6 – 36) at endpoint. Y-BOCS scores decreased a mean of 16.3% ± 22.7. The responder rate (≥25% decrease in Y-BOCS score) was 31.3%. All participants experienced at least one adverse event, but most were mild. The most common adverse effects were sedation (11/16) and fatigue (9/16).

Conclusion: Quetiapine augmentation may benefit SRI-resistant OCD. Despite the history of treatment resistance in our subjects, nearly one-third responded. Our responder rate (31.3%) falls within the range reported in other atypical neuroleptic augmentation trials (30–100%). Large-scale, double-blind, placebo-controlled trials comparing different atypical neuroleptic augmentors in treatment-resistant OCD are needed.

References:

NR55  Monday, May 19, 9:00 a.m.-10:30 a.m.
Psychiatric Recidivism: A Comparison of Single and Multiple Readmissions
Sanjoy Sathpathy, M.D., Department of Child Psychiatry, Brookdale Hospital, 68 Garden Terrace, North Arlington, NJ 07031; Nyapati R. Rao, M.D.

Summary:
Introduction: Purpose of the study is to identify the reasons for the high readmission rate to psychiatric in-patient units in an inner city hospital.
Methods: A sample of consecutive patients encountered in psychiatric emergency department of an inner city hospital (N=79) within a period of one month was obtained. A retrospective review of readmission over a period of 10 years was done from two different sources. Control group (N= 29), was chosen from subjects with a single readmission. Study group (N=50) was chosen from subjects with multiple readmissions. Data were compared across several variables in an effort to identify characteristic features such as socio-demographic status, substance use comorbidity, diagnosis, and length of inpatient stay.
Results: The variables predicting a high rate of multiple readmissions are: young (<35), comorbid substance use disorder and unmarried status. Drug abusers are more vulnerable than those with drug dependence for multiple readmission. Readmission rate was seen to increase as length of stay in inpatient unit increased. Diagnosis variation between first encounter and subsequent encounters does not influence readmission.
Conclusion: Intensive management protocol for younger patients with dual diagnosis and effective disposition for comorbid substance abusers should be considered as an attempt to reduce multiple readmissions of psychiatric patients to an inpatient service.

NR56  Monday, May 19, 9:00 a.m.-10:30 a.m.
Pretreatment Measures of Impulsivity, Aggression, and Sensation Seeking Predict Treatment Outcome for African-American, Cocaine-Dependent Individuals National Institute on Drug Abuse
Heather W. Murray, B.A., Department of Psychiatry, Thomas Jefferson University, 833 Chestnut East, Suite 210E, Philadelphia, PA 19107; Ashwin A. Patkar, M.D., Raman N. Gopalakrishnan, M.D., Edward Gottheil, M.D., Anup M. Desai, M.D., Loual A. Bilal, M.D., Michael J. Vergare, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should recognize the importance of impulsivity, aggression, and sensation-seeking as possible clinical predictors of treatment-outcome of cocaine patients.

Summary:
Objective: We investigated whether measures of impulsivity, aggression, and sensation seeking differed between cocaine-dependent subjects and controls, and whether these measures were related to treatment outcome for cocaine patients.
Method: Pre-treatment assessments of impulsivity (Barratt Impulsivity Scale [BIS]), aggression (Buss-Durkee Hostility Inventory [BDHI]), and sensation seeking (Zuckerman Sensation seeking scale [SSS]) were obtained for 141 African-American, cocaine-dependent individuals entering a 12-week, intensive outpatient treatment program and 60 controls. The outcome measures were number of negative urine drug screens, days in treatment, dropout rates, and number of treatment sessions.
Results: Cocaine patients reported significantly higher scores on the SSS, the BIS and the BDHI than controls. Furthermore, the SSS scores showed a significantly negative correlation with days in treatment and negative urines, and a significant positive correlation with the dropout rate. The BIS and the BDHI scores were significantly associated with days in treatment and dropout rates, respectively. A combination of the three behavioral variables contributed significantly toward predicting retention and abstinence.
Conclusion: Higher levels of pretreatment impulsivity and aggression and sensation seeking seem to predict poor treatment-outcome for cocaine abusers receiving intensive outpatient treatment. Combining these behavioral measures with other clinical predictors may help in early identification of ‘poor responders’ who may benefit from additional or alternative treatment approaches.

References:

NR57  Monday, May 19, 9:00 a.m.-10:30 a.m.
The Positive Effect of Mirtazapine in Benzodiazepines’ Detoxification Supported by Organon Pharmaceuticals Inc.
Kostas Papakonstantinou, M.D., Substitution Unit, Organization Against Drugs, 46 Kapodistriou Street 10432, Athens 10432, Greece; Georgia Spiropoulou, M.D., Emilos Katsoulakos, M.D., Barbara Vriniotou, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to have new options on benzodiazepines’ detoxification treatment

Summary:
Mirtazapine has been reported as an effective antidepressant agent. In a cohort of unselected patients addicted to benzodiazepines who had been also enrolled in a methadone substitution program, we estimated the efficacy of mirtazapine to relief anxiety symptoms and symptoms of withdrawal due to detoxification from benzodiazepines. Furthermore, we examined the influence of mirtazapine on the general course of these patients in the program.
Method: We randomized 80 patients in two groups of 30 patients each. The patients of the first group received a progressively reducing dose of diazepam for five weeks and the patients of the second group received diazepam and mirtazapine. The baseline characteristics of the patients between the two study groups, including age, sex, and severity of addiction, did not differ significantly, while patients with mental or pathological comorbidity were excluded. For a total period of 10 weeks, we were estimating the parameters of anxiety with Hamilton Scale of Anxiety and an auto-estimation scale. At the same time, we were transcribing the amount of benzodiazepines and other substances in the urine, trying to detect their possible "relapses".
Conclusion: The mirtazapine group presented a statistically significant reduction of many parameters and of total score in the Hamilton Scale, while there was some indicative data about the same group for a reduction of relapses in all substances. Our data suggest that mirtazapine may induce beneficial effects on adaptation in the substitution program when administered to patients also addicted to benzodiazepines.
References:

NR58 Monday, May 19, 9:00 a.m.-10:30 a.m.
Predictable Factors for Completion of Outpatient Detoxification and Retention in Ongoing Outpatient Treatment
Ayman M. Farreed, M.D., Department of Psychiatry and Substance Abuse, McLean Hospital, 115 Mill Street, Belmont, MA 02478-9106; Joseph G. Libertao, M.D., Paul Benson, Ph.D.

Educational Objectives:
The goal of this project was to identify factors associated with completion of outpatient detoxification and retention in ongoing outpatient treatment for patients treated at a large urban area Veterans Administration ambulatory detoxification program. Specifically, the project addressed the following questions:
1. Are certain patient characteristics predictive of detoxification completion and continuation in ongoing treatment (e.g., substance of choice, polydrug dependence, presence of psychiatric or medical illness)?
2. For opioid addicts in ambulatory detoxification, does the use of an opioid agonist-antagonist in treating opiate withdrawal improve the rate of detoxification completion compared to the use of medication targeted only at symptom relief?

Summary:

Background: High rates of drop out and relapse have been reported particularly for opioid-addicted patients in ambulatory detoxification settings. Since it is widely believed that longer periods of treatment result in better outcomes, and out of a need to improve the delivery of clinical services in their ambulatory detoxification program, the VA Maryland Health Care System (VAMHCS) Substance Abuse Treatment Program implemented the following Performance Improvement project.

Method: All ambulatory detoxification patients treated at the Baltimore VA between 01/01/2001 and 09/30/2001 had their charts reviewed for primary diagnosis at time of admission, medication used for detoxification and presence or absence of psychiatric and/or medical co-morbidity at time of admission.

Conclusion: Patients diagnosed with alcohol dependence had higher rates of completion of detoxification and retention in ongoing treatment than patients diagnosed with opiate dependence or polydrug dependence (83% vs 58%, 51% for completion of detoxification) and (81% vs 20%, 43% for retention in ongoing outpatient treatment). Similarly, patients with medical and/or psychiatric comorbidity had higher rates of completion and retention than did those patients without co-morbidity (75% vs 51% for completion of detoxification) and (100% vs 46% for retention in ongoing outpatient treatment). In addition, there was a higher rate for completion of detoxification for opioid addicted patients treated for the first three days with buprenorphine compared to those treated with clonidine (83% vs 50%).

References:
Summary:
Objective: Depressive symptoms in persons with dementia are often elicited from proxy sources by either a specific scale (e.g. Collateral Source Geriatric Depression Scale, CS-GDS) or as part of a global scale (e.g. the Neuropsychiatric Interview, NPI). This study compares the depression subscale of the NPI with the CS-GDS in identifying depression.

Method: Outpatients with an MMSE < 24 were included. A proxy source was questioned about the presence of depression with the screening question from the NPI. The sensitivity and specificity of the NPI screening question was compared to the CS-GDS. The mean number of symptoms endorsed by depressed vs. non-depressed patients on both the NPI and the CS-GDS were compared.

Results: The 272 subjects (73% female) had a mean age of 80.7, and 11.8 years of education. The NPI depression screen identified 167 patients as depressed. The sensitivity and specificity were 74% and 69% respectively, using a CS-GDS cut-off of 8. The mean number of symptoms on the CS-GDS was significantly greater in depressed patients (5.5 vs. 9.4, p < .0001).

Conclusions: The depression screening question of the NPI may be useful in identifying depression. When the NPI is used, it may be unnecessary to use an additional depression inventory.

References:

NR62 Monday, May 19, 9:00 a.m.-10:30 a.m.
Sustained Nuclear Translocation of ERK1/2 After Electroconvulsive Shock in the Rat Frontal Cortex
Yong Sik Kim, M.D., Department of Psychiatry, Seoul National University, 28 Yongon-Dong Chongno-gu, Seoul 110-744, Korea; Se Chang Yoon, M.D., Ung Gu Kang, M.D., Sook Ja Jun, Myoung-Sun Roh, M.D., Young Jin Koo, M.D., Hee Yeon Jung, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize ECS may modulate gene expression through sustained nuclear translocation of ERK1/2 in the brain.

Summary:
Electroconvulsive shock (ECS) can activate ERK1/2 in the brain. But this activation is only transient when observed in the whole tissue lysate, and its role in the regulation of gene expression is not clear. Therefore, we examined the effect of ECS on ERK1/2 in the nuclear preparation.

Male S-D rats were treated with ECS and sacrificed at predetermined time points. Frontal cortex, hippocampus, and cerebellum were dissected. Nuclear fractions were extracted and subjected to immunoblot analysis.

In the nuclear fraction from the frontal cortex, ERK1/2 were increased 2 to 180 minutes after ECS, and phospho-ERK1/2 were also increased until 180 minutes after ECS. There was no sustained nuclear accumulation of ERK1/2 in the cerebellum and the hippocampus. The phosphorylation of Elk-1. an ERK-downstream transcription factor, was well-correlated to the amounts of nuclear ERK1/2. In the whole tissue lysates, the complex formation of ERK1/2 and MEK1/2, ERK kinase and potentially “anchoring” molecule of ERK, was decreased after ECS. This effect was most prominent in the frontal cortex.

In short, we demonstrated that ECS induces sustained nuclear translocation of ERK1/2 in the rat frontal cortex, and we suggested that ECS may modulate gene expression via ERK1/2 pathways in regionally differential manner.

References:
Using TMS to Assess Cortical Excitability in Patients With Major Depression

Paul A. Zarkowski, M.D., Department of Psychiatry, CWRU/University Hospital, 11100 Euclid Avenue, Cleveland, OH 44106; Rajani Rajan, Pedro L. Delgado, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should understand a method for assessing cortical excitability using transcranial magnetic stimulation and motor evoked potentials. The participant should be able to recognize the pattern of decreased cortical excitability that may occur in patients with major depression.

Summary:
- **Introduction:** Transcranial magnetic stimulation (TMS) activates the corticospinal tract via stimulation of pre-synaptic interneurons. When combined with measurement of motor evoked potentials (MEP), it has been used to measure cortical excitability, which may be decreased in depressed patients.

- **Methods:** Five controls (mean age 27 y.o.) and four inpatients with major depression (mean age 32 y.o.) received TMS at 115% motor threshold in sets of 5 trains of 5 stimuli at 0.2 Hz, with 30 s pauses between trains. Pre-exercise MEPs were measured at the contralateral abductor pollicis brevis (APB) over multiple sets. APB MEP was exercised for 15 s at 20% maximum. 5 exercise periods and post-exercise TMS sets were performed. Hamilton Depression scale score for patient, ranged from 16 to 23. Psychotropic medications included paroxetine, citalopram, olanzapine, resperidone and zolpidem.

- **Results:** MEP for controls increased 78±27% after exercise while the patient’s increased only 8±13% (P=0.002). Variations included paroxetine, citalopram, olanzapine, resperidone and zolpidem.

- **Conclusion:** Attenuation of post-exercise MEP facilitation in depressed patients suggests decreased cortical excitability. Further study is required to identify the mechanism of this effect and the possible impact of psychotropic medications.

References:

Cortical Abnormalities in Autism: MRI Application of the Gyrification Index

Roger J. Jou, B.A., Department of Psychiatry, University of Pittsburgh, 88 22nd Street #3, PO Box 42316, Pittsburgh, PA 15203-0316; Antonio Hardan, M.D., Nancy J. Minshew, Ravi Varma, B.S., Macheri S. Keshavan, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should (1) appreciate the potential role of gyration in understanding neuropsychiatric disorders, (2) understand the implications of abnormal gyration in autism, (3) identify the limitations of the current study and interpret its results in the context of those limitations.

Summary:
- **Objective:** The gyrification index (GI) measures cortical convolutedness. Its examination in autism may yield valuable information about the developmental pathophysiology of this disorder.

- **Method:** Using MRI and modeling software, GIs were calculated in vivo for 52 non-meditating healthy men with autism and 52 normal controls. All 52 men and 39 of the healthy controls were right-handed. GIs were measured bilaterally using the first coronal slice anterior to the corpus callosum. Inner and outer contours were traced manually to allow the measurement of the GI.

- **Results:** Mean GI values did not differ between autistic and control groups. There was a decrease in GIs with age in the autistic group (left: R = -0.479, p = 0.006; right: R = -0.438, p = 0.012), but not in controls (left: R = -0.065, p = 0.725; right: R = -0.122, p = 0.507). Findings remained unchanged after adjusting for total brain volume.

- **Conclusions:** Whereas GI normally reaches a stable plateau after birth and remains stable afterwards, this pattern may be different in autism. These preliminary findings may account for some of the developmental abnormalities observed in autism and should be replicated in future studies examining multiple slices in different brain regions, and in subjects with a wide range of symptom severity.

References:

NR66  Monday, May 19, 9:00 a.m.-10:30 a.m.
The Neural Basis of Maternal Emotional Responsiveness: An fMRI Study of Mothers Viewing Videos of Infants
Supported by Welcome Trust
Sandeep Ranote, M.R.C., Department of Psychiatry, University of Manchester, 17 Thomas Telford Basin, Piccadilly Village M1 2NH, United Kingdom; Rebecca Elliott, Ph.D., Kathryn Abel, M.D., Rachel Mitchell, Ph.D., Bill Deakin, M.D., Louis Appleby, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize brain regions involved in maternal emotional responsiveness to infants and appreciate the distinct pattern of neural response in healthy mothers when viewing their own compared to someone else’s infant.

Summary:
Objectives: Abnormalities of maternal emotional responsiveness are seen in mothers with severe mental illness [1]. Parental lack of responsiveness inhibits bonding and the child’s development of secure attachments. This study’s aim was to develop an FMRI paradigm to examine the neural correlates of maternal emotional responsiveness in healthy mothers first. We predicted responsiveness to infants’ facial expressions would be associated with neural response in regions previously implicated in normal emotion response (medial prefrontal cortex, amygdala, orbitofrontal cortices, visual cortex, temporal lobe) [2] and would be enhanced when viewing ‘own’ compared to ‘other’ (genetically unrelated) infant.

Method: 10 healthy mothers viewed alternating blocks of video during one 8 minute experiment: i) 40s ‘own’ infant; ii) 20s ‘neutral’ video; iii) 10s ‘other’ infant and iv) 20s ‘neutral’ video, repeated four times.

Results: Areas activated when mothers viewed ‘infants’ compared to ‘neutral’ video included bilateral visual processing regions (superior temporal gyr; right medial occipital gyrus, left medial temporal lobe) and bilateral cerebellum. When viewing ‘own’ compared to ‘other’ activation in visual processing regions was stronger and prominent activation of right anterior temporal cortex and left amygdala were seen.

Conclusions: These results demonstrate the feasibility of using FMRI to study the neural correlates of maternal emotional responsiveness to infants’ facial expressions and are consistent with previous findings. Further studies must address this effect in more detail.

References:

NR68  Monday, May 19, 9:00 a.m.-10:30 a.m.
Increased 5-HT2a Receptor Binding in Depression, Post-Myocardial Infarction
Adriaan Honig, M.D., Department of Psychiatry, Brain and Behavior, P. Debyelaan 25, Maastricht 6202 AZ, Netherlands; Annette Schins, M.D., Marinus Kroonenburgh, M.D., Koen van Laere, M.D.

Summary:
Objective: In this study 5-HT2A binding was assessed in depressed post-myocardial infarction (post-MI) patients as compared to non-depressed, post-MI patients and healthy controls. The hypothesis was to find an increased 5-HT2A binding in depressed post-MI patients as compared with non-depressed post-MI patients and healthy controls.

Method: Twelve depressed post-MI patients and ten non-depressed post-MI patients underwent single photon emission computed tomography (SPECT). Patients had no psychotropic medication. Ten healthy subjects were individually matched with the MI patients for sex and age. SPECT images were obtained using 1-5-1-R91150, a new 5-HT2A receptor antagonist.

Result: Depressed post-MI patients have an increased 5-HT2A receptor binding as compared with non-depressed post-MI patients. Contrary to our expectations, MI patients have decreased 5-HT2A receptor binding as compared with age-matched healthy controls.

Conclusion: myocardial infarction is associated with decreased cerebral 5-HT2A receptor binding and depression post-MI is associated with increased cerebral 5-HT2A receptor binding as compared with non-depressed post-MI patients.
References:

NR69 Monday, May 19, 9:00 a.m.-10:30 a.m.
Association of Medical Factors to MRI Hyperintensities in Bipolar Disorder
Victoria M. Payne, M.D., Department of Psychiatry, Duke University Medical Center, Erwin Road, Box 3837, Durham, NC 27710; John L. Beyer, M.D., Frederick Cassidy, M.D., Melissa Moo Young, M.D., K. Ranga R. Krishnan, M.D.

Objective: To examine the relationship of medical factors in bipolar disorder to MRI hyperintensities.

Method: Brain MRI scans from 127 bipolar patients and 59 controls were evaluated for severity of periventricular (PVH), deep white matter (DWMH) and subcortical (SCH) hyperintensities. Data obtained from interviews included patient status (bipolar versus control), gender, age, age of bipolar onset, history of hypertension, cardiac disease, diabetes, suicide attempts, and family history of psychiatric disorder. The relationships between these medical factors and hyperintensity severity were examined using t-tests and Fisher’s Exact test. Logistic regression analyses were performed to evaluate predictive ability.

Results: Age was significantly older for bipolar patients with severe (versus non-severe) PVH (p<0.0001) and DWMH (p=0.0002). Late age of onset and hypertension were significantly associated with severity of DWMH hyperintensities (p-values=0.0205 and 0.0062). Other medical factors were not significantly associated. In logistic regression analyses including nonbipolar subjects, age was a significant predictor of PVH severity. Age and patient status were significant predictors of DMWH. Other medical factors did not predict hyperintensity severity.

Conclusion: Age, patient status, age of onset, and hypertension are associated with PVH and DMWH in bipolar disorder. Further studies are required to elaborate on these findings, and to help differentiate bipolar and unipolar disorders.

NR70 Monday, May 19, 9:00 a.m.-10:30 a.m.
Novel Antipsychotic-Induced Hyperlipidemia in Children and Adolescents With Psychotic and Aggressive Disorders
National Alliance for Research on Schizophrenia and Depression
Christoph U. Correll, M.D., 265-02 74th Avenue, Glen Oaks, NY 11004; Umesh H. Parik, M.D., John M. Kane, M.D., Anil Malhotra, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize & demonstrate that the children with a schizophrenic parent have seen to have psychopathology like more behavioral problems, poor attention, disordered thoughts & low IQ compared to children of normal parents.

Summary:
Objective: To assess the prevalence of behavioral problems, social competence, thought disorders, reaction times and intelligence in children born by schizophrenic vs. mentally healthy parents, and to compare these parameters in the two groups.

Method: Thirty school going children between ages 12–15 years born by a schizophrenic parent and thirty age-matched children born by mentally healthy parents were evaluated. The parameters mentioned above were assessed in both groups using CBCL, SAICA, reaction time apparatus and Weschler’s Intelligence Scale for Children. Comparison was performed using the Mann Whitney Test.

Results: Children of schizophrenic parents showed a greater number of behavioral problems like withdrawal behavior and greater number of social problems like not being liked and dependent behavior and poorer social competence. They also showed greater number of thought problems like positive formal thought disorder symptoms, greater number of attention problems like...
Conclusion: Children of schizophrenic parents show a greater number of thought disorders, behavioral, attention and social problems, poorer social competence, and longer reaction times. Our data thus shows the importance of screening the offspring of schizophrenic parents to identify early neurobehavioral dysfunctions.

References:

NR72 Monday, May 19, 9:00 a.m.-10:30 a.m.
Long-Term Sertraline Treatment in Children and Adolescents With MDD
Pfizer, Inc.
Moira A. Rynn, M.D., Department of Psychiatry, University of Pennsylvania, 3535 Market Street, Suite 670, Philadelphia, PA 19104-3309; Karen D. Wagner, M.D., Craig L. Donnelly, M.D., Paul J. Ambrosini, M.D., Phyllis Landau, M.D., Christopher Wohlberg, M.S.

Educational Objectives:
At the conclusion of this session, the participant should recognize the efficacy and safety of sertraline treatment in children and adolescents with major depressive disorder over a 24-week treatment period.

Summary:
Objective: Major depressive disorder (MDD) is a serious medical problem and can be associated with significant functional impairment that may persist into adulthood. The current study was designed to assess the efficacy and tolerability of open-label sertraline in children and adolescents with MDD who completed either of two 10-week, double-blind, placebo-controlled trials.

Methods: Children (6 to 11 years of age) and adolescents (12–18 years of age) with DSM-IV diagnosed MDD received sertraline in a flexibly-titrated dose range of 50–200 mg/day. The Children’s Depression Rating Scale - Revised (CDRS-R) was the primary measure of efficacy.

Results: 221 subjects (107 children, 114 adolescents) were treated for an average of 150 (children) and 157 (adolescents) days. 62.4% of subjects completed 24 weeks of treatment. The mean decline in CDRS-R score from double-blind baseline was 34.8 points ($p<0.001$) and subjects showed continued improvement in CDRS-R scores regardless of their treatment assignment in the double-blind phase. 6.4% of subjects discontinued from the study for adverse events and 3.6% discontinued for lack of efficacy. Headache, nausea, and insomnia were the most commonly occurring adverse events.

Conclusions: In this study, sertraline was effective and well-tolerated in children and adolescents with MDD over 24 weeks of treatment.

References:

NR73 Monday, May 19, 9:00 a.m.-10:30 a.m.
Medication Exposure in Bipolar Offspring With ADHD or Depression
National Alliance for Research on Schizophrenia and Depression
Kirti Saxena, M.D., Department of Psychiatry, Stanford University, 401 Quarry Road, Palo Alto, CA 94305; Kimberly Dienes, M.A., Kiki D. Chang, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the potential risks of treating bipolar offspring with psychotropic medications.

Summary:
Introduction: Children of parents with bipolar disorder (BD) (bipolar offspring) often present with attention-deficit/hyperactivity disorder (ADHD) and/or depression as children and are at high risk for development of BD. They often are treated with stimulants and antidepressants, which could cause mania in these susceptible children. We sought to characterize early medication exposure in children at genetic risk for BD, who did not yet have BD.

Methods: We collected medication histories from 120 children with at least one parent with bipolar I or II disorder. Parents were diagnosed by the SCID and offspring by the WASH-U-KSADS. Parental history of ADHD was obtained by parent interview. Medication histories (stimulants, antidepressants, antipsychotics, and mood stabilizers) were obtained from parents, physicians, and medical records.

Results: Bipolar offspring with ADHD (n=36) had more exposure to stimulants (27.7% vs. 0%) than depressed offspring (n=18). More subjects with ADHD had exposure to mood stabilizers (16.6%) than depressed children (5.5%). Of the depressed offspring, 50% had exposure to antidepressants, mostly non-SSRIs (78%). Bipolar offspring with ADHD compared with those with depression had a higher number of parents with ADHD ($p<0.02$).

Conclusions: Bipolar offspring are commonly treated with stimulants and antidepressants, which may put them at greater risk for BD development. Bipolar offspring with ADHD may be manifesting initial symptoms of a familial early-onset type of BD. Further studies addressing systematic use of psychotropics in bipolar offspring not yet diagnosed as bipolar are warranted.

References:

NR74 Monday, May 19, 9:00 a.m.-10:30 a.m.
Growing Concern of Lethal Violence Among Children: Trends in Emergency Room Referrals of Children for Psychiatric Evaluation
Valery M. Chernov, M.D., Department of Psychiatry, Bergen Regional, 230 East Ridgewood Avenue, Paramus, NJ 07652; Srikanth M. Reddy, M.D., Alex M. Gollin, M.D., Fouzia A. Aftab, M.D., Edward Hall, M.D.; M. Javed Iqbal, M.D.

Educational Objectives:
Audiences of this poster should be able to recognize the increasing referral of children for psychiatry evaluation in conjunction with assaultive behavior and homicidal threats as well as discuss requirements for future studies evaluating the outcomes of violence intervention policies.
Summary:

Objective: Following the Columbine High School tragedy in April 1999, the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the Substance Abuse and Mental Health Services Administration (SAMHSA) focused on violence among youths. In light of growing concern regarding lethal violence, we wanted to study the change from 2000 to 2001 in the number of referrals of children to our emergency room for reasons of homicidal threats or assaultive behavior as the presenting problems.

Method: Data were collected retrospectively from chart review of children referred to the emergency room at Bergen Regional Medical Center for psychiatric evaluation during March and April of 2000 and the same two months in 2001. Analysis of data was carried out via SPSS software using chi-squared test method.

Results: 87 patients between ages five and 17 were evaluated in year 2000 and 140 were evaluated in year 2001. This represents a statistically significant increase (p < 0.05) in referrals of children to the emergency room for psychiatric evaluation. Assaultive behavior was the reason for referral in 18% and homicidal threats in 7% of the year 2000 group. Assaultive behavior was the reason for referral in 40% and homicidal threats in 11% of the year 2001 group.

Conclusions: The increase in children presenting to a psychiatric hospital emergency room following assaultive behavior or homicidal threats raises questions. Are children becoming more violent, as evidenced by prior events at Columbine High School, or do these statistics reflect the outcome of zero tolerance policies and increasing concern among parents and teachers regarding the risk of lethal violence? Future studies should explore the outcomes of recommendations by the CDC, NIH and SAMHSA as well as the utility of using hospital emergency rooms for management of risk of lethal violence among children.

References:

NR76 Monday, May 19, 9:00 a.m.-10:30 a.m.
Autistic Disorder and Risperidone Direct and Indirect Benefits
Supported by Eli Lilly and Company
Philippe Granato, M.D., Nord, Hospital de Valenciennes, Avenue Desandreouins, Valenciennes 59300, France,

Educational Objectives:
At the conclusion of this session, the participant should recognize that risperidone can be an interesting therapeutic alternative in the spectrum of the autism.

Summary:
Introduction: Serious autistic disorders combine the absence of speech, self-inflicted mutilations, and refusal of contacts. Specialized institutions take care of autistic patients. One observes chronic stress of nursing staff. Work stoppages are an indication of this situation. For medication, there is no medical and therapeutic consensus.

Objectives: Evaluate the efficiency and tolerance of risperidone for serious autism treatment and analyze the socio-economic impact through the indirect benefits for nursing staff and the medical institution.

Method: Ten serious autistic patients : 32 ± 4 resisting traditional therapeutic treatment. Dosage: 16 ± 4 mg/day administered in four separate instances. We counted: (1) annual number of patients hospitalized for secondary traumatisms brought about by behavior disorders and self-inflicted mutilations, (2) number of work stoppage days by nursing staff, (3) annual cost of drugs.

Results: A) After two years of result evaluations, we observe an efficiency that was (1) outstanding for five patients, (2) average for three patients, (3) nonexistent for two patients. B) number of hospitalization decreased by 80%. C) number of work stoppages went from 17% to 9% for the first year and to 6.5% during the second year. D) cost of drugs went down by 19% for the two years.

Conclusion: (1) Risperidone seems to display real efficiency for serious cases of autism. Coprescription of a thymo-regulator enhances the efficiency of risperidone. (2) Indirect positive outcome of this molecule seem certain.

NR75 Monday, May 19, 9:00 a.m.-10:30 a.m.
Diagnosing Intermittent Explosive Disorder in Aggressive Adolescents
Paula Gaudino, M.A., CWS Department, George Washington University, 4480 MacArthur Boulevard, N.W., Washington, DC 20007; Mark J. Smith, M.D., Daniel Matthews, M.D.

Educational Objectives:
At the conclusion of this session, the participant should known the value of using a symptom oriented scale to diagnose intermittent explosive disorder in adolescents.

Summary:
Objective: Adults with unprovoked violent outbursts of rage are sometimes diagnosed with intermittent explosive disorder (IED). Aggressive adolescents are usually diagnosed with some externalizing behavior disorder, but not IED, in part because structured clinical interviews do not test for it. Some aggressive behavior in adolescents may be better explained by IED, and it may be overlooked when comorbid with other diagnoses.

Method: We evaluated 65 adolescents hospitalized for aggressive behavior with the observer-rated version of the IED Scale. The IED Scale consists of 12 yes or no questions on the characteristics of aggressive outbursts as described in DSM-IV and three yes or no rule-out criteria: outbursts not frequent enough, statutory exclusion due to certain DSM-IV diagnoses, and other. We calculated the optimal cut-off score on the 12 severity items. We hypothesized that some of the patients would satisfy criteria for IED and not other commonly used diagnoses of ADHD, CD, BAD, etc.

Results: Mean severity score was 9.42. Using an optimum cut-off of score of 10 and eliminating those with rule-out criteria, 23 (36%) had IED. Most, but not all, had other externalizing behavior diagnoses.

Conclusions: Aggressive behavior in adolescents patients may sometimes be due to IED.

References:
References:

NR77  Monday, May 19, 9:00 a.m.-10:30 a.m.
The Prevalence of QTc Prolongation in a Consultation-Liaison Psychiatry Population
Kien T. Dang, M.D., General Inpatient Department, CAMH
Clark Site, 250 College Street, Suite 530, Toronto, ON M5T 1P8, Canada; Rima Styra, M.D.

Educational Objectives:
At the end of the session, the participant should be able to recognize the high prevalence of QTc prolongation in a consultation-liaison psychiatry population and should be aware of the importance of monitoring the QTc when prescribing medications that can further prolong the QTc interval increasing the risk of sudden death.

Summary:
Objective: We investigated the prevalence of QTc prolongation in hospitalized patients who have received an ECG. We suspect that this population, served by a consultation-liaison psychiatry service, has a high prevalence of prolonged QTc.
Method: ECGs performed on all inpatients and patients seen in pre-admission clinics were collected over a 17-day period in a major teaching hospital. ECGs acquired in critical care units were excluded. Only the first available ECG per patient was included. The prevalences of QTc prolongation greater than 450 msec and 500 msec in all hospitalized patients who received an ECG were calculated.
Results: 2,064 ECGs were collected. After excluding ECGs from critical care and duplicates, ECGs from 823 individual patients were analyzed. 24.9% had QTc prolongation greater than 450 msec and 5.8% greater than 500 msec. The prevalences were slightly higher in females and higher in patients greater than 65 years of age. These results are collaborated in other literature. The prevalences are also higher in patients in medical subspecialties compared to surgical admissions.
Conclusions: One-fourth of hospitalized patients have prolonged QTc. A possible implication may be that, psychiatrists should obtain a baseline ECG when prescribing antipsychotics and exercise caution in baseline QTc prolongation patients.

References:

NR78  Monday, May 19, 9:00 a.m.-10:30 a.m.
Use of Psychotropics in Late-Onset Tay Sachs Disease (LOTS)
Mount Sinai Health Care Foundation of Cleveland
Susan H. Friedman, M.D., Department of Psychiatry, Case Western Reserve, 11100 Euclid Avenue, Hanna Pavilion, Cleveland, OH 44106; Barbara E. Shapiro, M.D., Jose A. Fernandez, M.D., Kyle Anthony, B.A.

Educational Objectives:
At the conclusion of this session, the participant should be able to better diagnose LOTS when it presents with psychiatric features. The participant will recognize which medications are safest for use in LOTS.

Summary:
Objective: This study's purpose was to provide epidemiologic confirmation of isolated reports that certain medications used to treat depression and psychosis in patients with late onset Tay Sachs Disease (LOTS) exacerbate the disease. LOTS is a lysosomal storage disorder, characterized by partial deficiency of hexosaminidase A with manifestations including psychosis, mania, depression, dementia, cerebellar ataxia, weakness, spasticity, dysarthria, and basal ganglia disorders.
Method: A retrospective survey with an extensive list of medications was completed by consenting adults with LOTS, indicating medications taken and effects, while a prospective diary of medications and effects was kept for four months. Percentage who worsened, improved, or had no effect from the medication were calculated.
Results: 41 patients participated 21 males and 20 females. Mean age was 39 years. Approximately 80% of surveys were returned. Medications most frequently worsening LOTS included haloperidol, risperidone, clonazapine, and bupropion. Medications that were relatively safe, and improved symptoms, included valproate, carbamazepine, and lithium.
Conclusions: The survey data confirmed reports of worsening symptoms and increased vulnerability to side effects in patients with LOTS exposed to certain psychotropic medications. Newer classes of psychotropic medications were also implicated. Other medications were found to be helpful and safe in LOTS.

References:

NR79  Monday, May 19, 9:00 a.m.-10:30 a.m.
Pathways to Care: Patterns of Referral of Patients Presenting at the Psychiatric Emergency Room
Ronny Bruffaerts, M.A., Department of Psychiatry, University Hospitals Gasthuisberg, Herestraat 49, Leuven 3000, Belgium; Marc Sabbe, Ph.D., Jean-Pierre Lepine, Ph.D., Koen Demyttenaere, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to provide knowledge on epidemiologic pathways, service use, and diagnostic problems of patients presenting at a psychiatric emergency room (PER). The participants should be able to have an advanced idea of the particularities of patients profiles observed in a psychiatric emergency room. A second educational objective lies in identifying the central role of a PER in the establishment of a psychiatric network.

Summary:
Objectives: Deinstitutionalizing and efforts of cost containment in mental health services have lead to an increased utilization of the psychiatric emergency room. This study aims to describe the patterns of referral and psychiatric history of patients in the psychiatric emergency room.
Method: The setting was a university hospital psychiatric emergency service (PES) between March 2000 and August 2001. All patients (N=2445) were monitored regarding sociodemographic
characteristics (age, gender, living arrangements, and working arrangements), patterns of referral, psychiatric history, and clinical characteristics (DSM-IV axis 1 diagnosis, presenting problems).

Results: Of the sample of 2,445 patients, 33.2% were referred by the emergency physician or the department of internal medicine, 28.9% by health care professionals (GP, psychiatrist, psychotherapist), 18.9% was self-referred, 12.2% was referred by family members, and 8.8% by the police; 64.8% did not have a previous psychiatric hospitalisation. Among patients with a previous hospitalisation (n=1,246), 35.8% was referred to the PES less than two months, 21.0% between two and six months, and 10.9% between six and 12 months after discharge.

Conclusions: A PET could overcome the discrepancy between the need of treatment and the effective use of mental health services.

References:

NR80 Monday, May 19, 9:00 a.m.-10:30 a.m.
Beyond Discharge: Risk Factors of Early Psychiatric Emergency Referrals After Psychiatric Hospitalization
Ronny Bruffaerts, M.A., Department of Psychiatry, University Hospitals Gasthuisberg, Herestraat 49, Leuven 3000, Belgium; Marc Sabbe, Ph.D., Jean-Pierre Lepine, Ph.D., Koen Demyttenaere, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to provide knowledge on epidemiologic pathways, service use, and diagnostic problems of patients with a psychiatric history presenting at a psychiatric emergency room. The participants should be able to see the differential impact of the concepts of 'aftercare' and 'continuity of care' with regard to the establishment of managed care in mental health.

Summary:
Objectives: We investigated the influence of sociodemographic, clinical, and treatment characteristics upon an early psychiatric emergency referral after discharge from previous psychiatric hospitalisation. The setting was a university hospital psychiatric emergency service (PES) between March 2000 and August 2001.
Method: All patients with at least one previous psychiatric hospitalisation (N=1243) were monitored regarding age, gender, living arrangements, work arrangements, DSM axis 1 diagnosis, any DSM axis 2 diagnosis, way of discharge, proposed aftercare, and continuity of care. Sociodemographic, clinical, and treatment covariates (expressed in odds ratios) were related to the time interval between discharge from previous hospitalisation and subsequent PES referral.
Results: The risk of a PES referral within 2 months after discharge was influenced by absence of a proposal for aftercare (OR=2.15, CI=1.47–3.14), discharge against medical advice (OR=3.89, CI=2.66–5.30), and absence of continuity of care within 1 week after discharge (OR=2.38, CI=1.16–4.88).
Conclusions: Early psychiatric referrals were exclusively associated with treatment characteristics of the previous psychiatric hospitalisation. In order to reduce early PES referrals after hospitalisation, treatment characteristics of a psychiatric hospitalisation should offer a well-organised discharge planning, including aftercare treatment proposals and continuity of care.

References:

NR81 Monday, May 19, 9:00 a.m.-10:30 a.m.
Cognitive Function and Life Quality According to Hematocrit Levels in ESRD
Heon-Jeong Lee, M.D., Department of Psychiatry, Korea University Ansan Hospital, Ansan-si, Sangbuk-Ku, Seoul 136-705, Korea; Sun-Young Lee, M.D., Kwang-Yoon Suh, M.D., Leen Kim, M.D., Min-Soo Lee, M.D.

Summary:
Objective: This study examined the putative association between the hematocrit levels and improvement of cognitive function as well as quality of life in patients with end-stage renal disease (ESRD).
Methods: Fifty-six ESRD patients were divided into two groups according to their hematocrit levels. Group A consisted of 26 patients with hematocrit levels lower than the median level (27.2 g%), while group B comprised the remaining patients. We compared the neurocognitive function and quality of life in these two groups.
Results: Although patients with higher hematocrit levels scored better in the neurocognitive-function tests such as forward Digit Span (p=0.034) and Digit Symbol (p=0.023) their quality of life evaluated by three scales (Karnofsky scale, Index of Well-Being, and SF-36) was not superior than those with lower hematocrit levels. However, there was a significant correlation between the Beck Depression Inventory score and quality of life (p<0.05).
Conclusions: These findings suggest that higher hematocrit levels improve neurocognitive function but not the quality of life in chronic hemodialysis patients. Psychiatric management for depressive moods is recommended in such patients.

References:

NR82 Monday, May 19, 9:00 a.m.-10:30 a.m.
Risperidone Treatment of Schizophrenia in Children and Adolescents
Texas Department of Health and Mental Retardation
Daniel Lane, Pharm.D., Pharmacy Department, University of Texas, 8701 West Parmer Lane #6228, Austin, TX 78731; Anthony De Leon, Pharm.D., Nick C. Patel, Pharm.D., Molly Lopez, Ph.D., M. Lynn Grimson, Pharm.D.

Summary:
Objective: The purpose of this study was to evaluate the effectiveness of risperidone in children and adolescents with schizophrenia from different ethnic backgrounds.
Methods: Total, internalizing, and externalizing Child Behavior Checklist (CBCL) scores were analyzed at baseline, 90-day, one-year, and two-year periods utilizing repeated measures analysis
of variance. Two-year hospitalization rates and time to hospitalization were measured by the Kaplan-Meier formula.

Results: All groups had significant improvements in CBCL scores at 90 days, one year, and two years post baseline (p<0.05). No significant differences existed between ethnic groups internalizing and externalizing CBCL scores at each time point. There was a significant difference between ethnic groups for total CBCL scores at 90 days (p=0.01), as Hispanic patients had lower scores compared to Caucasian patients. There was no significant difference between ethnic groups in 2-year hospitalization rates or time to hospitalization.

Conclusions: Risperidone was effective in children and adolescents with schizophrenia or schizoaffective disorder. Total, internalizing, and externalizing CBCL scores for all ethnic groups decreased over a two-year period. Hispanic patients had lower total CBCL scores at 90 days compared with Caucasian patients. There was no significant differences in two-year hospitalization rates or time to hospitalization between ethnic groups.

References:

NR83 Monday, May 19, 9:00 a.m.-10:30 a.m.
Catatonia From Clinical Presentation to Diagnosis
Antonio R. Lopez-Canino, M.D., Department of Psychiatry, University Hospital - SUNY, HSC T-10, Suite 020 SUNY-SB, Stony Brook, NY 11794; Bogdan P. Sasaran, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the core catatonic syndrome may decrease catatonia’s heterogeneity and increase its diagnostic confidence.

Summary:
Introduction: Catatonia is a complex syndrome that is diagnosed entirely clinically based on several signs. We hypothesize that certain signs are more observed than others in a way that may result in establishing the minimum clinical requirements for its recognition.

Method: A case control study was conducted on N=117 literature-reported cases of drug-induced catatonia. The DSM-IV-TR, ICD-10 criteria and the Bush-Francis Catatonia Rating Scale (BFCRS) were applied to these cases. A 13-item Sign Inventory for Catatonia (SIC) was created according to the signs' rate of occurrence and was then compared with the DSM, ICD and BFCRS criteria.

Results: Mutism (90.6%), negativism (84.6%), staring (78.6%), and autonomic abnormalities (59.8%) were the most elicited signs. Verbigeration and combative ness were absent in the stuporous group (18% and 41% in the excited group); similarly, there was no waxy flexibility in the excited group (47% in the stuporous group). There were no reports of echolalia phenomena or grasp reflex.

Conclusion: The core catatonic syndrome was established by high rates of mutism, negativism, and staring, which are in contradiction with the sign hierarchy in the DSM, ICD, and BFCRS. Further prospective studies taking into consideration both clinical and statistical significance of these factors are highly needed.

References:

NR84 Monday, May 19, 9:00 a.m.-10:30 a.m.
Do Anxiety and Depression Cause Cancer?
Arnstein Mykletun, M.A., Department of Psychiatry, University of Bergen, Hemil, Christiegt 12, N-5015 Bergen, Norway; Karina Nord, M.D., Sophie D. Fossa, Ph.D., Alv A. Dahl, M.D.

Summary:
Objective: The aim of the present study is to test the hypothesis that anxiety and depression is a risk factor for development of cancer.

Material: Anxiety and depression was measured using the Hospital Anxiety and Depression Scale (HADS) in the HUNT-II study in Nord-Trøndelag County, Norway, in 1995-97. HUNT-II was a population-based health study for the entire adult population (N=62591), with good participation rate (68%). Cancer was identified using the National Cancer Registry.

Methods: Episodes with cancer was included only if diagnosis was established after attendance to HUNT-II. Logistic regression analysis was used with adjustment for known possible founders.

Results: Of the participants in HUNT-II (N=62,591), 2161 persons was registered with malignant cancer diagnosis in the follow-up period, and additionally 849 with premalignancies. HADS anxiety and depression in HUNT-II was predictors of premalignancies (adjusted OR=1.29 and 1.24, respectively), but not malign diagnoses.

Discussion: It is from the literature not clear whether anxiety and depression are risk-factors for cancer, and which biological mechanisms that might be involved.

References:

NR85 Monday, May 19, 9:00 a.m.-10:30 a.m.
The Prevalence of Psychiatric Disorders in 95-Year-Olds
Anne M. Borjesson Hanson, M.D., Psychiatry Department, Clin Neuroscience, Sahlgrenska University Hospital, Goteborg 413 46, Sweden; Eva Edin, M.D., Thorstein Gislason, M.D., Ingmar Skoog, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be aware of how common psychiatric disorders are in the oldest old. Also a very old person with a psychiatric disorder could improve quality of life by receiving adequate treatment.

Summary:
Objective: To study the prevalence of psychiatric disorders in an extreme old population.

Methods: All 95-year-olds registered for census purpose in Göteborg, Sweden, and born between July 1, 1901 and December
31, 1903, were invited to participate in a psychiatric examination (N=531). Of these, 31 (6%) died before the examination, 142 (27%) refused to participate, 17 (3%) were not found, and three (0.6%) could not be examined due to a foreign language, leaving 338 (64%) (75 men, 263 women) for the study. The mean age was 95 years and two months. A telephone interview with a close informant was performed in 283 (84%) subjects by a trained nurse. All psychiatric diagnoses were defined according to the DSM-III-R criteria.

Results: The prevalence of dementia was 56% in women and 37% in men. Among the non-demented, the prevalence for depressive disorders was 20% in women and 13% in men, for psychotic disorders 20% in women and 13% in men, and for anxiety disorders 9% in women and 11% in men.

Conclusions: The prevalence of dementia and depression in this extreme old age are substantially higher in women than in men. Among all 95-year-olds, two-thirds suffer from either dementia or another psychiatric disorder.

References:

NR86 Monday, May 19, 9:00 a.m.-10:30 a.m.
Mania in the Swedish Twin Registry: Criterion Validity and Prevalence
AstraZeneca Pharmaceuticals, L.P.
Federico Soldani, M.D., Department of Epidemiology, Harvard School of Public Health, Department of Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139; Patrick F. Sullivan, M.D., Nancy L. Pedersen, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to appreciate the validity of lifetime-prevalence estimates of mania, as obtained in surveys using standard interview-methodology.

Summary:
Background: In population surveys, mania is commonly assessed by trained lay personnel with structured diagnostic instruments: We examined the criterion validity and prevalence of mania in a survey of Swedish twins conducted with standard interview-methodology.

Method: 41,838 individuals in the Swedish Twin Registry have been evaluated through a telephone questionnaire including the eight DSM-IV mania items, and these data were merged with discharge diagnosis from two comprehensive National registries (the criterion). An algorithm with eight cut-points was used to diagnose lifetime mania, and compared by a receiver operator characteristic (ROC) curve to the criterion. The cut-point requiring at least four positive items resembled a DSM-IV diagnosis.

Results: History of hospitalization for mania was present for 0.7% of all living twins, and predicted non-response to the survey (OR=0.5; 95% CI 0.4-0.6). Prevalence, sensitivity and specificity were at first cut point 3.6%, 39.0% and 96.6%, respectively; at fourth (DSM-IV-like) 2.6%, 36.5% and 97.6%; at last (8 items positive) 0.3%, 18.0% and 99.8%. Positive predictive values were respectively 5.7%, 7.0% and 29.8%.

Conclusions: Performance of the screening for mania in terms of positive predictive power was not satisfactory despite a high specificity. Low population prevalence of mania, criterion choice, non-response bias and inherent limitations of the interviewing-method are among the explanations.

References:

NR87 Monday, May 19, 9:00 a.m.-10:30 a.m.
Quality of Research Reports on Bipolar Disorder
Federico Soldani, M.D., Department of Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139; Nassir Ghaemi, M.D.

Summary:
Objective: To assess quality of recent research reports on bipolar disorder.

Method: All relevant studies (total=679 for 1998–2002) were identified by MEDLINE and PsycINFO searches in 5 journals with the highest ISI Impact-Factors, from which a random sample (n=100: 26 reviews, 74 original articles) was drawn, including 41 on treatment (37 pharmacological, two other somatic, two psychotherapies), 31 on biology (anatomy, genetics, pathophysiology), and 14 on psychopathology.

Results: Among reviews, only 2 (7.7%) were systematic (no qualitative meta-analyses), and 12 (46.2%) were in non-peer-reviewed journal supplements. Among original articles, we classified 26 treatment trials by presence of evidence at levels: [i] double-blind randomized, [ii] open randomized, [iii] large nonrandomized (n>50), [iv] small nonrandomized 50>n>10, [v] case reports/series. Only five (19.2%) reports met criterion i or ii, four (15.4%) met level iii, and 17 (65.4%) were at levels iv or v. Only one study provided a statistical power-analysis, and two included confidence intervals. Median cited methodological references/report was n=2 on validity-reliability, and n=0 for design or statistical methods.

Conclusions: This preliminary analysis suggests that even highly respected psychiatric journals include a majority of reports on bipolar research of limited quality, with insufficient attention to methodological issues, including risks of false-negative error and over-emphasis on hypothesis testing.

References:

NR88 Monday, May 19, 9:00 a.m.-10:30 a.m.
Quality of Randomized-Controlled Trials of Psychotherapies for Alcoholism
Marcelo Q. Hoexter, M.D., Department of Psychiatry, Federal University of Sao Paulo, Rua Andre Dreilis 109/122, Sao Paulo, SP 01252-0102, Brazil; Bernardo G.O. Soares, M.S.C., Mauricio S. Lima, M.D., Jair de Jesus Mari, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to critically appraise the trials that evaluate psychotherapies for...
Objective: To evaluate the quality of randomized controlled trials (RCTs) included in a systematic review and meta-analysis of psychosocial interventions for treating alcohol use disorders.

Methods: A randomized sample of RCTs was evaluated using two validated instruments applied by two independent subjects: Jadad Scale 1996 (3 items, score: 0 to 5), and Moncrieff checklist 1998 (30 items, score: 0 to 60), where higher score means better quality. Inter-rater reliability (Kappa Test) was established and the results of the instruments related.

Results: The search strategy resulted in 2,300 references which were evaluated using pre-established inclusion criteria: 400 papers were selected, and 90 RCTs included in the systematic review. The mean score for Jadad Scale was 2.6 (range: 1 to 3), and for Moncrieff 39.9 (33 to 45). There was no relation between scores of the instruments. The main aspects of good quality present in the studies are: proper description of the interventions and populations; and the main problems are: incomplete description of randomization procedure, dropouts, and results.

Conclusions: Methodological faults are common in the studies evaluating the efficacy of psychotherapies for alcoholism, what certainly limits their results. Quality instruments are very useful for grading the relevance of the studies and even for planning new ones.

References:

NR89 Monday, May 19, 9:00 a.m.-10:30 a.m.
Psychotropic Use Among Cognitively Intact Older Medical/Surgical Inpatients
Doris Duke Clinical Research Fellowship

Benjamin Kornitzer, A.B., Department of Geriatrics, Mount Sinai, 50 East 98th Street, Apt. 14R, New York, NY 10029; Rosanne Leibzig, M.D., Helen Fernandez, M.D., Shahla Bahariu, M.D., Deborah B. Marin, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the prevalence of psychotropic drug use among acutely hospitalized medical/surgical patients, and also be familiar with potential discrepancies between current psychotropic prescription patterns and recommended guidelines.

Summary:
Background: Psychotropic drugs may contribute to many of the "hazards of hospitalization," including delirium, sedation, incontinence, poor mobility, and prolonged hospitalization. Several of these drugs or specific doses have been identified as inappropriate for older adults. The purpose of this study is to characterize the drugs prescribed and their prevalence among cognitively intact older adults, hospitalized on medical/surgical floors.

Methods: This study is based on a random 25% sample of medical and surgical inpatients. Patients ≥65 years were enrolled from four pairs of matched medical/surgical units. Psychiatric, OB/GYN, and cognitively impaired patients were excluded. Psychotropic agents were defined as antipsychotics, anxiolytic/sedatives, and antidepressants.

Results: Of 1004 patients ≥65 years who met inclusion criteria, 440 Patients (43.8%) received at least one psychotropic. Of these, 67.3% received only a single psychotropic medication, 22.7% took two different medications, and 10% took three or more different medications. 32.1% of all older patients received a sedative/hypnotic; 20.1% received an antidepressant; and 7% received an antipsychotic.

Conclusions: Almost half of cognitively intact older patients on acute medical/surgical floors received a psychotropic. We are currently doing a chart review to determine the reason for these prescriptions and whether the administered doses are consistent with current guidelines.

References:

NR90 Monday, May 19, 9:00 a.m.-10:30 a.m.
Epidemiology of Migraine in a Bipolar Population

Nancy C. Low, M.D., Department of Mood & Anxiety Disorders, NIMH, 15K North Drive, Room 208 (MSC2670), Bethesda, MD 20892-2670; Guillaume Galbaud Du Fort, M.D., Pablo Cervantes, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the increased prevalence and clinical correlates of migraine in the bipolar population; increase the awareness of the underdiagnosis and treatment of migraine in the bipolar population.

Summary:
Background: The relationship between migraine and mood disorders has been of longstanding interest to researchers and clinicians. Although a strong association has been demonstrated consistently for migraine and major depression, there has been less systematic research on the links between migraine and bipolar disorder.

Methods: A migraine questionnaire (based on International Headache Society criteria) was administered to 108 out-patient bipolar subjects. Information on the clinical course of bipolar illness was also collected.

Results: The overall lifetime migraine rate was 39.8% (43.8% among females and 31.4% among males). In the subgroup of bipolar disorder type II subjects, the lifetime prevalence of migraine was 64.7%. The (bipolar with migraine) group was younger, tended to be more educated, was more likely to be employed or studying, and had fewer psychiatric hospitalizations. They were more likely to have a family history of migraine and psychiatric disorders, and a greater number of affected relatives. Migraine was assessed by a neurologist in only 16% of affected subjects. The prevalence of the use of specific anti-migraine medications (triptans) was 27.9%.

Conclusions: The prevalence of migraine is higher among the bipolar population compared to the general population. Migraine in bipolar disorder subjects is underdiagnosed and undertreated.

References:

NR91 Monday, May 19, 9:00 a.m.-10:30 a.m.
Length of Stay Comparison Between Adjudicated and Nonadjudicated Psychiatric Inpatients
Patrick J. Rowan, M.D., Psychiatry Department, NYMC Saint Vincent’s, 144 West 12th Street, Room 175, New York, NY 10011; Stephen B. Billick, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the effect of the decision to go to court requesting discharge on the treatment of inpatients.

Summary:
Objective: This study attempts to assets the prolongation of hospitalization in civilly committed psychiatric patients who request discharge and are evaluated for judicial hearings.
Methods: Hospital records for forensically evaluated patients who went to court (N=16) and for forensically evaluated patients who decided not to go to court (N=6) were retrospectively reviewed. These results were compared with non-forensic psychiatric inpatients.
Results: The average total length of stay (LOS) for adjudicated patients was 39.23 days longer than for non-adjudicated patients, which was statistically significant. The average LOS from court date to discharge for adjudicated patients was 24.37. The average LOS from court date to discharge for adjudicated patients was 15.84 days longer than for non-adjudicated patients, which was statistically significant. The average LOS for non-forensic patients was 13.04.
Discussion: The finding that LOS was so much longer for patients who went to court seems to indicate that these are two distinct populations. Patients who went to court likely had far more impaired insight and judgment. They may have cooperated less with the treating team. The treating team may have dealt with them differently since they decided to go to court. Once the decision to treat has been made, the LOS for non-forensic patients (13.04) was still much shorter than the LOS for adjudicated patients from court date to discharge (24.37).
Conclusion: The prolongation of LOS for adjudicated patients over non-forensic patients appears to be due to two distinct factors: (1) lack of cooperation with the treatment team, and (2) greater severity of illness requiring longer treatment.

References:

NR92 Monday, May 19, 9:00 a.m.-10:30 a.m.
Association Study of the 5HT2A Gene in the Puerperal Triggering of Bipolar Disorder
West Midlands Regional Health Authority
Emma K. Robertson, Ph.D., Department of Women’s Health, UHNL, 657 University Avenue, ML20048, Toronto, ON M5G2N2, Canada; Ian R. Jones, M.D., Nick Craddock, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the genetic investigation of bipolar affective puerperal psychosis.

Summary:
Introduction: Bipolar affective puerperal psychosis is the most severe form of postnatal affective illness, affecting one to two per 1,000 deliveries. Women with bipolar disorder are at very high risk of an episode in the puerperium, and compelling evidence points to familial (probably genetic factors) influencing vulnerability to puerperal triggering episodes in bipolar women. We examined whether variation at two common polymorphisms, T102C and -1438AG, of the serotonin 2A gene (5HT2A) are involved in the puerperal triggering mechanism of bipolar affective puerperal psychosis. This study is the first to examine the role of 5HT2A within this illness.
Methods: 242 UK Caucasian parous women diagnosed with bipolar disorder were genotyped for the two polymorphisms. The puerperal psychosis group comprised 165 women who had experienced a manic or psychotic episode, according to DSM-IV criteria, within six weeks of childbirth. The comparison group comprised 77 parous women who had not experienced psychiatric disturbance following childbirth.
Results: No significant differences between genotype or allelic frequencies were found between the two groups for either polymorphism.
Conclusions/Discussion: The results indicate that variation at two common polymorphisms of the 5HT2A gene do not appear to play a major role in the development of bipolar affective puerperal psychosis. These results need to be replicated in other samples.

References:
oping certain psychiatric disorders. Counseling recommendations varied depending on the disorder, with pregnancy termination recommended most commonly for autism (19.8%), schizophrenia (11.5%) and antisocial personality disorder (10.2%).

Conclusions: This is a first step in assessing psychiatrists’ preparation for the clinical application of genetic knowledge, and suggests areas where additional education may be needed.

References:

NR95 Monday, May 19, 9:00 a.m.-10:30 a.m.
The Effect of Bodily Pain on Time to Remission in Late-Life Depression
Jordan F. Karp, M.D., Department of Psychiatry, Western Psychiatric Institute, 3811 O’Hara Street, Pittsburgh, PA 15213; Karen Seligman, M.Ed., Patricia Houck, M.S.H., Charles F. Reynolds III, M.D.

Educational Objectives:
At the conclusion of this session, the participant should (1) recognize the interaction of depression and bodily pain in late life depression. (2) understand the importance of and ability to treat the elderly with bodily pain and depression to full remission.

Summary:
Objective and Method: Depression and bodily pain are common disorders among the elderly, and depression has been found to be persistent when bodily pain is comorbid (Geerlings et al, 2002). We were interested in a possible interaction between subjectively described bodily pain on time to remission during the acute phase of treatment in a sample of elderly outpatients (age ≥ 70) with depression who were treated with paroxetine and interpersonal psychotherapy. We hypothesized that higher levels of bodily pain, as measured by the Medical Outcome Survey (Ware 1994) bodily pain index (MOS-BPI) would predict a longer time to remission. Remission was defined as three consecutive weeks of HRSD ≤ 10.

Results: The sample consisted of 171 subjects, 66% female and 92% white, with an age range from 69–95 years. Of these, 133 have remitted (78%). Cox proportional hazards model revealed a significant relationship between baseline MOS-BPI scores and time to remission. For every ten-unit decrease in pain scores, there was an increased “risk” of remission of 9% (X² = 6.50, p = 0.01). However, covarying for baseline depression severity (performed because of a correlation between baseline HRSD and MOS-BPI [r = –0.29, p = 0.01]) caused this relationship between baseline MOS-BPI and time to remission to disappear. Trichotomizing the sample into low, medium, and high bodily pain revealed no difference between the three groups for time to remission (Kaplan-Meier Survival Analysis: Wilcoxon Test: X² = 2.05, df = 2, p = 0.36). Although there was a significant relationship between medical comorbidity as measured by the CIRS-G and MOS-BPI scores (r = –0.29, p = 0.0002), we found no relationship between the CIRS-G and time to remission (Kaplan-Meier Survival Analysis: Wilcoxon Test: X² = 0.03, df = 1, p = 0.87). Finally, there was no difference between patients with low and high levels of suicidal ideation as measured by HRSD and level of bodily pain (t = –1.40, df = 162, p = 0.16).

Conclusions: While our hypothesis was not supported by these results, we feel they are significant as they suggest that elderly patients with high levels of physical pain or medical comorbidity can still achieve a robust remission from their depression. These findings imply that perhaps the diagnosis of depression in late life should be more inclusive and less etiologic as even patients with pain and somatic complaints are likely to benefit from treatment.

References:
fluid (CSF) following electroconvulsive shock. The present study investigated whether or not this property exists in human CSF. Three experimental groups were compared to control human CSF. ANOVA with repeated measures and t-tests were used for analysis.

For the tonic seizures, the 1 Hz TMS group (F=4.75; p=0.045) was not significantly different than control. There were no significant “group x time” interactions for onset of myoclonic seizure. There was a “group x time” interaction compared with control CSF for the 10 Hz TMS (F=11.15; p<0.001) and the 1 Hz TMS (F=8.52; p<0.001) groups for onset of myoclonic seizure. The aCSF and ECT groups were not significantly different than control.

Conclusions: This study suggests that there is no anticonvulsant property in the CSF 48–72 hours following ECT. CSF taken from subjects treated with 1 Hz rTMS may have an anticonvulsant property, which is not present in those treated with 10 Hz rTMS.

References:

Summary:
Objective: While literature supports the efficacy and value of integrating on-site clinical psychiatric services into the general practice of medicine, there is a paucity describing the demographics of actual joint practice. This study analyzes the first 75 consecutive patients referred by an internist for assessment by a psychiatrist/social worker within the general practitioner’s office.

Method: Comprehensive evaluation included administration of the Structured Clinical Interview I for DSM IV, the 24-item Hamilton Depression Rating Scale, Mini-Mental State Examination, as well as a clinical assessment of the patient’s history and presenting problem. Self-administered questionnaires were distributed to all patients.

Results: The majority of patients were female and of late onset of age. Medical diagnoses included 26.7% cardiac, 21.3% neurological, 8.7% cancer and 22.7% miscellaneous and 22.7% psychiatric (50%, major depressive disorder; 16%, cognitive impairment; 12%, generalized anxiety disorder; 2%, anorexia nervosa; 2%, posttraumatic stress disorder; and 10.7%, no diagnosis). Within the diagnosis on major depressive disorder, 64% were recurrent episode, 21% were single episode, 14% were bipolar, the mean age was 68 years old, the mean Hamilton score was 20, and the mean Mini Mental Status score was 27.

Conclusion: A large number of elderly psychiatric and cognitively impaired patients initially present to an internist rather than a psychiatrist. When the internist requests a psychiatric referral, most likely the patient does not pursue the consult. However, if an immediate diagnostic evaluation is made by a trained clinician in the setting of the physician’s office, the institution of subsequent off-site psychiatric intervention, that might otherwise be neglected, will be achieved.

NR98 Monday, May 19, 9:00 a.m.-10:30 a.m.
Changes in Regional CBF in Bipolar Disorder Following Transient-Induced Sadness Measured With PET
Stephanie Krueger, M.D., Department of Psychiatry, University of Dresden, Fetscherstr 74, Dresden, Germany; David Seminowicz, B.S.; Kim Goldapple, B.S., Sidney H. Kennedy, M.D., Helen S. Mayberg, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize abnormalities in rCBF in bipolar disorder, understand that clinical euthymia does not equal normal brain metabolism, and understand some of the functional neuroanatomy of mood regulation.

Summary:
Remitted patients with bipolar disorder remain sensitive to various external stressors that can be associated with triggering of new episodes. Imitating such stressors by the controlled transient exposure of these patients to an emotional stimulus may help to further identify brain regions involved in these aberrant behavioral responses. Transient sadness was induced in nine euthymic subjects and in 11 currently depressed subjects. Regional blood flow (rCBF) changes were measured using 150-water PET. Common changes were seen with induced sadness in both remitted and depressed BD subjects; increased rCBF was seen in anterior insula, cerebellum, and decreased rCBF was seen in dorsal and ventral medial frontal cortex, posterior cingulate, hippocampus, inferior parietal, and temporal cortex. More robust decreases in medial frontal cortex were seen in remitted subjects relative to depressed. Unique to remitted subjects were rCBF increases in dorsal anterior cingulate and in premotor cortex. Prefrontal rCBF decreases were unique to depressed subjects. Comparison of remitted to depressed subjects at baseline revealed a unique...
rCBF increase in remitted subjects in dorsal anterior cingulate and orbitofrontal cortex, but comparable prefrontal cortex decreases relative to healthy controls. The common change pattern seen in both groups may identify sites of disease vulnerability. Unique cingulate and orbital frontal changes may identify regional interactions important to the euthymic state in this population.

References:

**NR99** Monday, May 19, 9:00 a.m.-10:30 a.m.
**Factor Analysis of the Catatonia Rating Scale in Four Diagnostic Groups**
Supported by Eli Lilly and Company

Stephanie Krueger, M.D., Department of Psychiatry, University of Dresden, Fetscherstr 74, Dresden, Germany; Peter Braeunig, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to diagnose catatonic symptoms, and learn that catatonia is a heterogenous syndrome that occurs across diagnoses.

Summary:
Background: Catatonia is a frequent psychomotor syndrome, which has received increasing recognition over the last decade. The assessment of the catatonic syndrome requires systematic rating scales that cover the complex spectrum of catatonic motor signs and behaviours. The Catatonia Rating Scale (CRS) is such an instrument that has been validated and which has undergone extensive reliability testing.

Method: In order to further validate the CRS, the items composing this scale were submitted to principal components factor extraction followed by a varimax rotation. An analysis of variance (ANOVA) was performed to assess group differences on the extracted factors in patients with schizophrenia, pure mania, mixed mania, and major depression (N = 165).

Results: Four factors were extracted, which accounted for 71.5% of the variance. The factors corresponded to the clinical syndromes of (1) catatonic excitement, (2) abnormal involuntary movements/mannerisms, (3) disturbance of volition/catalepsy and (4) catatonic inhibition. The ANOVA revealed that each of the groups showed a distinctive catatonic symptom pattern and that the overlap between diagnostic groups was minimal.

Conclusions: This four-factor symptom structure of catatonia challenges the current conceptualization, which proposes only two symptom subtypes.

References:

**NR100** Monday, May 19, 9:00 a.m.-10:30 a.m.
**Neuropsychiatric Symptoms in Kleine-Levin Syndrome: Long-Term Follow-Up**
Magdalena M. Berkhoff, M.D., Department of Psychiatry, University of Zurich, Cullmannstrasse 8, Zurich, CH 8091, Switzerland; Giuseppe Distefano, M.D., Christian W. Hess, M.D., Claudio Bassetti, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to improve their diagnosis and neuropsychiatric assessment of patients with Kleine-Levin syndrome.

Summary:
Objective: To assess personality features and neurocognitive functioning in patients with Kleine-Levin syndrome (KLS). This rare disease is characterized by periodic hypersomnia, hyperphagia, and abnormal behavior. A potential association with persistent cognitive impairment is still discussed.

Method: We assessed all patients (n=10) diagnosed as KLS at the University of Berne since 1965 by interview and standardized self-assessment scales including personality features (FPI-R), depression (BDI), sleep (PSQI) and daytime sleepiness (ESS). Cognitive assessment included measures of intelligence, attention, memory, and executive functioning.

Results: As to personality features, Stanines were below average in five or more patients for frankness (6/10), inhibition (5/10), and emotionality (5/10). BDI sum score was low compared with a normal population (3.44 vs. 6.45, p=0.035, two-tailed). PSQI global score was higher than in normal controls (mean 4.3 vs. mean 2.67, p=0.014, two-tailed), whereas no divergence was found in daytime sleepiness (ESS scores 5.89 and 5.9, respectively). IQ and neurocognitive functions were within normal range in 7/8 patients.

Conclusion: These findings support the assumption that no permanent neurocognitive dysfunction is associated with KLS. However, personality features such as frankness, inhibition, and emotionality might differ compared with a normal population.

References:

**NR101** Monday, May 19, 9:00 a.m.-10:30 a.m.
**A Randomized-Treatment Trial in Mild Traumatic Brain Injury**
Physicians Services, Inc.

Omar Ghaffar, M.D., Department of Psychiatry, SWCHSC, 2075 Bayview Avenue, Toronto, ON M4N3M5, Canada; Donna Ouchterlony, M.D., Anthony Feinstein, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize whether six months treatment of mild TBI offers neurobehavioral benefit and recognize which patients may be most likely to benefit.

Summary:
Hypothesis: Multidisciplinary treatment of mild traumatic brain injury (TBI) improves neurobehavioral outcome at six months post-injury.

Methods: Subjects with mild TBI were randomly assigned to treatment (n = 97) or non-treatment (control, n = 94) groups. Treated patients were assessed within one week of injury and subsequently managed by a multidisciplinary team according to clinical need for a further six months. Control subjects were not offered treatment. Six-month outcome measures included severity of post-concussive symptoms (Rivermead Post-Concussion Disorder Questionnaire), psychosocial functioning (Rivermead Follow-up Questionnaire).
NR102  Monday, May 19, 9:00 a.m.-10:30 a.m.
Residents’ Attitudes to Information From Pharmaceutical Representatives

Fatimah A. Tahil, M.D., Department of Psychiatry, Saint Luke’s–Roosevelt, 310 Riverside Drive #1522, New York, NY 10025;

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the significance of psychiatric residents’ attitudes and perception of information received through interactions with pharmaceutical company representatives.

Summary:
Objective: To assess the attitudes of psychiatric residents toward promotional information received from pharmaceutical company representatives (PCRs).
Methods: A questionnaire study of PGY-2 psychiatric residents (n = 18) enrolled in the St. Luke’s-Roosevelt Hospital Center, between 2000 and 2003, was designed to determine their attitudes toward information originating from PCRs. The study instrument was administered before and after a three-part course on the influences of the pharmaceutical industry on current psychiatric practice. The survey used a Likert scale, and was designed to assess residents’ attitudes concerning various information received from PCRs on psychotropic medications, their delivery and communication of such information, and residents’ actions in verifying the information provided by PCRs.

Results: Prior to the course, 39% of residents considered PCRs as an important source of information for psychotropic medications; half of all respondents regarded the information as accurate. Post-course responses show that a substantial number of residents (67%) verified the verbal information received, and that most residents (78%) recognized the importance of developing a framework to evaluate promotional drug information.

Conclusions: Continued efforts to educate physicians on the influences of the pharmaceutical industry must also include critical appraisal methods if residents are to be better consumers of information.

References:

NR103  Monday, May 19, 9:00 a.m.-10:30 a.m.
Adequacy of Antidepressant Treatment by Psychiatric Residents

Rachel E. Dew, M.D., Department of Psychiatry, Wake Forest University, Medical Center Boulevard, Winston-Salem, NC 27157; W. Vaughn McCall, M.D., Stephen I. Kramer, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the relationship of training level, severity of illness, and time in treatment to adequacy of treatment for depression in a psychiatric residents’ clinic.

Summary:
Objective: To evaluate adequacy of pharmacologic treatment of depressive disorders in a psychiatric residents’ clinic.
Background: Research indicates that depression is typically undertreated; gaining facility in psychopharmacologic treatment of depression is a major goal of psychiatric residency. This study quantifies adequacy of pharmacotherapy provided to depressed patients presenting to the Wake Forest University resident clinic during a specified calendar year.
Methods: Charts of all patients seen in the outpatient triage clinic during 2000 were reviewed. Of 285 patients, 116 were followed by 12 different residents and had diagnoses of major depression, dysthymia, depressive disorder NOS, adjustment disorder with depressed mood, or bipolar disorder with a documented depression during the studied period. Four patients treated with psychotherapy alone were excluded. Pharmacologic treatment was rated using the Antidepressant Treatment History Form (ATHF). Other variables analyzed included comorbid diagnoses, weeks in treatment, training level of the treating resident, and Clinical Global Impression (CGI) score assigned by the reviewer.

Results: Of 112 charts, 55 (49.1%) documented adequate treatment, defined as at least one ATHF score ≤ 3. Maximal ATHF ratings increased with treatment duration (r = 0.73, p < 0.001). No correlation was found between ATHF ratings and training level, or between scores and CGI severity ratings.

Conclusions: Results suggest that time retained in treatment plays a major role in determining if patients receive adequate treatment. This reinforces the importance of residency training not only in psychopharmacology but also in developing therapeutic alliance.

References:

NR104  Monday, May 19, 9:00 a.m.-10:30 a.m.
Atypical Antipsychotics Increase Engagement in Psychosocial Rehabilitation

Matthew E. Bernstein, M.D., Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02478-9106; Paul J. Barreira, M.D.
NR105 Monday, May 19, 9:00 a.m.-10:30 a.m.
Drinking Patterns and Personality Traits by ALDH2 Genotype Variances in Alcoholics
Jong-II Lee, M.D., Department of Psychiatry, Hangyang University Hospital, Haeng-Dang-Dong, Seoul 133-792, Korea; Jung-Hyun Nam, M.D., Byung-Hwan Yang, M.D., Eun-Ki Chung, M.D., Young-Gyu Chai, Ph.D., Seok-Hyeon Kim, M.D.

Educational Objectives:
The purpose of this study is to evaluate the pathophysiology of alcoholics with investigation of differences in frequency of ALDH2 genotypes and ALDH2 alleles between patients with alcohol dependence and controls, and in drinking pattern and personality trait by ALDH2 genotype variances in Korean male alcoholics.

Summary:
Methods: ALDH2 genotypes were typed with Mbol RFLP(Restriction Fragment Length Polymorphism) method in 53 controls and 98 patients with alcohol dependence. The resultant products were analyzed with 'genescan 3.1'.

Results: (1) The genotypic frequencies of subjects with ALDH2/1 were higher and those with ALDH2/2 were lower in patients than in controls; (2) Alcohol dependence could be found in ALDH2/2 homozygote individuals. (3) Variant ALDH2 alcoholics had more family problems in AU than normal ALDH2 alcoholics. (4) Variant ALDH2 alcoholics experienced more flushing and cardiovascular responses after alcohol ingestion than normal ALDH2 alcoholics. (5) Variant ALDH2 alcoholics had less altruistic personality traits in NEO-PI-R than normal ALDH2 alcoholics. (6) Variant ALDH2 alcoholics tended to have more tolerance about alcohol than normal ALDH2 alcoholics.

References:

NR106 Monday, May 19, 9:00 a.m.-10:30 a.m.
Psychopathology as a Risk Factor for Being Overweight
Swiss National Science Foundation
Gregor Hasler, M.D., Department of Mood & Anxiety Disorder, NIMH, 15K North Drive, Bethesda, MD 20892; Kathleen Merikangas, Ph.D., Dominique Eich, M.D., Richard Herrell, Ph.D., Wulf Roessler, M.D., Alex Gamma, Jules Angst, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize which psychiatric disorders and symptoms are related to being overweight; have increased the awareness of the risk of being overweight among psychiatric patients.

Summary:
Background: Obesity is the most common and costly nutritional problem in Western countries. The goals of the present study were to describe: (1) the stability of being overweight, (2) the longitudinal association of psychopathology and overweight, and (3) the gender differences, personality traits, and socio demographic characteristics related to the regulation of body fat.

Methods: The sample is a cohort of 591 young adults from the general population of Zurich, Switzerland, aged 18–19 at study entry, who have been followed to age 40.

Results: 18.9% of the participants were classified as being overweight. Sociopathy, binge eating, and atypical depression were positively associated with being overweight among both males and females. However, among males alone, hypomanic symptoms were associated with being overweight, while generalized anxiety disorder was negatively related to being overweight. The association between psychopathology and body mass index (BMI) remained statistically significant even after controlling for medication, social and educational variables.

Conclusion: These findings demonstrate the importance of longitudinal investigation of the psychopathology BMI association.
and demonstrate the need for long-term studies on the regulation of body fat.

References:

NR107  Monday, May 19, 9:00 a.m.-10:30 a.m.
Current Trend in Psychiatric Research
Arun R. Kunwar, M.D., Department of Psychiatry, Upstate Medical University, 750 East Adams Street, Syracuse, NY 13210; Subhdeep Virk, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the present trend in psychiatric research. The funding sources, topic areas in which research is carried out, and common methodologies. Participant will be able to identify the topics that lack research and the need for balance funding of different topics in psychiatry.

Summary:
Objective: To study the present trend in psychiatrist research as captured in the published research articles of the American Journal of Psychiatry (AJP).

Method: The 265 research articles published in AJP in the year 2002, were taken. They were categorized according to the source of funding, field of research, and methodological approach.

Results: Source of grant for 76% of published research was of non-industry (drug companies) origin, Industry accounted for 11.5%, and 12% were non-funded. Schizophrenia and psychotic disorders accounted for 22% of the research, affective disorders accounted for 20% and other disorders accounted for the remainder. Almost half (44%) of the published research articles used cross-sectional methods, 22% used case control methods, 22% used cohort/perspective methods, and 12% were clinical trials.

Conclusions: This study concludes (that with in a major psychiatric journal), that the majority of the research funding comes from public funding and not industry. This could very well be do to editorial policies in the journal. Public policy for funding future mental health research can most effectively be directed through the examination of funding streams, research approaches, and disorders studied, which will help clarify where research resources are being directed and which disease states are being overlooked.

References:

NR109  Monday, May 19, 9:00 a.m.-10:30 a.m.
Treating Depression Among Low Income Women in Primary Care Santiago, Chile
National Institute of Mental Health
Graciela Rojas, M.D., Department of Psychiatry, University of Chile, Auda La Pas 1003, Santiago, Chile; Ricardo Araya, M.D., Greg Simon, Rosemarie Fritsch, Jorge Gaete

Educational Objectives:
At the conclusion of this session, the participant should be able to learn more effective ways of treating depression among women in primary care clinics from deprived neighborhoods.

Summary:
Objective: To compare the effectiveness of a multi-component, stepped-care program with usual care for the treatment of depression in primary care.

Method: Randomized controlled trial. 240 female primary care patients aged 15–70 who met DSM-IV major depression criteria were randomly allocated to either usual care or the ‘stepped-care’ programme. Non-medical health workers led this programme that involved a psycho-educational group intervention, a structured and systematic follow-up, and pharmacotherapy. The main outcome measure was the Hamilton Rating Scale for Depression. All patients completed blinded assessments at three and six months after randomization.
Results: 90% of randomized subjects completed outcome assessments. There was a large and highly significant difference in all outcome measures between treatment groups, in favor of the stepped-care program. The adjusted difference in mean HDRS between the two groups was 9.0, 95% CI 6.8, 11.2, p<0.001. At six-months, 70% (CI 60.79) of the intervention group compared with 30% (CI 21.40) of the usual care had recovered (HDRS score=8).

Conclusions: In spite of the lack of resources and marked socioeconomic deprivation, depressed women responded well to our treatment programme, which is now being introduced nationwide.

References:

NR110  Monday, May 19, 9:00 a.m.-10:30 a.m.
Drop-Out Treatment: Relevant Factors
Blanca Reneses, L.C.P., Department of Psychiatry, San Carlos Hospital, Rafael Calvo 30, Madrid 28010, Spain; Elena Munoz Marron, L.C.P., Juan J. Lopez-Ibor, Jr., M.D.

Summary:
Objectives: Assessment of factors associated to outpatient dropout of treatment.
Methods: Retrospective study of patient drop out of treatment in a mental health center corresponding to all outpatient new cases seen in 1999 and followed between 1999 and 2001. Data were obtained from the Madrid (Spain) Psychiatric Case Register and by chart review. Total number of patient drop out from treatment was 789 (31% of all new cases). Dropout treatment cases were compared with a sample of patients who adhered to treatment.
Results: No differences in sociodemographic characteristics were found between both groups. Patients that abandoned treatment significantly had less frequent previous psychiatric history, and were seen by more than one doctor more often. Patients that adhered to treatment received more often psychopharmacologic treatment only. Psychiatric illnesses significantly more frequent in the drop out group were: personality disorders alcohol abuse and dependence, drugs abuse and dependence and eating disorders.

Conclusions/Discussion: Despite known higher prevalence of medical comorbidities among mentally ill, the population in the present study professed to suffering from these disorders less than the general population. The mentally ill may be less aware of their physical health due to lack of access to primary care physicians and patient education. A cross-sectional study of the entire Clubhouse needs to be done. Additionally, the 241 patients in the study need to be reevaluated blindly by a physician, and the physician diagnosis compared with the self-reported diagnosis to confirm our hypothesis.

References:

NR112  Monday, May 19, 9:00 a.m.-10:30 a.m.
Treatment Patterns and Involvement of Bosnian Refugees Clinical Mental Health Services
Schuyler W. Henderson, M.D., Department of Psychiatry, New York University, 21 East 108th Street, Apt. 2D, New York, NY 10029; Stevan M. Weine, M.D., Amer Smajic, M.D., Zvezdena Zdjuric-Bijedic, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the demographic features that contribute to treatment patterns and involvement in therapeutic services of a cohort of Bosnian refugees and discuss the implications of these findings for future clinic-based interventions.

Summary:
Objective: To describe the patterns of treatment and involvement in services of Bosnian refugees receiving mental health services at a refugee mental health clinic.
Method: The charts of 84 Bosnian refugees were retrospectively reviewed for demographic characteristics and patterns of treatment and involvement.

Results: Nearly all persons received basic services of psychiatric evaluation (100%), psychiatric medication (96%), and supportive counseling (95%). 51% also received psychotherapeutic services of individual psychotherapy (19%), group psychotherapy (26%), or both (6%). Loss of a primary relative was associated with receiving psychotherapeutic services and also receiving group therapy, whereas low levels of education were associated with receiving individual psychotherapy. Statistical models constructed to predict psychotherapeutic services, individual psychotherapy, or group psychotherapy were built on the basis of factors including level of education, loss of a primary relative, as well as self-referral and marriage.

Conclusion: Treatment patterns vary with respect to demographic characteristics such that psychotherapeutic services are deployed for those with less familial and social resources.

References:

NR113 Monday, May 19, 9:00 a.m.-10:30 a.m.
Gender and Age Effects on Salivary DST, 24-Hour Urinary Cortisol, and Metyrapone Challenge in PTSD
National Institutes of Health

Christian Otte, M.D., Department of Mental Health, Veterans Administration Medical Center, 4150 Clement Street, San Francisco, CA 94111; Maryann Lenoci, M.A., Melissa Magiline, M.A., Thomas Metzler, M.A., Charles R. Marmar, M.D., Thomas C. Neylan, M.D.

Summary:
Objective: To examine gender and age effects on hypothalamus-pituitary-adrenal-(HPA) activity in posttraumatic stress disorder (PTSD).

Method: We studied 30 patients with PTSD (10 female, 20 male, mean age 44.4 ± 9.3 years) with a 0.5 mg salivary dexamethasone suppression test, a collection of 24-hour urinary cortisol and a metyrapone challenge.

Results: Repeated measures-MANOVA revealed significant effects for gender (F=5.6, p=0.03) and age (F=4.5, p=0.05) on log-transformed pre- and post-dexamethasone cortisol values indicating higher values for women and older subjects. MANOVA for change scores of ACTH, cortisol and 11-deoxycortisol concentrations after metyrapone administration showed a significant effect for age (F=6.3, p=0.003) and a trend for gender (F=2.1, p=0.12). There was no gender effect on 24-hour cortisol values but a significant positive correlation between age and 24-hour cortisol (r=0.43, p=0.02) when examining the whole sample.

In women, but not in men, depression and PTSD measures (BDI, CAPS, IES-R) correlated strongly with cortisol values pre- and post-dexamethasone and -metyrapone, respectively.

Conclusions: Age and gender effects might in part be responsible for equivocal results in earlier studies examining HPA activity in PTSD. As has been described in depression, the relationship between HPA activity and psychopathology seems to be stronger in women.

References:

NR114 Monday, May 19, 9:00 a.m.-10:30 a.m.
Thyroid Abnormalities and Violent Suicidal Behavior
Sriram Ramaswamy, M.D., Department of Psychiatry, Creighton Nebraska, 3528 Dodge Street, Omaha, NE 68131; William A. Marci, M.D., Pirzada Sattar, M.D., Frederick Petty, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the hypothesized link between thyroid abnormalities and violent suicidal behavior.

Summary:
Objective: Several studies have explored the link between suicidal behavior, especially violent behavior and altered thyroid stimulating hormone levels, suggesting a hypothalamic-pituitary axis (HPA) dysfunction in such patients. We attempted to study the relationship between violent suicidal attempts and TSH levels.

Method: We retrospectively examined charts of patients who presented to the hospital after suicide attempts over a two-year period. Patients were divided in two groups: those with violent attempts and those with nonviolent attempts. Their TSH values were compared and data analyzed using t-tests.

Results: The sample consisted of 46 patients, 42 males and four females, mean age was 53.23 years. The prevalence of a high TSH value in the violent group was 5.8%. The mean TSH value in the violent group was 1.79 and in the nonviolent group was 1.49. Statistical analysis using two-tailed paired t-test did not suggest significance (p=0.9425). However, TSH values of the violent group were observed to be higher than those for the nonviolent group.

Conclusions: Our results do not suggest a significant link between high and violent suicidal behavior, but further work with bigger samples may be needed.

References:
Summary:

Objective: To determine whether the presence of suicidal ideation at time of initial treatment for major depression predicts treatment response to antidepressants in the primary care setting when a systematic depression management protocol is used.

Method: A retrospective review of 63 patients who had received treatment for depression in a primary care practice based on a formal, systematic depression management protocol was completed. Suicidal ideation was evaluated at the onset of treatment and nine depressed patients acknowledged suicidality upon interview and on the PHQ-9 depression rating scale, while five patients did not report any suicidal ideation. A family physician, family nurse practitioner, and a psychiatric consultant systematically followed both groups over four months of treatment. DSM-IV major depression symptoms, PHQ-9 depression rating scale scores and functional disability scores were used to evaluate for partial response and full remission from depression symptoms.

Results: In this study there was no statistically significant difference in partial response or full remission rates in regards to self-reported functional disability, PHQ-9 scores, nor the DSM-IV depressive symptoms of depression between suicidal or non-suicidal patients.

Conclusion: The presence of suicidality as a depressive symptom does not seem to predict a poorer clinical outcome when treating depression in the primary care setting with antidepressants.

References:

NR117 Monday, May 19, 9:00 a.m.-10:30 a.m.
Is a Partial Remission Specifier Clinically Relevant for PTSD?
Dawn Johnson, Ph.D., Department of Psychiatry, Brown University, 345 Blackstone Boulevard, Duncan Bldg, Providence, RI 02906; Caron Zlotnick, Ph.D., Mark Zimmerman, M.D.

Summary:

Objective: Although research suggests that residual symptoms of PTSD are associated with considerable impairment, no research has specifically evaluated the clinical relevance of a partial remission specifier for PTSD. This study compared partial PTSD with current PTSD and PTSD in full remission in degree of impairment and clinical correlates of PTSD in a sample of outpatients.

Method: PTSD was assessed with the SCID-I/P (2). Patients were also interviewed about psychiatric hospitalizations, suicide attempts, and their desire for PTSD treatment. The GAF scale and items from the SADS (3) were used to assess impairment.

Results: Of the 261 patients, 29% (n=75) met criteria for PTSD in partial remission. A majority of the partial remission group met diagnostic criteria for the re-experiencing PTSD criterion while they were least likely to meet full criteria for avoidance. The partial remission group displayed impairment at a level that was between the current PTSD and PTSD in full remission groups. Patients with PTSD in partial remission were significantly more likely to request treatment for PTSD than were patients with PTSD in full remission.

Discussion: This study lends preliminary support to the clinical relevance of a partial remission specifier with PTSD. The existing binary diagnostic system for PTSD may exclude important clinical information.

NR116 Monday, May 19, 9:00 a.m.-10:30 a.m.
Intimate Partner Violence in Vietnamese and Chinese Immigrant Communities
California Academy of Family Physicians
Lan T. Vu, Department of Psychiatry, University of California San Francisco, 117 Behr Avenue, San Francisco, CA 94143; Nang Du, M.D., Stacy Tsai, Linna Li

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the importance of questioning about both emotional and physical forms of intimate partner violence and the need for culturally sensitive community education.

Summary:

Objectives: Intimate partner violence (IPV), a major health issue in the Asian immigrant population, has not been comprehensively examined due to several factors, including the absence of cultural sensitivity and language barrier on the part of researchers and health care providers and the fear of disclosure on the part of the community. The objectives of this study were to (1) quantitatively and qualitatively describe the type of IPV that occurs in this community, and (2) develop a culturally sensitive IPV screening questionnaire for the Vietnamese and Chinese immigrant population.

Methods: The list of IPV behaviors, compiled from a literature review of several English domestic violence screening questionnaires, was assessed and modified for cultural appropriateness and accurate translation by Vietnamese and Chinese community service providers and IPV survivors through individual interviews and focus groups, respectively. Validity and reliability testing for the questionnaire will be conducted in a future study.

Results: Qualitative analysis of the five focus groups (n = 42) confirmed the categories of IPV in the screening questionnaire as follows: physical abuse, emotional abuse (verbal, restrictions, and threats), and sexual abuse. Among both Vietnamese and Chinese IPV survivors (n = 33), 12 women admitted to emotional and sexual abuse, but denied any form of physical abuse. In addition, all 21 women who admitted to physical abuse, also experienced emotional and sexual abuse. Among the Vietnamese immigrants in the community center, the prevalence of IPV was estimated at 64% (16/25). In addition, eight women denied any history of IPV, but responded affirmatively to at least two of the questions on the questionnaire.

Conclusions: Screening for emotional and sexual abuse is a sensitive method for identifying IPV survivors and victims in the Vietnamese and Chinese immigrant community. Community education, which is currently lacking, remains one of the key methods to prevention and intervention of IPV.

References:
PTSD Symptoms After Car Accidents
Supported by Aker University Hospital, Janssen
Pharmaceutica, Cilag, Inc., Norway; H. Lundbeck, Inc.,
Gjensidige Nor Insurance
Thor B. Kvakkested, M.D., M.Sc., Lillestromklinikken, PO Box 80,
kjeller 2027, Norway; Alv A. Dahl, M.D.

Educational Objectives:
- PTSD- and anxiety symptoms are found in 20% of those willing
to take part in a study of the claim-holders after car accidents.
Doctors should be observant to psychic reactions after car accidents.

Summary:
Background: Posttraumatic stress disorder (PTSD) is a common occurence after traffic accidents. In this pilot study we tried to avoid selection biases by addressing those insured in a big insurance company who sent claims after their accidents.

Methods: 88 consecutive claim holders to the insurance company got an invitation to take part in a questionnaire study over six months in order to study psychological reactions to car accidents. The reactions were measured by Hospital Anxiety and Depression Scale and Davidson Trauma Scale (DTS).

Results: Twenty-four of 88 (27%) claim holders filled in the questionnaires at six months after the accident. The most frequent age category was 26–33 years (29%), 46% were permanently employed and 62% had formerly been involved in a car accident 25% had a possible anxiety disorder, and 8% a possible depression. Five claim holders (21%) had a DTS-sum score over the cut-off on all three measures, and they were flagged as in need of interventions.

Conclusions: Only a minority of those involved in a car accident is willing to take part in a prospective study of mental problems. Among those participating, 20% show a symptom load after six months that show need of treatment.

References:

Psychoeducational Family Intervention on Caregivers of Bipolar Patients
Stanley Medical Research Institute
Maria Reinares, Ph.D., Department of Psychiatry, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain; Eduard Vieta, M.D., Francesc Colom, Ph.D., Anabel Martinez-Aran, Ph.D., Mercè Comes, Ph.N., Jose M. Goikolea, M.D., Barbara Corbella, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to recognize the importance to involve the caregivers in the treatment of bipolar patients.

Summary:
Objective: Several studies suggest that family beliefs about bipolar disorder may predict family burden, and this burden could influence the patients’ outcome. Our aim was to assess the impact of a psychoeducational family intervention on caregivers of bipolar patients.

Methods: 45 medicated bipolar outpatients in remission for at least three months were divided into an experimental and a control group. Relatives of patients from the experimental group received 12 psychoeducational 90-minute sessions about bipolar disorder. The caregivers’ knowledge about bipolar disorder, the relationship subscales of the Family Environment Scale, and a Spanish version adapted from the family burden subscales of the Social Behaviour Assessment Schedule were assessed for both groups before and after the intervention.

Results: Psychoeducated caregivers significantly improved their knowledge about bipolar disorder and reduced both the subjective burden and their view of the role of the patient in the objective burden. There were no significant differences neither in the objective burden nor in the family environment subscales.

Conclusions: Family psychoeducation improves the caregiver’s knowledge about bipolar disorder, reduces the caregiver’ distress associated with the patient’s behaviours (subjective burden) and also the caregivers’ belief about the link between their objective burden and the patient.

References:
References:

NR121 Monday, May 19, 9:00 a.m.-10:30 a.m.
To Determine the Occurrence of Mania or Hypomania During Treatment With ECT in Patients With Bipolar Depression
Jaskaran Singh, M.D., National Institute on Mental Health, 9000 Rockville Pike, Building 10, Room 35243, Bethesda, MD 20892; Andrew D. Krystal, M.D., Richard D. Weiner, M.D., C. Edward Coffey, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to determine the occurrence of mania or hypomania during treatment with ECT in patients with bipolar depression.

Summary:
Objective: Electroconvulsive therapy (ECT) is highly efficacious for bipolar depression and its antimanic effects suggest the possibility of a lower rate of inducing mania/hypomania than antidepressant pharmacotherapy. We sought to determine the occurrence of mania or hypomania during treatment with ECT in patients with bipolar depression, and to assess its relation to unilateral vs. bilateral electrode placement because of evidence that bilateral ECT may have greater antimanic effects. This effect might lead some clinicians to preferentially administer bilateral ECT for bipolar depression to prevent mania/hypomania, however; bilateral ECT has greater associated cognitive impairment and the switch rate for mania/hypomania for unilateral and bilateral ECT has never been studied.

Method: We carried out a retrospective chart review in 159 patients diagnosed with bipolar depression who received index ECT at Duke from 1987–2002.

Results: Mania/hypomania occurred in 3.8% of the patients (6/149). The rate of mania/hypomania did not differ for unilateral (3.4%-3/89) and bilateral (5%-3/60) ECT.

Conclusion: Our results confirm the low-rate of mania/hypomania with ECT in Patients with bipolar depression. We did not find a different rate of mania/hypomania for unilateral and bilateral ECT, suggesting bilateral electrode placement does not offer any protective advantage against the occurrence of this outcome during an index course of ECT.

References:

NR122 Monday, May 19, 9:00 a.m.-10:30 a.m.
Methohexitone, Propofol, and Etomidate in ECT: A Comparative Analysis
Graham Pluck, Ph.D., Andrew J. Mogg, M.R.C., Declan M. McLoughlin

Educational Objectives:
At the conclusion of this session, the participant should understand that different anaesthetics influence ECT practice in different ways.

Summary:
Objective: The recent lack of availability of methohexitale has led to use of other agents that differ in their influence on seizure characteristics. The purpose of this study was to compare seizure characteristics and therapeutic responses to ECT when using different anaesthetic agents.

Method: Patients who received ECT during 1999–2000 at the Maudsley & Bethlem Royal Hospitals, London, were included in this retrospective case note study.

Results: 69 courses of ECT were given to 55 patients. Three different anaesthetics were used: methohexital (Brietal (n = 19) and Brevimytal (n = 20)), propofol (n = 8) and etomidate (n = 16) were used. Response to ECT or the average number of ECTs in each course did not differ between any of the groups. The mean seizure duration was lowest (p=0.01) in the propofol group and the mean stimulus charge was highest in the propofol group (p<0.0001). There was a trend for confusion/amnesia to be higher in the propofol group (p=0.06).

Conclusions: Use of propofol for ECT does not alter the therapeutic outcome, though the stimulus charge required is higher and the seizure duration is lower. Use of propofol may be associated with increased cognitive dysfunction due to higher stimulus charge required.

References:

NR123 Monday, May 19, 9:00 a.m.-10:30 a.m.
Peak Heart Rate During ECT
Shyam K. Bhat, M.D., Department of Psychiatry, SIU School of Medicine, 901 West Jefferson, Springfield, IL 62702; Conrad M. Swartz, M.D.

Educational Objectives:
At the conclusion of this session the participant should be able to predict the maximal attainable peak heart rate in a subject, during ECT. Also, to utilize a comparison between the observed heart rate and the predicted maximal peak heart rate as a measure of seizure quality.

Summary:
Background: Peak heart rate (PHR) is a useful measurement of ECT treatment quality. A comparison of observed ECT PHR to a predicted maximum attainable ECT PHR should help to evaluate seizure quality. This resembles the use of predictive PHR in cardiac stress tests.

Objective: We aimed to identify a relationship between maximum attainable ECT PHR on one hand and age and sex on the other.

Method: PHR were determined from ECG strips with calipers or by digital HR devices for a total of 177 patients. These represented all patients treated by one of us (CS) in three university hospital sites for which such measurements were available. Also recorded were age, sex, and weight.

Results: The lower limits of PHR were as follows.
For men: < age 35: 150 bpm; 35–45: 125 bpm; 45–60: 120 bpm; > 60: 105 bpm
For women: < age 40: 156 bpm; 40–60: 135 bpm; > 50: 125 bpm

Conclusion: These results show a fairly simple relationship between PHR and age, although different between males and females. The peak heart rates during ECT are lower than maximal heart rates predicted by the formula (220-age +/- 15) used for exercise stress testing. Detailed statistical analysis, including a predictive model, is in process and will be presented.

References:

NR124 Monday, May 19, 9:00 a.m.-10:30 a.m.
Spirituality Among Psychiatry Outpatients
Shyam K. Bhat, M.D., Department of Psychiatry, SIU School of Medicine, 901 West Jefferson, Springfield, IL 62702; Vivek Jain, M.D.

Educational Objectives:
1. To learn about the spiritual attitudes and beliefs of patients with different psychiatric disorders— their prevalence and nature.
2. To recognize that patients with different psychiatric disorders have varying spiritual beliefs and needs, and to understand how these might impact treatment and history taking.

Summary:
Background: Although there is a growing appreciation of the role of spirituality as an integral part of well-being and health, there are little data about spiritual beliefs among psychiatric patients. In addition, there are no data on psychiatric patients and their attitudes and needs regarding spiritual exploration by treating psychiatrists.

Objective: We aimed to study spiritual attitudes among psychiatric patients, and to examine if there was a perceived need for more spiritual exploration by treating psychiatrists.

Methods: All participants (n=110) were administered the 26-item Spiritual Involvement and Beliefs Scale (SIBS, r=0.92 and Cronbach’s alpha = 0.92), along with an addendum to evaluate their need for further spiritual exploration by their treating psychiatrist. Also recorded were age, gender, diagnosis, religion, and race.

Results: Statistically significant results included (1) patients with major depressive disorder (MDD) in remission had lower scores than patients not in remission and (2) there was a perceived need for further spiritual exploration by treating psychiatrists only for patients who had MDD not in remission.

Conclusion: These results suggest that patients with MDD not in remission may have different spiritual attitudes and needs as compared with patients who are either in remission, or have other psychiatric diagnoses. They also have a greater perceived need for an exploration of their spirituality by the treating psychiatrist.

References:

NR125 Monday, May 19, 9:00 a.m.-10:30 a.m.
Effects of ECT Electrical Parameters on Clinical Outcome
Jenna A. Hiestand, M.D., 406 W Kirkham Avenue, Webster Groves, MO 63119; Keith E. Isenberg, M.D., Carol S. North, M.D.

Educational Objectives:
1. To describe the effects of different ECT electrical parameters on clinical outcome and their contributions to seizure threshold.

Summary:
Objectives: The impact of electrical impulse delivery characteristics on the seizure threshold of patients receiving ECT remains unclear. The purpose of the current investigation was to determine the impact of variables upon ECT seizure threshold and clinical outcome.

Method: Medical records of all patients receiving ECT titrations during the years of 1996 through 1998 (N=350) were reviewed, and data manually extracted. The sample was titrated using the same ECT device, employing three sets of stimulus parameters (0.5 ms, 30 Hz; 0.5 ms, 60 Hz; 1.0 ms, 30 Hz). A model to predict seizure threshold was constructed using independent variables including age, electrode placement, frequency, pulse width, and train duration. A clinical outcome rating was developed to assess clinical improvement. Data from standard rating scales (BDI, BPRS, YDS) were also collected.

Results: Age, electrode placement, frequency, pulse width and train duration largely predict seizure threshold (91% of variance explained). These variables had no impact on clinical response to ECT.

Conclusions: A model can be constructed that predicts most of the variance for seizure threshold. This data suggests that elements of this model have little implication for clinical improvement. This observation does not address the prediction of side effects, such as memory problems, related to variations in electrical parameters.

References:

NR126 Monday, May 19, 9:00 a.m.-10:30 a.m.
Enhanced Creativity in Bipolar Disorder Patients Compared to Caregivers
National Institute of Mental Health
Andrea M. Alarcon, B.A., Department of Psychiatry, Stanford University, 401 Quarry Road, Room 2130, Stanford, CA 94305-5723; Deborah A. Perlick, Ph.D., Karen Menard, M.A., Natalie Baloga-Mintz, Matthew Schumacher, M.A., Connie M. Strong, Ph.D., Terence A. Ketler, M.D.

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

Summary:
Objective: To explore creativity in bipolar disorder patients (BD) compared with their caregivers (CG).

Method: Eighteen BD and their 18 CG, 27 age-matched healthy controls (HC), and 28 age-matched (unipolar) major depressive
disorder patients (MDD), were assessed with the Barron-Welsh Art Scale (BWAS). As BWAS decreases with age and CG were older than other groups, the analysis was repeated age-matching other groups to CG.

**Results:** BD had higher BWAS scores (21.6 ± 11.6) compared to their CG (11.6 ± 8.0, p < 0.01), age-matched HC (15.3 ± 9.8, p < 0.05), and age-matched MDD (14.6 ± 9.7, p < 0.05). This pattern of BWAS scores was similar when groups were age-matched to CG.

**Conclusion:** BD had enhanced creativity compared to their (older) CG. This effect may not be simply accounted for by age, as it persisted in a bipolar sample age-matched to the CG. These preliminary data need to be considered with caution due to the small sample size and the heterogeneity of the CG group, which included individuals that were both related (five parents/siblings) and unrelated (13 spouses/partners) to BD.

**References:**

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**NR127**

**Monday, May 19, 9:00 a.m.-10:30 a.m.**

**Measurement of Creativity in Bipolar Adults and Their Offspring**

**National Alliance for Research on Schizophrenia and Depression**

Diana Simeonova-Lennon, M.S., Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford, CA 94305; Kimberly Dienes, M.A., Christine Blasey, Ph.D., Terence A. Ketter, M.D., Kiki D. Chang, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should learn about creativity measures in individuals with and at high risk for bipolar disorder.

**Summary:**

**Introduction:** Many artists in the past have been retrospectively diagnosed with bipolar disorder (BD), giving rise to the hypothesis that there is some association between creativity and BD. We hypothesized that adults with BD and their offspring would score higher on the Barron Welsh Art Scale (BWAS; a measure of creativity) than healthy controls and their children.

**Methods:** 17 BD adults (mean age = 42.0, 6 males) and 18 of their children (mean age = 13.0, 14 males) and 12 adults with no diagnosis (mean age = 42.5, one man and 11 women) and 14 of their diagnosis-free children (mean age = 12.8, 9 males) completed the BWAS.

**Results:** The adults with BD scored significantly higher than the control adults on the dislike scale of the BWAS (p = .01), but not on the total score. The subgroup of children with BD did not differ significantly from control children or children with ADHD but their mean scores were higher.

**Conclusion:** The bipolar adults did score higher than the controls on the dislike subscale, although the results were not significant for overall score. However, although the children of bipolar adults did have higher scores on the BWAS than children of controls, this difference was not significant. Further investigation with a larger sample size will present a better picture of the difference between bipolar adults and their children with BD and controls and their children.

**References:**

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**NR128**

**Monday, May 19, 9:00 a.m.-10:30 a.m.**

**Treatment and Outcomes of Patients With Comorbid Depression and Schizophrenia**

Kiran Khanuja, M.D., HSR&D, Veterans Affairs, 2215 Fuller Road, Ann Arbor, MI 48105; Karen Austin, M.P.H., Frederic C. Blow, Ph.D., Richard R. Owen, Jr., M.D., Marcia T. Valenstein, M.D.

**Educational Objectives:**
Through this session, participants should be able to recognize the extent and patterns of utilization in patients with comorbid schizophrenia and depression as compared to patients with schizophrenia alone or depression alone. Participants will also understand the implications of comorbidity for treatment and system planning.

**Summary:**

**Objectives:** This study assessed the patterns of health care utilization in patients with comorbid schizophrenia and depression as compared with patients with depression or schizophrenia alone. **Methods:** Data were obtained from the V.A. National Registry for Depression and the V.A. National Psychosis Registry. Using multivariate analyses that adjusted for age, race, and gender, patients with comorbid schizophrenia and depression (N=26,322) were compared with patients with depression alone (N=279,568) and schizophrenia alone (N=81,455) in terms of hospitalizations, other institutional care, and outpatient utilization during fiscal year 2001.

**Results:** There was a two-fold increase in psychiatric hospitalizations in patients with schizophrenia and depression as compared with patients with schizophrenia alone (p<0.0001) and a three-fold increase as compared with patients with depression alone (p<0.0001). Patients in the comorbid group had significantly increased utilization in residential rehabilitation, domiciliary care, and vocational programs as compared with patients with schizophrenia or depression alone (p<0.0001). The number of outpatient visits doubled for comorbid patients as compared with patients with either depression or schizophrenia alone (p<0.0001).

**Conclusions:** Although it is well known that comorbidity in serious mental illness increases health care utilization, this study documents the extent and patterns of utilization among this vulnerable group of patients.

**References:**

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**NR129**

**Monday, May 19, 9:00 a.m.-10:30 a.m.**

**Cholesterol Screening and Intervention in a Chronic Mental Health Setting**

Candace R. Good, M.D., Department of Psychiatry, Penn State College of Medicine, PO Box 850, 500 University Drive,
NR130 Monday, May 19, 9:00 a.m.-10:30 a.m.
The Internet Usage Patterns of Adult Psychiatric Outpatients

Benjamin W. O'Brien, M.D., Department of Psychiatry, University of Oklahoma, 4502 East 41 Street, Tulsa, OK 74135; William R. Yates, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be informed of the Internet usage patterns of their outpatient adult psychiatric patients, and of the possible ways in which psychiatrists can guide this use.

Summary:

Objective: To gather information from the patients' perspective regarding their Internet use as it relates to their illness, in an attempt to understand how their psychiatrist can guide their Internet experience and maximize the potential benefit.

Method: A patient survey was compiled and approved by the University of Oklahoma's Institutional Review Board. Participants, aged 18 to 80 years, were established at the adult psychiatric clinic. The participants were voluntary and anonymous. Chi-square, probability, and distribution frequency was conducted on the 100 completed surveys.

Results: 77% of patients used the Internet to gather information about their illness, 99% were comfortable discussing what they read with their psychiatrists. 78% were unaware of the agencies sponsoring the websites. 69% selected the websites using a search engine. 27% changed their treatment because of what they read on the Internet. 78% would be interested in communicating with their psychiatrist via email. 80% want to receive a list of websites regarding their disorder from their psychiatrists. Those without a college degree were less likely to use the Internet. Those with a college degree were more likely to change their treatment after using the Internet.

Conclusion: Outpatient adult psychiatric patients use the Internet to learn about their illness and change their treatment as a result. They are open to having their psychiatrist guide their Internet use.

References:


**NR132** Monday, May 19, 9:00 a.m.-10:30 a.m.

**A Biopsychosocial Model of Mood Changes During Pregnancy and the Postpartum**

Canadian Institutes for Health Research

Lori E. Ross, Ph.D., Department of Psychiatry and Behavioral Neurosciences, McMaster University, 50 Charlton Ave. E, WHCC, 6th Fl, Font Bonne, Hamilton, ON L8N 4A6, Canada; Edward M. Sellers, Ph.D., Myroslava K. Romach, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should understand the application of structural equation modeling techniques to mental health conditions with multiple causal variables.

**Summary:**

**Introduction:** Women are vulnerable to mood changes during pregnancy and the postpartum period. While it is generally believed that hormonal changes interact with psychosocial stressors to result in this vulnerability, this hypothesis has not been empirically tested in the published literature.

**Method:** We developed an integrative model of perinatal mood changes on the basis of mood, hormone, and psychosocial data collected from 150 women in late pregnancy and at six weeks postpartum. Structural equation modeling was used to quantify relationships between psychosocial stressors (social support, recent stressful life events), biological variables (progesterone concentrations, genetic risk), and symptoms of anxiety and depression (measured using standardized continuous scales).

**Results:** Biological variables had no direct effect on prenatal depressive symptoms, but acted indirectly through their statistically significant effects on both psychosocial stressors and symptoms of anxiety. The same model did not fit the postpartum data, suggesting that other variables such as obstetrical or infant factors may be relevant to postpartum mood.

**Conclusions:** The indirect nature of the relationship between biological variables and perinatal mood may explain the negative findings of previous research attempting to link these variables in a linear relationship. Our model provides empirical support for a multidimensional understanding of perinatal mental health.

**References:**


**NR133** Monday, May 19, 9:00 a.m.-10:30 a.m.

**Prevalence of Postpartum Obsessions in a Community Sample**

Katherine M. Moore, M.D., Psychiatry, Mayo Clinic, 200 First Street SW, Rochester, MN 55905; Stephanie A. Schwartz, Ph.D., Stephen P. Whiteside, Ph.D., Brett J. Deacon, Ph.D., Sarah A. Kalsey, M.A., Kristi R. Luenzmann, B.S., Manheruh Khandker, B.S., Jonathan S. Abramowitz, Ph.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should recognize how common intrusive thoughts may be in a postpartum population of mothers and fathers and describe them; characterize strategies used to manage intrusive thoughts.

**Summary:**

**Introduction/Hypothesis:** Obsessive-compulsive disorder (OCD) onset in pregnancy and the postpartum has been recognized, with the most prominent symptoms being intrusive thoughts of harming the newborn. We examined the prevalence of intrusive thoughts in a postpartum sample and hypothesized that intrusive thoughts would be fairly common, but in most cases, would not cause significant distress. We also predicted the use of a variety of strategies for managing intrusions.

**Method:** 146 parents (60 fathers and 86 mothers) of babies <6 mos. (M = 4.4 mos.) completed a questionnaire of intrusive thoughts and coping strategies that included the obsessions subscale of the Yale-Brown Obsessive-Compulsive Scale (YBOCS).

**Results:** 68% of mothers and 58% of fathers reported intrusive thoughts (e.g., baby's death; harming the infant). Mean YBOCS-obsessions score was 2.03 (SD = 2.23), indicating subclinical severity. Main strategies to manage thoughts included self-reassurance, checking, and avoidance.

**Conclusions:** Although parents experience upsetting thoughts regarding their infants, in most cases such thoughts are not experienced as highly distressing. Nevertheless, they may lead to coping strategies similar to those observed in OCD. Education about postpartum obsessional symptoms may be useful to parents. Further research on postpartum obsessions may help better understand OCD.

**References:**


**NR134** Monday, May 19, 9:00 a.m.-10:30 a.m.

**Irritability in Women: A New Clinical Measure Supported by Eli Lilly and Company**

Leslie E. Born, M.S.C., WHCC, St. Joseph’s Healthcare, 50 Charlton Avenue East, FB639, Hamilton, ON L8N4A, Canada; Meir Steiner, M.D., Gideon Koren, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be familiar with irritability as a phenomenon and a new clinical measure for rating its severity in female-specific emotional disturbances.

**Summary:**

**Objective:** To develop a new rating scale of irritability for women suffering from emotional disturbances related to reproductive cycle.

**Method:** A questionnaire designed to elicit key words and/or descriptive phrasing that described irritability was distributed to premenstrual/antenatal/postnatal/perimenopausal patients and healthy women in the community. Using Nudist Nvivo and SPSS programs, 121 questionnaires were analyzed in order to generate an item pool, and this was reduced using frequencies of endorsement. The self-rating scale was initially piloted for content and comprehension, and then tested for reliability on 50 patients and healthy volunteers.
Results: The core symptoms of irritability include: annoyance, anger, tension, hostile behaviour, and sensitivity. The new self-rating measure includes 10 items from existing measures and 26 items written from spontaneous descriptions. Reliability statistics showed mean inter-item correlations are close to 0.5, with a minimum variance close to 0, and Alpha = 0.9721.

Discussion: The results to date indicate a high consistency of measurement. A high alpha may indicate redundancy in the measure.

Relevance: A new scale for measuring severity of irritability will assist clinical decision making. The burden of illness associated with severe irritability in women reinforces the importance of timely assessment and appropriate treatment.

References:

NR135 Monday, May 19, 9:00 a.m.-10:30 a.m.
Behavioral Disturbances Associated With Problem Drinking in Late Life
Syed P. Sattar, M.D., Department of Psychiatry, Creighton University, 3528 Dodge Street, Omaha, NE 68131; Delores McArthur-Miller, M.A., Prasad K. Padaia, M.D., William J. Burke, M.D.

Educational Objectives:
At the end of reviewing this poster, the reviewer should be aware of behavior disturbances that may be linked to problem alcohol use.

Summary:
Background: Little research has focused on behavior problems among older alcoholics living in the community. We compared the behavioral symptoms of patients with and without drinking problems.

Method: Charts of patients undergoing geriatric assessment at the University of Nebraska Medical Center were reviewed. All patients received comprehensive medical psychological and psychiatric assessments. A collateral source completed the Neuro-psychiatric Inventory (NPI) and provided a history of alcohol use.

Results: 349 patients were evaluated; mean age was 79.1, 69% were female and mean education was 12 years. Subjects were divided into two groups based on their alcohol use, those with drinking problem (N=86) and those without (N=263). Caregivers of problem drinkers reported more caregiver distress (p<0.05), sleep (p<0.05) and irritability (p<0.01). Problem drinkers had a higher total NPI symptom score (p<0.05) and greater disturbances on the NPI-subscalses for agitation (p<0.05), sleep (p<0.05) and irritability (p<0.01).

Conclusions: Older patients with a history of problematic alcohol use may display more behavioral symptoms compared to those without such use. This in turn may cause increased caregiver distress. Therefore, problem alcohol use may be linked to increased behavior disturbances in later life.

References:

NR136 Monday, May 19, 1:00 p.m.-2:30 p.m.
Normal People Have Vivid Recollections of Things That Did Not Happen
Ron Wright, M.D., Psychiatry Department, University of Arizona, PO Box 245002, Tucson, AZ 85724-5002; C.J. Brainerd, Ph.D., D.G. Payne, Ph.D., V.F. Reyna, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe memory illusions; explain differences between gist and verbatim memories; understand how feeling verbatim details are reconstructed from lasting gist memories; understand how memories can be gist true, but verbatim false; specify when gist-true-but-verbatim-false memories arise and when they are problematic; and understand developmental trends in gist and verbatim memory.

Summary:
Introduction/Hypothesis: Memory is essential to psychiatry, both patients' memories of their past and psychiatrists' memories of their patients. Recent basic science research on memory has shown independent storage for meaning ("gist") and verbatim details. For recent memories, verbatim details are strong and provide verisimilitude. More distant memories are reconstructed from longer-lasting gist memories. Sometimes gist-consistent, but incorrect verbatim details are reconstructed resulting in hallucatory experiences of exact verbatim memories. This research tested the hypothesis that strongly gist-consistent, but nonpresented material would be recalled with imputed verbatim details.

Methods: In three experiments, 271 normal volunteers studied lists of words designed to evoke strong gist memories of specific nonpresented words. Responding pitted gist memories against verbatim memories (conjoint recall), so introspective experience could be assessed via overt responses.

Results: The data suggest high levels of imputed verbatim details to gist-consistent-but-verbatim-false memories. Memory processes for true and false memories were distinct and independent.

Conclusions/Discussion: Carefully controlled study showed reliable memory illusions: Hallucinated details for gist-consistent-but-verbatim-false memories. Limitations include using words as stimuli, but studies using narratives produce parallel findings. Gist memories reflect rememberers' understanding/interpretation; true verbatim information is required to correct misperceptions. False memories based on persistent gist may be more enduring than true verbatim-based memories.

References:

NR137 Monday, May 19, 1:00 p.m.-2:30 p.m.
Prevalence of Menstrual Disorders and Eating Disorders in Female NCAA Athletes
Kristy M. Griffith, M.D., Psychiatry Department, University of Oklahoma, 1704 South Delaware Avenue, Tulsa, OK 74135; William R. Yates, M.D., Craig Johnson, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss the differences in menstrual functioning and eating disordered behavior among female NCAA athletes, comparing the high risk groups gymnastics and cross-country with other sport categories.
Summary:

Objective: To estimate the prevalence of menstrual disorders for female NCAA athletes.

Method: 1,445 student athletes from 11 Division-1 schools were surveyed using a 133-item questionnaire.

Results: Female gymnasts and cross-country runners had lower anthropomorphic measures and higher rates of amenorrhea (gymnasts, 60.6% and cross-country, 59.8%, p<0.001) than athletes in other sport categories. Gymnasts reached menarche at a later age than all other female athletes (mean 15.2 yrs, p<0.001), and cross-country athletes had a significantly longer duration of amenorrhea (mean 8.6 months, p=0.007) and a lower BMI when amenorrheic (mean 17.1, p<0.001) than other female athletes. Currently amenorrheic female cross-country runners had a significantly lower current BMI (mean 18.0, p=0.027), age when first reached lowest weight (mean 15.9 yrs, p=0.001), age when first restricted food intake (mean 14.3 yrs, p=0.001), body fat % (mean 9.0%, p=0.046), and ideal body fat% (mean 9.0%, p=0.025) than runners who were not currently amenorrheic. Gymnasts who had ever been amenorrheic had a significantly lower current body fat % (mean 13.4%, p=0.007) than gymnasts without a history of amenorrhea. The majority of athletes with current amenorrhea exhibit eating disordered behavior (mean 70.2%, p<0.0001).

Conclusion: Female cross-country and gymnastic NCAA athletes are at risk for menstrual disorders, and this finding may help identify those at risk for eating disorders.

References:

NR138 Monday, May 19, 1:00 p.m.-2:30 p.m.
Psychiatrists’ Understanding of Medical Statistics
Arun R. Kunwar, M.D., Department of Psychiatry, Upstate Medical University, 750 East Adams Street, Syracuse, NY 13210; Geoffrey M. Hopkins, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the importance of statistics knowledge in accurate interpretation of medical studies.

Summary:
Objective: To investigate the understanding of medical statistics by psychiatrists.
Methodology: The questionnaire was a self-report and anonymous. It consisted of questions on demographics, confidence, difficulty in interpreting medical statistics, specific understanding of statistical techniques, and on the need for a statistics tutorial in medical journals. Both general and specific understanding of different medical statistics used in psychiatric literature was examined.

Results: Out of 50 psychiatrist surveyed, 33 responded. Overall confidence in interpretation of medical statistics was 44.2% (SD 21.0%). Overall difficulty perceived was 56% (SD 25.1%). The cohort reported that they had no comprehension of 51% of the statistical methods probed. No statistically significant difference existed between the academic and non-academic psychiatrists in reporting confidence and difficulty. Statistically significant difference existed for understanding specific statistical techniques; (56% vs 41%; p 0.0009). The majority (64%) of respondents agreed with the need for a simplified statistical tutorial in medical literature.

Conclusions: This pilot study reveals that the overall understanding of key statistical concepts by psychiatrists was insufficient for accurate interpretation of medical studies. The majority of the respondents agreed with the need for a simplified statistical tutorial in medical journals. The limitations of this study includes: limited sample size and self-reported questionnaire.

References:

NR139 Monday, May 19, 1:00 p.m.-2:30 p.m.
The Impact of Initial Authorization on Outpatient Mental Health Treatment
Harvard Medical School, Department of Psychiatry; NIMH Post-Doctoral Training Grant
Rebecca A. Kornbluh, M.D., Department of Public Health, UCLA, 2409 San Mateo Court, Claremont, CA 91711; Amy Lewis, M.P.H., Karen Richards, M.S.W., Dale Mickey, M.B.A., Qi Zhou, M.D.

Educational Objectives:
At the conclusion of the session, the participant should be able to recognize that even apparently simple care management techniques can exert a significant influence on the treatment that patients receive.

Summary:
Background: With the onset of mental health parity legislation in the majority of states, many traditional mental health management techniques, including copayments and deductibles, are no longer available to HMOs.

Objective: To examine the impact of initial authorization, a remaining management technique in many parity-states, on the utilization of psychotherapy visits. Initial authorization requires an initial telephone request for authorization of visits at the start of treatment, and then a subsequent one-page form request if further visits are desired.

Methods: Data from a large HMO were abstracted for information on outpatient psychotherapy utilization in two different initial authorization conditions. In the first year of the study, patients were uniformly given authorization for eight visits, and in the second year of the study, patients were uniformly given authorization for 12 visits.

Results: In the eight visit year, the hazard of treatment termination exactly at the eighth visit was significantly higher than in the 12-visit year (p<0.01). In the 12-visit year, the hazard was higher for treatment termination exactly at the twelfth visit (p<0.01).

Conclusions: Initial authorization, in spite of its relative simplicity, exerts a significant impact on the duration of treatment for outpatient psychotherapy.

References:
Clinical Presentation of Bipolar Patients With and Without Diabetes Mellitus
Supported by Eli Lilly and Company

Martina Ruzickova, M.D., Department of Psychiatry, Dalhousie University, 5909 Jubilee Road, Room 4031, Halifax, NS B3H 2E2, Canada; Claire Slaney, R.N., Julie Gamham, R.N., Martin Alda, M.D.

Educational Objectives:
At the conclusion of this session, the participant should realize that diabetes mellitus is an important condition comorbid with bipolar disorder. It affects the clinical presentation of bipolar disorder and may lead to poor outcome.

Summary:

Introduction: Patients with bipolar disorder (BD) have about three times higher risk of diabetes mellitus (DM) compared with the general population. Various reasons such as lifestyle, medications, or signal transduction alterations, possibly on a genetic basis may underlie this comorbidity. As a starting point in investigating the relationship between the two disorders, we carried out a study comparing the clinical picture between bipolar subjects with and without DM using data from the Maritime Bipolar Registry.

Methods: The sample (n = 222) consisted of 86 males and 136 females, in the age range of 15 to 82 years, diagnosed with bipolar I (n = 151), bipolar II (n = 65), or bipolar NOS (n = 6) disorders. We analyzed the data with chi-square for categorical, and Wilcoxon test for continuous variables. The variables contributing to differences between the groups were analyzed using logistic regression with DM as a dependent variable.

Results: The prevalence of DM was 11.7% (n = 26). The diabetic group showed significantly higher age (p = 0.0001), increased rates of rapid cycling (p = 0.017), hypertension (p = 0.003), and lower GAF score (p = 0.009). Non-diabetics had higher prevalence of episodic course of BD (p = 0.006). Lifetime history of antipsychotic treatment was associated with an insignificant elevation of the risk (p = 0.16).

Conclusions: Presence of comorbid diabetes in patients with bipolar disorder has relevance for their prognosis, and outcome.

References:

Leuprolide Acetate Treatment of Juvenile Sexual Deviancy

Fabian M. Saleh, M.D., Psychiatry Department, University of Massachusetts, 55 Lake Avenue North, Worcester, MA 01527, Philip Clemency, Ph.D., Marc Fishman, M.D.

Educational Objectives:
This descriptive study examines the effects of leuprolide acetate (leuprolide) on sexual arousal, drive and behavior in juvenile subjects with paraphilic disorders. It also examines the tolerability and safety of leuprolide. At the conclusion of this session, the participants should be able to recognize and treat treatment-resistant juvenile paraphilia.

Summary:
Introduction: Paraphilias are psychiatric disorders primarily characterized by a pattern of deviant sexual thoughts, fantasies, and/or behaviors. Though afflicted individuals usually become aware of the unconventionality of their sexual fantasies by their mid-teens, most do not seek treatment preemptively and/or voluntarily. Once identified, paraphilias can be effectively treated and managed psychotherapeutically and pharmacologically. Leuprolide acetate (leuprolide), a luteinizing hormone-releasing-hormone agonist, has been used with some success in adult paraphilias. Data on its effectiveness and tolerability in the juvenile patient population remain scarce.

Method: Adolescent/young adult patients are followed longitudinally after receiving leuprolide for treatment-resistant paraphilias. Data on the type and frequency of inappropriate sexual thoughts and behaviors are gathered at baseline and at regular follow-up intervals. A 14-item survey serves as the primary outcome measure.

Results: All subjects (current N=6) reported a reduction in target symptoms. One subject continued to engage in sexually offending behaviors, and required augmentation with medroxyprogesterone acetate. Except for one subject, no one reported a decrease in ejaculate function. Baseline Dual-Energy X-ray-Absorptiometry (DEXA) results were within normal limit Follow-up DEXA data are pending.

Conclusion: This study provides preliminary data on the safety and efficacy of leuprolide in previously treatment-resistant paraphilic juveniles.

References:

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Conclusion: This study provides preliminary data on the safety and efficacy of leuprolide in previously treatment-resistant paraphilic juveniles.

References:
and history of ECT. 88% of RD+ vs. 54% of RD− patients had 
early extrapyramidal symptoms and 75% of RD+ vs. 56% of RD−
had a diagnosis of dementia. 

Discussion/Conclusions: Approximately one in seven older de
ovo TD patients developed RD. This is consonant with other 
frequency rates reported in this age group in non-neuroleptic naïve 
patients. Early EPS and presence of dementia may predispose 
TD patients to RD. Standardized scales to measure diverse RD 
features are wanting and a proposed scale is presented.

References:
1. Rich MW, Radwany SM: Respiratory dyskinesias. An underrec-
2. Woerner MG, Alvir JMJ, Saltz BL, Lieberman JA, Kane JA: 
Prospective study of tardive dyskinesia in the elderly: rates 

NR143 Monday, May 19, 1:00 p.m.-2:30 p.m.
Loss of Sustained Antidepressant Response After 
Initial Remission
Jacob B. Kagan, B.A., Weill Medical College, 313 East 81st 
Street, 3FW, New York, NY 10028; Joseph F. Goldberg, M.D., 
Carrie J. Endick, C.S.W.

Educational Objectives:
At the conclusion of this session the participant should be 
able to identify the significant predictors of loss of sustained response to 
fluoxetine treatment, with particular emphasis on the relationship 
between relapse and early response.

Summary:
Objective: Controversy persists about the extent to which early 
antidepressant response may predict sustained response or even-
tual relapse in major depression. We report a prospective analysis of 
sustained vs. lost response to continued fluoxetine treatment 
in depressed, initially responsive outpatients.

Method: 55 DSM-IV unipolar depressed outpatients took fluoxe-
tine for 10 weeks. Acute responders continued open treatment 
for up to one year. Hamilton Depression Scale (HAM-D) scores 
were followed to rate initial response and sustained response 
versus relapse.

Results: (1) Initial patient response occurred at a mean dose 
of 30.9 mg/day. (2) Patients who lost initial responses had an 
earlier age at onset (p=.044) and longer duration of illness (p= 
.028), and tended to have greater baseline illness severity (p= 
.055). (3) Lost responses occurred more frequently among acute 
partial than full remitters (p=.016). (4) Patients who had at least 
a 20% reduction from baseline HAM-D scores by week two were 
more likely to be full responders by the end of the acute phase 
(p=.007), but two-week response did not predict eventual relapse 
during long-term treatment. No significant differences were 
observed in relapse rates between early/transient and late/persistent 
acute response patterns.

Conclusions: Age of onset and residual depressive symptoms 
strongly predict eventual loss of an initial SSRI antidepressant 
response. Signs of initial response after two weeks may not be 
a useful indicator of longevity of a sustained antidepressant re-
sponse.

References:
1. Stewart OW, Quitkin FM, McGrath PJ, Amsterdam J, Fava M, 
Fawcett J, Reimtze F, Rosenbaum J, Beasley C, Robins K: Use of 
Pattern Analysis to Predict Differential Relapse of Remit-
ted Patients with Major Depression During 1 Year of Treatment 
with Fluoxetine or Placebo. Arch Gen Psychiatry 1998; 

2. Tranter R, O'Donovon C, Chandarana P, Kennedy S: Preva-
ience and outcome of partial remission in depression. J Psychiatry 

NR144 Monday, May 19, 1:00 p.m.-2:30 p.m.
Is There a Delay in the Antidepressant Effect? A 
Meta-Analysis
Michael A. Posternak, M.D., Department of Psychiatry, Rhode 
Island Hospital, 235 Plain Street, Providence, RI 02905; Mark 
Zimmerman, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be 
able to describe the time course of improvement on antidepressant 
médication and placebo.

Summary:
Objective: To determine whether or not a delayed antidepres-
sant effect can be observed by analyzing the results of a large 
collection of antidepressant trials conducted over the last two 
decades.

Method: We utilized the results of a recently published meta-
analysis that evaluated placebo response rates in 76 double-blind, 
placebo-controlled trials published between 1981 and 2000. Of 
these 76 trials, 39 studied antidepressant medications with proven 
efficacy, performed weekly or bi-weekly evaluations, and pre-

tected weekly rates of changes in symptom severity scores as 
measured by the Hamilton Depression Rating Scale (HDRS). To 
augment this database, we also manually reviewed each issue 
of six psychiatric journals from January 1990 through December 
2000, from which we located eight additional trials that met our 
inclusion criteria.

Results: Most of the improvement that occurred on antidepres-
sant medication and placebo took place during the first two weeks 
of treatment. Although patients receiving active medication clearly 
fared better, the time course of improvement was nearly identical:
60.2% and 61.6% of the improvement that occurred on active 
médication and placebo, respectively, took place during the first 
two weeks of treatment. Drug-placebo differences were also most 
pronounced during the first two weeks, and diminished in a step-
wise fashion thereafter. Very little drug-placebo differences were 
found between Week 4 and Week 6.

Conclusions: These results challenge the notion that there is a 
two to three week delay before a true antidepressant effect occurs. 
These findings also raise the possibility that a four-week antide-
pressant trial may be more appropriate than a six-week trial.

References:
1. Quitkin FM, Rabkin JG, Ross D, Stewart JW. Identification of 
true drug response to antidepressants. Use of pattern analysis. 
Arch Gen Psychiatry 1984; 41:782-786.
2. Stassen JJ, Angst J, Delini-Stula A. Delayed onset of action 
of antidepressant drugs? Survey of results of Zurich meta-

NR145 Monday, May 19, 1:00 p.m.-2:30 p.m.
The Prevalence of the Metabolic Syndrome Among 
Patients Treated With Atypical Antipsychotic Drugs
David A. Straker, D.O., Department of Psychiatry, Zucker 
Hillside Hospital, 75-59 263rd Street, 2nd Floor, Glen Oaks, NY 
11004; Elayna Rubens, M.D., Fiju Koshy, D.O., Elisse Kramer, 
Ph.D., Peter Manu, M.D.

Educational Objectives:
After reviewing the poster presentation, the participants should 
be able to recognize the feature of metabolic syndrome and devise
cost-effective strategies for its detection among patients treated with newer antipsychotic agents.

**Summary:**

**Background:** The metabolic syndrome (METSYN) is diagnosed in patients with three or more of the following: abdominal obesity (OBES), hypertriglyceridemia (TG), low high-density lipoprotein cholesterol (HDL), high blood pressure (HBP), and high fasting glucose (GLUC). The age-adjusted prevalence of the syndrome among US adults is approximately 25%. OBES, TG, and GLUC are common in patients treated with newer (atypical) antipsychotic agents, but the prevalence and characteristics of METSYN in this population have not been elucidated.

**Methods:** Data regarding METSYN criteria were collected on admission from a near-consecutive group of 94 patients taking newer antipsychotic agents to determine the sensitivity (SENS), specificity (SPEC), positive likelihood ratio (PLR) and posterior probability (PROB) of the individual criteria.

**Results:** The prevalence of METSYN in this sample of psychiatric patients was 29%.

<table>
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<tr>
<th>SENS</th>
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<td>68%</td>
<td>90%</td>
<td>17</td>
<td>82%</td>
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**Conclusions:** Cost-effective screening for METSYN among patients treated with atypical antipsychotic drugs should rely on the high sensitivity of OBES and high predictive value of GLUC.

**References:**

**NR146**

**Monday, May 19, 1:00 p.m.-2:30 p.m.**

**Depressed Patients With Overdrive of the HPA System Have More Severe Benzodiazepine Withdrawal Symptoms**

Adam Wichniak, M.D., Max Planck Institute of Psychiatry, Kraepelinstrasse 10, Munich 80804, Germany; Hans Brunner, Marcus Ising, Francesco Pedrosa, Florian Holsboer, Elisabeth Friess

**Educational Objectives:**
- At the conclusion of this session, the participant should learn about association between overdrive of hypothalamic-pituitary-adrenocortical system and severe benzodiazepine withdrawal symptoms.

**Summary:**

**Objective:** Benzodiazepines are commonly used in the early phase of treatment of depression. Due to the risk of dependence, they should be discontinued as soon as relief of the symptoms of depression has occurred. In some patients, this leads to a transient worsening of symptoms or even to a reoccurrence of depression. In the present study we investigated whether patients with severe benzodiazepine withdrawal syndrome show hyperactivity of the hypothalamic-pituitary-adrenal (HPA) system.

**Method:** We performed the combined dexamethasone/CRH test in 14 depressed patients (13 f, 1 m, mean age 54.6 ± 14.6) before their benzodiazepine medication was discontinued. The diagnoses were established according to DSM-IV criteria. The benzodiazepine taper off was performed with maximal speed of 5 mg diazepam-equivalents per week. The severity of withdrawal symptoms was measured using the Clinical Institute Withdrawal Assessment-Benzodiazepines (CIWA-B). The depressive psychopathology was monitored using the HADRS, MADRS and BDI.

**Results:** Patients (n=7) whose CIWA-B total score increased over 14 points during benzodiazepine withdrawal did not differ from patients (n=7) with low increase of CIWA-B total score (<14 points) in the pre-taper psychopathology ratings. The first groups of patients, however, showed a larger cortisol and ACTH response in the dexamethasone/CRH test preceding the discontinuation of benzodiazepines than those patients displaying less severe withdrawal symptoms (ANCOVA with covariate initial benzodiazepine dose, p<0.05).

**Conclusions:** In depressed patients, HPA overdrive is associated with more severe benzodiazepine withdrawal.

**References:**

**NR147**

**Monday, May 19, 1:00 p.m.-2:30 p.m.**

**The Beck Cognition Checklist for Mania: A New Scale**

Susan J. Wenze, B.A., Psychiatry Department, Weill Medical College Cornell, 525 East 68th Street, Box 140, New York, NY 10021; Joseph F. Goldberg, M.D., Tara M. Singer, Ph.D., Aaron T. Beck, M.D.

**Educational Objectives:**
- At the conclusion of this session, the participant should understand about patterns of maladaptive, automatic cognitions in manic patients.

**Summary:**

**Objectives:** Cognitive dimensions of depression have long been considered fundamental to both its phenomenology and pathogen- esis. Underlying cognitive dysfunction in mania has not been as thoroughly examined. The current study sought to investigate and characterize faulty cognitive beliefs in bipolar manic patients.

**Methods:** We administered a new, validated, 61-item, self-report questionnaire by Beck et al., to assess automatic thought patterns in mania to outpatients with bipolar mania (n=30, YMRS>15), unipolar depression (n=32, HAM-D>15), or non-psychiatric controls (n=29). Seven dimensions related to maladaptive cognitive beliefs were evaluated in mania relative to depression.

**Results:** Bipolar manic, unipolar depressed, and control sub- jects' scores differed on subscales measuring self-importance (p=.041), interpersonal frustration (p=.001), and past and future outlooks on life (p=.000). Significant interassociations (r>.5, p<.05) were observed between most of the modules within each of the three diagnostic groups. Manic symptoms were associated with lower scores on the subscale measuring past and future outlooks on life in control subjects (r=.462, p=.023). Depressive symptoms were associated with lower scores on the subscale measuring self-importance (r=.415, p=.028) and the subscale measuring past and future outlooks on life (r=.378, p=.047) in unipolar depressed patients. No significant inter-diagnostic differences were seen in subscales assessing relationship views, spending, excite- ment, or activity.
NR148  Monday, May 19, 1:00 p.m.-2:30 p.m.
Longitudinal Assessment of Emotional Schemas in Bipolar Outpatients
Susan J. Wenze, B.A., Psychiatry Department, Weill Medical College Cornell, 525 East 68th Street, Box 140, New York, NY 10021; Joseph F. Goldberg, M.D., Tara M. Singer, Ph.D., Carrie J. Endick, C.S.W., Robert L. Leahy, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be informed about patterns of emotional response, cognitive processes, and related psychopathologic domains in bipolar disorder.

Summary:

Introduction: Emotional schemas have been implicated in the cognitive aspects of depression. The objective of this study was to longitudinally investigate patterns of emotional and cognitive response in affectively non-syndromal bipolar individuals.

Methods: We administered a validated, 50-item, self-report questionnaire to assess emotional schemas in a sequential group of non-syndromal (HamDc=14, YMRS=10) bipolar outpatients and evaluated 14 dimensions related to thought patterns. Responses were assessed at two points in time approximately eight weeks apart.

Results: Significant inter-associations (r=5, p<0.05) were observed between most dimensions. Subsyndromal depressive symptoms were associated with lower scores on the “expressivity” module (r=0.531, p=0.034) and the “higher values” module (r=-0.530, p=0.035). Hypomanic symptoms were associated with lower scores on the “validation” module (r=-0.532, p=0.034) and the “expression” module (r=-0.580, p=0.018). Substantial, significant correlations (r=0.645-0.890, p<0.05) were observed from the first to second assessment in 10 of the 14 schema domains.

Conclusion: Bipolar individuals possess distinct patterns of cognitive processing of emotions. Such schemas appear relatively stable across time, though some domains vary with even subsyndromal states.

References:


NR150  Monday, May 19, 1:00 p.m.-2:30 p.m.
Cardiovascular Risk Factors and MDD Relapse
Dan V. Ioifulescu, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114; George I. Papakostas, M.D., Nicoletta Clementi-Craven, M.D., Julie L. Ryan, B.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Maurizio Fava, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the impact of cardiovascular risk factors during the continuation phase of antidepressant treatment in major depressive disorder.

Summary:

Objective: We examined the impact of cardiovascular risk factors on the rate of relapse of major depressive disorder (MDD) during 28-week continuation therapy with the antidepressant fluoxetine.

Method: We studied 119 outpatients meeting DSM-IV criteria for MDD (63 women and 56 men; mean age: 39.9 years) who entered the continuation phase of an antidepressant treatment study. Patients had achieved remission (defined as a 17-item Hamilton Rating Scale for Depression (HAMD-17) score <8 after eight weeks of treatment with fluoxetine 20 mg/day. We recorded for each subject the age, gender, smoking status, family history, total cholesterol, arterial hypertension, diabetes, concomitant medications. We calculated a cumulated cardiovascular risk score (range = 0–5) following the NIH ATP III guidelines (based on the
Framingham Heart Study). Patients were followed for 28 weeks of continued treatment with fluoxetine 40 mg/day. We used logistic regression to assess the relationship between depressive relapse and cardiovascular risk score, as well as individual cardiovascular risk factors.

Results: 44 patients (37%) did not complete and eight patients (6.7%) relapsed during the 28-week continuation phase. Among cardiovascular risk factors, total cholesterol level significantly predicted relapse of MDD (p<.05). There was also a trend for the association between total cholesterol and increases in HAM-D-17 scores (p=.056). Other cardiovascular risk factors, as well as the total cardiovascular risk score, were not significantly associated with depressive relapse.

Conclusion: Higher total cholesterol levels significantly predict relapse of major depressive disorder during continuation treatment with the antidepressant fluoxetine.

References:

NR151  Monday, May 19, 3:00 p.m.-5:00 p.m.
Efficacy of Thyroid Hormone (T3) Addition to Paroxetine in Major Depression
Bente C. Appelhof, M.D., Department of Endocrinology, Acad. Med. Center, Meibergdreef 9, Room F5-173, Amsterdam 1105AZ, Netherlands; Jantien P. Brouwer, M.D., Richard Van Dyck, M.D., Eric Fliers, M.D., Witte J. Hoogendijk, M.D., Jochanan Huysers, M.D., Aart H. Schene, M.D., Jan G. Tijssen, M.D., Wilmar M. Wiersinga, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to form an evidence-based opinion about the role of thyroid hormone (T3) addition to SSRI as an augmentation strategy in the treatment of major depressive disorder.

Summary:
Objective: Guidelines for the treatment of major depressive disorders propose the addition of triiodothyronine (T3) to antidepressants as an augmentation strategy. However, evidence derives from relatively small studies and the efficacy of T3 has not been investigated in combination with selective serotonin reuptake inhibitors. We investigated the efficacy of T3-addition to paroxetine in major depression.

Methods: 113 patients with major depressive disorder and a baseline 17-item Hamilton Rating Scale for Depression (HRSD) score ≥16 were randomly assigned to eight weeks of double-blind outpatient treatment with low-dose T3 (25 µg), high dose T3 (25 µg twice daily), or placebo in addition to paroxetine 30 mg daily.

Results: 106 patients started treatment and were included in the outcome analysis. Response rate after eight weeks, defined as a reduction of HRSD score ≥50%, was 46% in all three treatment arms (p=0.99). Remission rate, defined as a HRSD score ≤8 at endpoint, was 32% in both T3 groups and 36% in the placebo group (p=0.92). Patients on T3-addition reported significantly more side effects than patients on placebo-comedication.

Conclusion: These results do not support a role for T3-addition to SSRI in the treatment of major depressive disorder.

References:

NR152  Monday, May 19, 3:00 p.m.-5:00 p.m.
Injectable Ziprasidone in the Psychiatric Emergency Service
Steven G. Klotz, M.D., Department of Psychiatry, SUNY Stony Brook, Health Science Center T-10, Room O20, Stony Brook, NY 11794-8101; Horacio Preval, M.D., Robert Southard, R.N., Andrew J. Francis, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to treat agitation using ziprasidone in a psychiatric emergency service setting.

Summary:
Objective: Injectable atypical neuroleptics may supplant benzodiazepine and/or butyrophenone alternatives. Published studies of intramuscular [IM] ziprasidone excluded severe psychiatric agitation [AGIT], and that from alcohol [ETOH] or other substances [SUBS].

Method: We determined BARS agitation scores [min=1, max=7] and duration of physical restraints in a naturalistic study of IM sedatives in our psychiatric emergency service during a three-month period. Dosages were 20 mg for ziprasidone, and varied for conventional IM sedatives [86% haloperidol and/or lorazepam].

Results: Baseline BARS scores were high for AGIT [N=40], ETOH [N=10] and SUBS [N=19] [respective means 6.5, 6.9, 6.5, P=NS]. Ziprasidone decreased agitation scores rapidly [means 5.7, 5.3, 5.6 at 15 min and 3.2, 3.3, 3.0 at 45 min (P<0.01)]. At 2 hr, scores were 2.5, 2.1, and 2.3. For conventional sedatives [N=7] baseline scores were 6.4, 5.4 at 15 min, 3.3 at 45 min, and 2.7 at 2 hr [P=N.S. from ziprasidone]. Restraint duration decreased from 91±4 to 45±4 min with ziprasidone [P<0.01]. Of 17 EKGs, none had prolonged QTc; one dystonic reaction occurred with ziprasidone.

Conclusion: IM ziprasidone appears effective for severe agitation including alcohol or substance-induced intoxication. It may lead to reduced time in restraints compared with conventional agents.

References:

NR153  Monday, May 19, 3:00 p.m.-5:00 p.m.
EPS With Atypical Neuroleptics in Bipolar Disorder
Klara J. Rosenquist, B.S., Department of Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139; S. Nassir Ghaemi, M.D., Douglas J. Hsu, B.S., Frederick K. Goodwin, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the relative risks of extrapyramidal symptoms with atypical neuroleptics in bipolar disorder.
Summary:

Objective: To examine, in a real-world clinical setting, the risk of extrapyramidal symptoms (EPS) with atypical neuroleptics in patients with bipolar disorder.

Methods: We assessed results of 27 atypical trials (9 risperidone, 9 quetiapine, 9 ziprasidone, 3 olanzapine) in 20 patients with bipolar disorder Type I. Risk of EPS was assessed using the Abnormal Involuntary Movement Scale, Barnes Akathisia Rating Scale, and the Simpson-Angus Scale. Median duration of treatment was 18 weeks (range 5–94 weeks) and 74% of patients were female.

Results: 48.1% of trials resulted in EPS. Frequency of EPS and frequency of discontinuation did not differ statistically between specific neuroleptic agents or between high potency (risperidone/ziprasidone; 8/15 trials, 53.3%) and low potency (quetiapine/olanzapine; 5/12 trials, 41.7%) agents. 22.2% of trials were discontinued due to side effects, including three trials in two patients that were discontinued due to tardive dyskinesia.

Conclusions: About one-half of patients experienced EPS in this real-world clinical setting. This rate is much higher than the 5% to 15% range reported in clinical trials, suggesting problems with clinical trial generalizability. The apparent tardive dyskinesia rate in our sample was about 7%, which is higher than expected from studies of schizophrenia, and may require further investigation in bipolar disorder.

References:

NR154 Monday, May 19, 3:00 p.m.–5:00 p.m.
The Monoamine Transporter Gene Polymorphisms and the Antidepressant Response

Hyeran Kim, M.D., Department of Psychiatry, Samsung Medical Center, 50 Ilwon-Dong, Kangnam-gu, Seoul 135-710, Korea; Shih-Won Lim, M.S., Doh Kwon Kim, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize genetic polymorphisms of the serotonin transporter and the nortriptyline transporter are associated with individual patient antidepressant responses to SSRI antidepressants or to nortriptyline.

Summary:

Objective: Genetic polymorphisms of the serotonin transporter (SERT), the major site of action for selective serotonin reuptake inhibitor (SSRI) antidepressants, are reportedly associated with the SSRI drug response. The norepinephrine transporter (NET) is also a target for antidepressants such as nortriptyline, and the NET has a similar structure and mode of action as the SERT. We investigated whether genetic polymorphisms of SERT and NET were associated with individual patient antidepressant responses to SSRI antidepressants or to nortriptyline.

Method: One hundred eighty-three Korean patients with major depressive disorder were enrolled and placed in an SSRI-treatment group (102 patients) or a nortriptyline-treatment group (81). We examined SERT and NET gene polymorphisms for each group, and compared their responses to medication after six weeks of treatment. We analyzed s/l variations of the promoter region and intron 2 in the SERT gene, and the T/C nucleotide variation (NET1) of exon 2 and G/A variation (NET8) of exon 9 in the NET gene, using polymerase chain reactions and electrophoresis.

Results: We found that SERT intron 2 polymorphism had significant associations with both the SSRI and nortriptyline responses. SERT promoter polymorphism was associated with the SSRI response, and NET8 polymorphism was weakly associated with the nortriptyline response. NET1 polymorphism had no relation with any antidepressant response.

Conclusion: These results could help us to explore the genetic components that play a role in producing an individual's characteristic response to an antidepressant, and thus will help the clinician to individualize each patient's therapy.

References:

NR155 Monday, May 19, 3:00 p.m.–5:00 p.m.
QTc Values in Children and Adolescents: Machine Versus Hand-Derived Values

Fida Hassan, M.D., 2371 Stone Road, Ann Arbor, MI 48105-2538; Madhvi P. Richards, M.D., Paul E. Quinlan, D.O., Norman E. Alessi, M.D.

Educational Objectives:

At the conclusion of this session, the participant should have a better understanding of the significance of machine-generated vs hand-derived QTc intervals in making clinical decisions when prescribing psychotropic medications that may cause QTc alterations.

Summary:

Objective: Suggestions that hand-derived QTc values are more accurate than machine-generated values is of concern as QT prolongation may cause adverse cardiac consequences. Our objective is to compare machine- and hand-derived QTc values in a pediatric population on whom data are lacking.

Method: EKGs were obtained by retrospective inpatient chart review of 15 children and adolescents taking ziprasidone. QT and RR intervals in lead II were measured manually using calipers by a single observer. QTc values were calculated using Bazett and Fridericia formulas and rounded off to the closest millisecond. Data were analyzed using ANOVA.

Results: Mean age of the patients was 12.60 ± 3.25 years. Mean baseline QTc using machine-generated values and those using Bazett and Fridericia formulas were 413.27 ± 13.05, 428.33 ± 22.40, and 401.00 ± 16.40 milliseconds, respectively. On post-EKGs the mean values were 415.80 ± 13.68, 425.40 ± 18.38, and 398.40 ± 12.92 milliseconds, respectively. Differences in values obtained by the three methods at either time point were not significantly different statistically.

Conclusion: Results suggest that machine-generated QTc values are not significantly different from hand-derived values. Therefore, clinicians can use machine-generated values to make clinical decisions when prescribing psychotropic medications that may cause QTc alterations.

References:
NR156  Monday, May 19, 3:00 p.m.-5:00 p.m.
Low Incidence of Lamotrigine Treatment-Emergent Rash With Dermatology Precautions
Supported by GlaxoSmithKline
Rebecca A. Chandler, B.S., Department of Psychiatry, Stanford University, 401 Quarry Road, Room 2130, Stanford, CA 94305-5723; Colette O’Keeffe, M.D., Po W. Wang, M.D., Kamin Giri, M.D., Cristin Davenport, Matthew Schumacher, M.A., Terence A. Ketter, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that dermatology precautions (limiting antigen exposure) during the first three months of treatment with lamotrigine may yield a low incidence of rash.

Summary:
Objective: To assess treatment-emergent rash incidence when using dermatology precautions (limited antigen exposure) during lamotrigine initiation.

Method: In a retrospective chart review, rash incidence was assessed in 66 bipolar disorder patients instructed for the first three months on lamotrigine, NOT to ingest other new medicines or new foods, or utilize new cosmetics, conditioners, deodorants, detergents, or fabric softeners, and to avoid sunburn or poison ivy/oak exposure. Lamotrigine was not started within two weeks of having a rash, viral syndrome, or vaccination.

Results: No patient had serious rash, and only 1/66 (1.5%) discontinued lamotrigine due to benign rash. One additional patient with recurrent mouth sores whose mother had pemphigus discontinued due to allergy concerns. 5/66 (7.6%) had benign rash. However, two of these patients were not adherent to dosing recommendations or dermatology precautions. Among the remaining patients, 3/64 (4.7%) had benign rash, with 2/64 (3.1%) considered related to lamotrigine.

Conclusion: 4.7% of patients adhering to dermatology precautions and dosage recommendations developed treatment-emergent rash, lower than the 10% incidence in other clinical studies. Systematic studies are needed to confirm these preliminary findings suggesting that dermatology precautions may yield a low incidence of rash with lamotrigine.

References:

NR157  Monday, May 19, 3:00 p.m.-5:00 p.m.
Topiramate for Clozapine-Induced Weight Gain
APA/GlaxoSmithKline Fellows
Christine J. Truman, M.D., Department of Psychiatry, New York Presbyterian Hospital, 525 East 68th Street, Box 140, New York, NY 10021; Jill Ann Jacobson, M.D., Joseph F. Goldberg, M.D., James H. Kocsis, M.D.

Educational Objectives:
The purpose of this poster is to better understand the relationship between treatment with topiramate and reduction of weight gain due to clozapine treatment.

Summary:
Objective: The purpose of this pilot study is to determine if treatment with topiramate facilitates weight loss in patients reporting weight gain with clozapine treatment. Despite good antipsychotic efficacy in the treatment of refractory psychosis, the antipsychotic medication, clozapine, has been associated with obesity, hypertriglyceridemia, and diabetes, all risk factors for cardiovascular disease and other serious medical illnesses. This poses significant health risks and contributes to noncompliance in a population that is already vulnerable to psychiatric and medical morbidity. Topiramate, a novel anticonvulsant agent, has been associated with the side effect of weight loss.

Method: Outpatients with DSM-IV-diagnosed schizophrenia or schizoaffective disorder with reported weight gain of ≥10% of baseline on clozapine were treated with open-label topiramate up to 75mg twice daily for 16 weeks.

Results: After 16 weeks of treatment with topiramate, all ten subjects lost weight (mean (± SD) weight loss = 6.0 (± 4.3) kg). Topiramate was well tolerated. No subjects experienced exacerbation of psychiatric symptoms.

Conclusions: Based on this pilot study, topiramate appears to facilitate weight loss in patients experiencing weight gain with clozapine treatment. Controlled data with a larger sample size are needed to confirm these preliminary findings.

References:
which may be adjusted by varying shifts or providing recreational activity at the time of shift change.

choice of medications, violence in history of present of illness, ethnicity, length of stay, number of admissions, diagnosis, and the control group indicated no significant differences in terms legal and substance history.

patients were most likely to be given prn psychotropics at 1500 distribution among all prn users and higher users. Furthermore, compare the difference between high prn use and the control group by age, sex, and unit.

Five-week period. These 16 high prn users accounted for 33% of all prn use in the 300 bed hospital. An additional 16 control patients without prn administration were matched by age, sex, and unit. PRN use was observed at least once in 91 patients. In addition, high prn users were identified from the 91 patients who had more than six prn administrations during the five-week period. These 16 high prn users accounted for 33% of all prn use in the 300 bed hospital. An additional 16 control patients without prn administration were matched by age, sex, and unit.

T test was applied to study the shift and hourly distributions of prn use; T test with unequal variance and Fisher's exact test were utilized to compare the difference between high prn use and the control groups.

Results: There was significant difference in hourly and shift distribution among all prn users and higher users. Furthermore, patients were most likely to be given prn psychotropics at 1500 (around shift change). Comparisons between the high prn users and the control group indicated no significant differences in terms of ethnicity, length of stay, number of admissions, diagnosis, choice of medications, violence in history of present of illness, legal and substance history.

Conclusion: High prn use is likely related to management factor, which may be adjusted by varying shifts or providing recreational activity at the time of shift change.

References:

NR159 Monday, May 19, 3:00 p.m.-5:00 p.m.
Administration of PRN Psychotropics in a Chronic Hospital
Hong Chen, M.D., Department of Psychiatry, Hershey Medical Center, 32 University Manor East, Hershey, PA 17033; Paul A. Kett, M.D.

Educational Objectives:
This study is to examine whether environmental management or patient factors were associated with PRN use.

Summary:
Introduction: Patients hospitalized for treatment of psychiatric illness commonly receive prn psychotropics. Little is known about the reasons for prn use. The purpose of the present study was to examine whether environmental, management or patient factors were associated with prn use.

Method: A retrospective review of all prn use was carried out in a chronic care hospital over a five-week study period (2002) in three units. The shift and hourly distributions of prn use among three units were analyzed. PRN use was observed at least once in 91 patients. In addition, high prn users were identified from the 91 patients who had more than six prn administrations during the five-week period. These 16 high prn users accounted for 33% of all prn use in the 300 bed hospital. An additional 16 control patients without prn administration were matched by age, sex, and unit.

Statistical Analysis: One sample Goodness of Fit test was applied to study the shift and hourly distributions of prn use; T test with unequal variance and Fisher's exact test were utilized to compare the difference between high prn use and the control groups.

Results: There was significant difference in hourly and shift distribution among all prn users and higher users. Furthermore, patients were most likely to be given prn psychotropics at 1500 (around shift change). Comparisons between the high prn users and the control group indicated no significant differences in terms of ethnicity, length of stay, number of admissions, diagnosis, choice of medications, violence in history of present of illness, legal and substance history.

Conclusion: High prn use is likely related to management factor, which may be adjusted by varying shifts or providing recreational activity at the time of shift change.

References:

NR161 Monday, May 19, 3:00 p.m.-5:00 p.m.
Metabolic Consequences of Ziprasidone and Quetiapine: A Retrospective Study
Ritu Chahil, M.D., Department of Psychiatry, University of Virginia at Roanoke/Salem, 1940 Roanoke Boulevard, Building 11, 116A7, Salem, VA 24153; Ali Iranmanesh, M.D., Joann Hawley, Pharm.D., Melissa Maxwell, Pharm.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the effects of atypical antipsychotic agents on serum lipid profile.

Summary:
Introduction: Atypical antipsychotic agents have superior side effect profile regarding extrapyramidal symptoms however they have been reported to cause weight gain, diabetes mellitus, and hyperlipidemia. Although the metabolic effects of clozapine, olanzapine and risperidone are well documented there is limited and controversial data on quetiapine and ziprasidone. The present study was conducted to assess the effects on lipid profiles of patients on ziprasidone or quetiapine.

References:
Methods: In this retrospective study, medical records of 48 patients treated with ziprasidone or quetiapine were reviewed for serum cholesterol, triglycerides, low density lipoproteins (LDL), and high density lipoproteins (HDL). Drug-induced changes were determined by comparison of data at baseline (prior to onset of treatment) and within one year of therapy. Results are presented as mean ± SEM and compared for statistical significance using Student T-Test.

Results: There were no statistically significant changes in serum cholesterol with treatment with either ziprasidone (196.21 ± 36.99 vs. 203.58 ± 47.85; p=0.5) or quetiapine (194.34 ± 36.38 vs. 213.37 ± 33.42; p=0.065). Additionally there were no significant changes in serum LDL, HDL and triglycerides.

Conclusion: Quetiapine or ziprasidone do not appear to have any effect on serum lipid levels. Routine clinical monitoring of serum lipids may not be indicated on patients on these agents.

References:

NR162 Monday, May 19, 3:00 p.m.-5:00 p.m.
Patient Expectation as a Predictor of Outcome in Antidepressant Treatment
Supported by Pharmacia
Heather V. Krell, M.D., Department of Psychiatry, UCLA/NPI
760 Westwood Boulevard, Los Angeles, CA 90103
Andrew F. Leuchter, M.D., Ian A. Cook, M.D., Melinda Morgan, Ph.D., Michelle Abrams, R.N.

Summary:
Background: There has been little systematic study of the relationship between patient expectations of improvement and outcome of the pharmacological treatment of depression. This study was conducted to examine subject expectations for treatment as a predictor of treatment response.

Methods: 25 subjects meeting DSM-IV criteria for major depression with Ham-D ≥17 were enrolled. Subjects were treated for eight weeks with reboxetine 8–10 mg per day. At the initiation of this study, subjects were asked to report their expectations for the effectiveness of the medication.

Results: Of the patients who reported their expectation that the medication would be “very effective” 90.0% responded with a significant level of response while only 33.3% of those who reported “somewhat effective” responded (n=5) [X2=7.819 p=.005]. There was no association between other potential predictors of treatment response.

Conclusion: These findings suggest that individuals with high baseline expectation of improvement with treatment demonstrate a significantly higher level of response than those with lower expectations.

Significance: Subject expectation should be examined as a predictor of outcome in pharmacologic treatment trials. Future research should examine methods for altering expectations to determine which can affect response rates in clinical trials.

NR164 Monday, May 19, 3:00 p.m.-5:00 p.m.
Retrospective Cohort Study of Diabetes Mellitus and Antipsychotic Treatment in a Geriatric Population in the U.S.
Supported by Eli Lilly and Company
Peter D. Feldman, Ph.D., Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285
Linda K. Hay, Ph.D., John S. Kennedy, M.D., David Hutchins, Ph.D., Kenneth Hornbuckle, D.V.M., Walter DeBerdt, M.D., Alan F. Breier, M.D.

Educational Objectives:
At the conclusion of this presentation, the attendee should be familiar with the findings that suggest that the risk of diabetes mellitus among elderly patients receiving antipsychotics is higher than for those receiving conventional antipsychotics.

Summary:
This analysis investigated the risk of developing diabetes mellitus among elderly patients aged 60+ during treatment with antipsychotic medications.

Diabetes risk was studied by analyzing new prescription claims for antihyperglycemic agents in the AdvancePCS claim database among elderly patients who initiated antipsychotic therapy within a three-month period. The following cohorts were studied: (1) an
elderly reference population [no antipsychotics used: n=1,836,799], (2) all conventional antipsychotics [n=11,546], (3) haloperidol [n=6481], (4) thioridazine [n=1658], (5) all atypical antipsychotics [n=19,407], (6) clozapine [n=117], (7) olanzapine [n=5382], (8) quetiapine [n=1664], and (9) risperidone [n=12,244]. The incidence of new diabetes was higher in every antipsychotic cohort than in the standard reference population. Risks were not different overall, however, between the atypical and conventional antipsychotic cohorts (2 & 5). For the individual antipsychotic cohorts, risk was highest for patients treated with thioridazine (95% CI: 3.1–5.7) and lowest for quetiapine (95% CI: 1.3–2.9). Risks for the haloperidol, olanzapine, and risperidone cohorts were intermediate. Among atypicals, only patients treated with risperidone had a significantly higher risk (95% CI: 1.05–1.60, p=0.016) than haloperidol. Conclusions about clozapine were hampered by the low number of patients in the cohort.

Although causality remains to be demonstrated, diabetes risk was higher among elderly patients receiving antipsychotic treatment than among the general elderly patient population. As a group, risk for atypical antipsychotics was not higher than for conventional antipsychotics, but risperidone’s risk uniquely was significantly higher than haloperidol’s.

References:

NR165 Monday, May 19, 3:00 p.m.–5:00 p.m.
Lamotrigine Augmentation in Unipolar Depression
Fabio L. Rocha, M.D., Department of Psychiatry, IPSEMG, Rua Dos Otoni-106, Belo-Horizonte 30150-270, Brazil; Claudia Hara, M.S.C.

Educational Objectives:
At the conclusion of this session, the participant should recognize the efficacy and tolerability of lamotrigine as an augmentation drug in treatment-resistant unipolar depression.

Summary:
Introduction: A significant number of patients with unipolar depression fail in achieving remission after one or a series of antidepressants. We present the result of a retrospective chart review of the efficacy and tolerability of lamotrigine as an augmentation drug in the treatment-resistant unipolar depression.

Methodology: Previous absence of response was defined as clinically significant presence of depressive symptomatology after six weeks of treatment with an antidepressant, with at least three weeks at the maximum dose tolerated by the patient. The patients were rated retrospectively using the Clinical Global Impression rating scale.

Results: Seventy-six percent of the patients improved. Gender, age, baseline severity of the episode, and degree of previous nonresponse were not statistically associated with response to lamotrigine augmentation. Comorbidity showed a tendency to be negatively related with response to lamotrigine. Three patients abandoned the treatment with lamotrigine due to side effects. Complaints were excessive somnolence, headache, dizziness, nausea, and malaise.

Discussion/Conclusion: Data suggest that lamotrigine is a promising drug for treatment-refractory unipolar depression. Double-blind studies are necessary to substantiate its use as an augmentation agent.

References:

NR166 Monday, May 19, 3:00 p.m.–5:00 p.m.
Is There a Link Between Antipsychotics and Low Bone Mineral Density?
Supported by AstraZeneca Pharmaceuticals
Oliver D. Howes, M.R.C., Psych Med, Institute of Psychiatry, Camberwell, London SE5 8AF, United Kingdom; Lindsay Simpson, M.R.C., Shubulade Smith, M.R.C.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that patients taking antipsychotics may be at increased risk of osteoporosis or osteopenia.

Summary:
Introduction: To determine whether antipsychotics are associated with low bone mineral density secondary to hyperprolactinaemia. Hyperprolactinaemia due to pituitary pathology is linked to osteoporosis. It is established that most antipsychotics can cause chronic hyperprolactinaemia, although some have little effect on prolactin secretion (clozapine, quetiapine, olanzapine).

Method: The study used a case-control design. Subjects were consecutive clinic attendees taking an antipsychotic for ≥2 years, and controls were a local population reference sample. Main outcome measures were DXA absorbiometry (DXA) scan of lumbar spine, and prolactin levels. DXA scans are reported as t-scores. Results: A total of 95 subjects were assessed (mean age 46y, SD±13.06, 54% male, mean medication dose 279 mg chlorpromazine equivalent, SD±36.1). Mean spinal t-score: –0.65 (SD±1.4, p<0.001), prolactin 725 m U/L (SD±1127, upper limit of reference range 450mU/L). Controlling for confounding factors did not alter the significance of the reduced bone mineral density. 37.8% of subjects showed spinal osteoporosis or osteopenia.

Conclusions: The data indicate that spinal bone mineral density is significantly lower than the controls. This supports an association between antipsychotic treatment and reduced trabecular bone mineral density (the pattern of bone change associated with hyperprolactinaemia associated with pituitary pathology). Patients taking antipsychotics may be at increased risk of osteoporosis or osteopenia.

Funding: Astra-Zeneca, Eli Lilly, SELHA grant.

References:

NR167 Monday, May 19, 3:00 p.m.–5:00 p.m.
Evidence of Publication Bias in Estimates of NMS Incidence
Ronald J. Gurrera, M.D., Department of Psychiatry, VA Boston Health Care, 940 Belmont Street, #116A, Brockton, MA 02301; John C. Simpson, Ph.D., Ming T. Tsuang, M.D.
Educational Objectives:
At the conclusion of this session, the participant should be able to cite evidence of publication bias in published estimates of neuroleptic malignant syndrome incidence, and identify several methodological factors associated with increased risk of publication bias.

Summary:
Introduction: Published estimates of the incidence rate for neuroleptic malignant syndrome (NMS) are notoriously variable, ranging from 0% to 3.23%. This dramatic variation has been attributed to the combined effects of a real decline in incidence over time and the low reliability of earlier studies, most of which used a retrospective methodology and inconsistent diagnostic criteria. Inconsistent estimates of NMS incidence estimates have hindered risk factor identification and evaluations of prevention strategies. This study examined published reports of NMS incidence for sources of experimental bias and time-related trends that might account for this excessive variability.

Methods: A National Library of Medicine computerized search was conducted to identify potentially eligible studies, supplemented by a manual search of one of the author's (RJG) own library of NMS publications. Twenty-two previously reported estimates were identified as candidates for analysis. The relationship of estimated NMS incidence (I) to time, study size (N), and case ascertainment (C) was examined using standard graphical and statistical methods.

Results: No NMS incidence trend over time was found (r Spearman's ρ = .269, p = .226). Log(I) was significantly linearly related to log(N) (β = −.823, R² = .677, p = .000) for all studies, as well as in a select subgroup (N=13) of studies that satisfied minimum methodology requirements (β = −.739, R² = .546, p = .004). Mean weighted incidence rate was significantly lower in the select subgroup of studies (4.70 vs. 9.32 cases per thousand, X² = 57.75, df = 1, p = .000). These findings indicate a substantial publication bias effect in the NMS incidence literature. Among studies that met minimum design standards, the best estimate of NMS incidence is −0.1%. This estimate is based exclusively upon psychiatric inpatients, so NMS incidence in the population of all patients receiving antipsychotic medication is likely to be much lower.

References:

NR169  Monday, May 19, 3:00 p.m.-5:00 p.m.
Polypharmacotherapy of Inpatients With Schizophrenia
Supported by Eli Lilly and Company
Zhongyun Zhao, Ph.D., Department of Outcomes Research, Eli Lilly and Company; Lilly Corporate Center DC 4025, Indianapolis, IN 46285; Peter F. Wang, M.D., Benjamin Gutierrez, Ph.D., Barbara L. Gaylord, M.B.A.

Educational Objectives:
At the conclusion of this presentation, participants should gain a better understanding how polypharmacotherapy is prescribed and identify factors associated with for inpatients with schizophrenia.

Summary:
Objective: To examine recent pharmacologic treatment patterns for hospitalized schizophrenia patients.

Methods: Premier’s Perspective™ database, the largest U.S. hospital drug utilization database, was used to identify hospitalized schizophrenia patients discharged between 01/1999 and 09/2001. Treatment regimens for five classes of psychotropics were analyzed. Regressions examined relationships between polypharmacy compared with those in managed care and commercial programs. Atypical antipsychotic use increased and lithium use decreased from 1999-2001.

Results: Of 42,233 patients (55% male, mean age 42 years), 94.9% received antipsychotics; 74.4% atypicals, most commonly olanzapine (46.5%). Mood stabilizers were used by 40.9% of patients, antidepressants by 47.6%, anxiolytics by 66.8%, and hypnotics by 23.4%. Only 7.9% of patients received monotherapy. On average, patients received 3.67 psychotropics; 74.2% received ≥3 and 27.4% received ≥5 psychotropics. Most common regimens were antipsychotic and anxiolytic combinations (13.6%); this combination plus either antidepressants (12.2%), mood-stabilizers (10.5%), or both (9.9%); and antipsychotics alone (9.6%). Greater severity, being female, paranoid or schizoaffective diagnoses, and non-teaching- and for-profit-hospitals were associated with increased polypharmacy use. Patients in public programs (Medicaid/Medicare) received less atypical antipsychotics but more polypharmacy compared with those in managed care and commercial programs. Atypical antipsychotic use increased and lithium use decreased from 1999-2001.

Conclusions: Polypharmacy is common among hospitalized schizophrenia patients. Patient and institution characteristics influenced treatment.

References:

NR170 Monday, May 19, 3:00 p.m.-5:00 p.m.
Long-Acting Risperidone in Hospital Inpatients With Schizophrenia
Supported by Janssen Pharmaceutica Products, L.P.

Stephen Rodriguez, M.A., Janssen Pharmaceutica Products, L.P., 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Cynthia Bossie, Ph.D., Robert Lasser, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss the benefits of using long acting risperidone in hospital inpatients with schizophrenia.

Summary:

Introduction: Medication adherence in schizophrenia is vital to optimal response and outcome. Daily dosing regimens are frequently associated with partial compliance, which can contribute to poor symptom control, relapse, and hospitalization. This analysis looked at the effect of treatment with long-acting risperidone in hospital inpatients.

Methods: Data were derived from a 12-week, multicenter, double-blind study of placebo or long-acting risperidone (25 mg, 50 mg, or 75 mg every two weeks).

Results: Subjects were hospital inpatients at study entry (n = 151 long-acting risperidone, n = 51 placebo). Mean number of previous hospitalizations: 8.9 ± 14.3 in the long-acting risperidone group, 8.1 ± 9.2 in the placebo group. Mean PANSS total scores improved with long-acting risperidone and worsened with placebo (-6.6 and +4.5, respectively, p < 0.001). Response rates for > = 20%, 40%, or 60% reduction in PANSS total scores at endpoint were significantly (p <0.05) higher with long-acting risperidone (43.1%, 20.5%, 8.8%, respectively) than placebo (17.7%, 0%, 0%, respectively). Severity of EPS was mild at baseline and throughout the trial in both groups. Injection-site pain was rated as low by the patients, consistent with the investigators' ratings of the injection site.

Conclusions: These data show that long-acting risperidone can be used in hospital inpatients to provide significant clinical benefits.

References:

NR171 Monday, May 19, 03:00 p.m.-05:00 p.m.
Differences Among Antipsychotics in the Time to All-Cause Drug Discontinuation: Results From a Longitudinal Naturalistic Study of Schizophrenia
Supported by Eli Lilly and Company

Baojin Zhu, Ph.D., Department of Information, Eli Lilly and Company, Lilly Corporate Center, DC #4025, Indianapolis, IN 46285; Haya Ascher-Svanum, Ph.D., Douglas E. Faries, Ph.D., Joseph P. Gibson, Ph.D., Frank Ernst, R.Ph., Marvin S. Swartz, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss the clinical impact and importance of continuous medication treatment for patients with schizophrenia.

Summary:

Objective: Time to treatment discontinuation for any cause was previously identified as an important outcome parameter in the medication management of schizophrenia. This study compared the following four antipsychotics: olanzapine, risperidone, quetiapine, and haloperidol - on the time to all-cause discontinuation.

Methods: Participants (N=964) were new initiators of olanzapine, risperidone, quetiapine or haloperidol in the Schizophrenia Care and Assessment Program (SCAP), a 3-year longitudinal, observational study of schizophrenia. Time to all-cause discontinuation of the antipsychotic during the 1 year following its initiation was measured by (a) the total number of days on the antipsychotic, and (b) the number of days of continuous treatment up to the first gap of >14 days. Analyses employed Mantel-Haenszel and Cox proportional hazard model. Results were further confirmed using a mixed-model approach.

Results: Olanzapine-treated patients were on their medication significantly longer than patients receiving risperidone, quetiapine, or haloperidol. Compared with olanzapine, the likelihood of discontinuation was 26%, 54%, and 158% greater among patients receiving risperidone, quetiapine, or haloperidol, respectively.

Conclusions: Antipsychotics were found to significantly differ in the time to all-cause discontinuation, such that olanzapine-treated patients evidenced the longest time to discontinuation, followed by risperidone, quetiapine, and haloperidol.

References:
the PANSS score indicated a 20% drop in compliance predicts a 3.1-point increase in PANSS total scores (p < 0.001). Improvements in PANSS scores were significantly greater in patients with higher compliance scores (p < 0.001). Controlling for compliance, a regression model indicated a 4.7-point or approximately 30% greater improvement in PANSS scores with risperidone than conventional agents (p < 0.0026).

Conclusion: The finding of a direct correlation between degree of partial compliance and clinical outcome emphasizes the importance of treatment strategies that promote continuous medication treatment with an atypical antipsychotic.

References:
2. Jolley AG, Hirsch SR, McRink A, Manchanda R: Trial of brief treatment with an atypical antipsychotic. Monday, May 19, 03:00 p.m.-05:00 p.m.

NR174 Monday, May 19, 3:00 p.m.-5:00 p.m.
Effect of Smoking on Clozapine Levels
Huma Aziz, M.D., Department of Psychiatry, University of Pittsburgh, 3811 O’Hara, #1227, Pittsburgh, PA 15213; Mujer U. Shad, M.D., Jaspreet Brar, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the impact of cigarette smoking on the plasma levels of clozapine, and should have an idea about the potential clinical significance of increased clearance of clozapine.

Summary:
Objective: To examine the impact of smoking on clozapine levels.
Background: Clozapine is primarily metabolized to norclozapine by Cytochrome P450 (CYP) enzyme, 1A2. Since cigarette smoking induces CYP1A2, clozapine patients who smoke may develop lower clozapine levels as compared to non-smokers. This may compromise effectiveness of clozapine. Differences in amount of smoking inside versus outside the hospital may at least partially contribute to the rehospitalizations sometimes observed in clozapine patients. To quantify impact of smoking, we compared clozapine and norclozapine levels in smoking versus non-smoking clozapine patients.

Methods: The data were collected from medical charts of 15 middle-aged schizophrenic outpatients (males=11) on clozapine treatment from January 01 to September 02. Nine out of 15 subjects were smokers consuming from 0.7 to 2.5 PPD (Mean=1.3PPD/day). All clozapine levels were analyzed using the same laboratory. Patients’ confidentially was maintained via linkage codes assigned by an honest broker. Concomitant medications were recorded.

Results: A 52 and 40% decrease in clozapine and norclozapine clearance was observed in non-smoking versus smoking schizophrenics, respectively (i.e., 0.54 vs. 1.12 ng-mL/min and 1.40 vs. 2.32 ng-mL/min, respectively). Decrease in norclozapine levels may be due to increased preload.

Conclusion: Smoking decreases clozapine levels by increasing its clearance.

References:

NR175 Monday, May 19, 3:00 p.m.-5:00 p.m.
Maternal Depression Before and After Birth, Child Temperament, and Cortisol
Janet M. Fairbanks, M.D., NYS PI Department, Columbia University, 1051 Riverside Drive, Unit 74, New York, NY 10032
NR176 Monday, May 19, 3:00 p.m.-5:00 p.m.
A Comparison on Clinician Versus Electronic Monitoring of Antipsychotic Adherence in Supported by Janssen Pharmaceutical Products, L.P.
Matthew J. Byerly, M.D., University of Texas Southwestern Psychiatry, 5509 Harry Hines Blvd Suite 600, Dallas, TX 75235; Robert Fisher, B.S., A. John Rush, M.D., Rhiannon Holland, B.A., Femina Varghese, B.A.

Educational Objectives:
At the conclusion of this session, the participant should be able to compare the ability of electronic monitoring and clinician assessment to detect antipsychotic nonadherence in schizophrenia.

Summary:
Objective: To evaluate the concordance of electronically-monitored (MEMS® cap) antipsychotic adherence with that determined by clinician-rated assessment and clinical outcomes among public sector outpatients with schizophrenia and schizoaffective disorder.

Methods: In 21 public-sector outpatients with schizophrenia or schizoaffective disorder, antipsychotic medication adherence was determined for three consecutive months by two different methods: (1) electronic monitoring (MEMS® caps) and (2) the Clinician Rating Scale (CRS), an ordinal scale of 1-7, with higher numbers representing greater adherence (blinded to MEMS® data). Clinically meaningful nonadherence was defined as daily adherence of ≤70% according to MEMS® caps or a CRS rating of ≤4 during any one of three monthly evaluations.

Results: Detection of clinically meaningful nonadherence was more likely when determined by MEMS® cap assessment (11/21) than CRS ratings (1/21) (χ² = 15.43, df = 1, p<0.0001). Additionally, MEMS® cap assessment found that seven of the 21 patients were ≤50% adherent, four were ≤30% adherent, and three were ≤10% adherent during at least one of the three monthly assessments.

Conclusions: MEMS® cap monitoring found high levels of clinically meaningful nonadherence among these public sector outpatients with schizophrenia and schizoaffective disorder. Compared to electronic monitoring, clinician assessment dramatically underestimated antipsychotic medication nonadherence.

References:

NR177 Monday, May 19, 03:00 p.m.-05:00 p.m.
Schizophrenia Dosing of Atypical Antipsychotics for Inpatients With Schizophrenia Supported by Eli Lilly and Company
Benjamin Gutierrez, Ph.D., Pharm Research, Premier Healthcare, 2320 Cascade Point Boulevard, Charlotte, NC 28268; Zhongyun Zhao, Ph.D., Peter F. Wang, M.D., Barbara L. Gaylord, M.B.A.

Educational Objectives:
At the conclusion of the presentation, participants should be able to recognize current dosing strategies and understand relative benefit and risk of high-dose usage across major atypical antipsychotics.

Summary:
Objective: To systematically examine overall atypical antipsychotic dosing; extent, outcomes, and characteristics of patients receiving high-dose therapy; and dosing trends over three years.

Methods: Pharmacological therapy of about 33,000 inpatients with schizophrenia discharged from 03/1999 to 09/2001 was assessed using Premier’s Perspective™ database, the largest U.S. hospital drug utilization database. Several dosing measures including average daily dose (ADD), starting dose, days to maximum dose, and outcomes variables (length of therapy, switch, and use of EPS drugs) were examined.

Results: From 1999 to 2001, quetiapine ADD increased 25.7% (from 261.9 to 329.2mg/d). Olanzapine and risperidone ADD increased slightly, from 16.8 to 17.8mg/d and from 4.9 to 5.3mg/d, respectively. Prevalence of high-dose prescribing was 38.2% for olanzapine (>20mg/d), 17.9% for quetiapine (>750mg/d), and 26.0% for risperidone (>8mg/d). Young age, white race, “treated by psychiatrists,” and “located in northeast” predicted high-dose usage. High-dose use was associated with less switch and longer therapy. Only risperidone high-dose use was associated with increased EPS drug usage (OR=1.71, 95%CI=1.58–1.88). Olanzapine had the shortest time to maximum dose (<2 days) among atypical antipsychotics.

Conclusions: High-dose atypical antipsychotics were commonly prescribed for inpatients with schizophrenia. Effectiveness and safety issues relating to high-dose use vary across atypical antipsychotics.
NR178  Monday, May 19, 03:00 p.m.-05:00 p.m.
Changes in Plasma Cholesterol in Bipolar Patients: Does Treatment Make a Difference?
Adel A. Gabriel, M.D., Department of Psychiatry, Peter Lougheed Centre, 3500 26th Avenue, NE, Calgary, AB T1Y 6J4, Canada; Scott B. Patten, M.D.

Educational Objectives:
1. Participants will have an increased awareness of the relationship between blood lipids mood disorders, and the complexity of factors that impact on cholesterol levels, e.g. genetic, psychological stresses, dietary and neuropsychological factors; 2. Participants will identify the impact of treatment on levels in bipolar patients

Summary:
Objectives: To examine the impact of treatment on the blood levels of total cholesterol in patients with manic or hypomanic episodes and comorbid generalized anxiety symptoms.

Method: A consenting series of patients with 27 acute relapses, both inpatients and outpatients, with DSM IV-R-confirmed manic or hypomanic episodes were included. Patients were followed for eight weeks. The modified mania state rating scale (MMRS), and Hamilton anxiety scale (HAM-A), were utilized to evaluate clinical symptoms. Fasting blood samples were drawn for cholesterol estimations, on two occasions over time, once before treatment started, and once after remission of the acute clinical symptoms. The relationship between changes in plasma cholesterol levels and severity of psychiatric symptoms, were analysed.

Results: There was a statistically significant reduction of total cholesterol levels in patients with manic or hypomanic episodes and comorbid generalized anxiety symptoms.

Conclusion: Various studies have examined the relationship in the manic phases of bipolar disorder, and no studies to our knowledge have reported significant reduction of levels during treatment of acute phases of the illness. Further studies however, are needed to examine the clinical implications of these results with regard the cardiovascular risk, and to examine whether there is a casual relationship between manic/hypomanic phases of bipolar disorder and cholesterol. Other hypothesized explanations for these results are discussed.

References:

NR180  Monday, May 19, 3:00 p.m.-5:00 p.m.
Prevalence of Diabetes Among Outpatients Receiving Clozapine
J. Steven Lamberti, M.D., Department of Psychiatry, University of Rochester, 1650 Elmwood Avenue, Rochester, NY 14620, Geanina O. Costea, M.D., John F. Crilly, C.S.W., David Olson, Ph.D., Kumar Maharaj, R.Ph., Margaret Bushey, N.P., Marci B. Dietz, R.N.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify the point prevalence of diabetes mellitus among severely mentally ill outpatients receiving clozapine. Participants should also be able to recognize the risk imposed by demographic factors including age, family history, race, and gender.

Summary:
Objective: Treatment with antipsychotic drugs has been associated with increased risk for developing diabetes mellitus. Recent evidence suggests that clozapine may pose an especially high risk. This study examines the prevalence of diabetes mellitus among outpatients with schizophrenia and schizoaffective disorder receiving clozapine.

Method: A retrospective chart review was conducted on 141 outpatients receiving clozapine at the University of Rochester Department of Psychiatry. Diagnosis of diabetes was established through the presence of documentation in the medical record.
Results: Mean (SD) age was 41.7 (9.8) years, and 66% were male. Seventy-seven percent were Caucasian. Mean (SD) duration of clozapine treatment was 5.8 (3.8) years. Point prevalence was 17.7%. Chi-square analysis revealed a significant effect for family history of diabetes (χ²=19.06, p=.000). Physical assessment with 66 of the 141 clients to date has revealed a mean (SD) body mass index of 33.8 (7.9), a waist/hip ratio of .97 (.08), and a percent body fat of 36% (.11).

Conclusion: Patients receiving clozapine are at significant risk for developing diabetes, although the level of risk relative to that associated with other atypical antipsychotic medications remains somewhat unclear. Clinicians should regularly monitor blood glucose levels on all severely mentally ill patients receiving antipsychotic drugs.

References:

NR181 Monday, May 19, 3:00 p.m.-5:00 p.m.
Prevalence of Diabetes Among Outpatients Receiving Antipsychotic Drugs
J. Steven Lamberti, M.D., Department of Psychiatry, University of Rochester, 1650 Elmwood Avenue, Rochester, NY 14620; John F. Crilly, C.S.W., David Olson, Ph.D., Kumar Maharaj, R.Ph., Geanina O. Costea, M.D., Margaret Bushey, N.P., Marci B. Dietz, R.N.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify the point prevalence of diabetes mellitus among severely mentally ill outpatients receiving antipsychotic medications. Participants should also be able to recognize the risk imposed by demographic factors including age, family history, race, and gender.

Summary:
Objective: Growing evidence suggests that individuals with schizophrenia or schizoaffective disorder receiving antipsychotic drugs are at increased risk for developing diabetes mellitus. The purpose of this study is to examine the prevalence of diabetes among outpatients with schizophrenia and schizoaffective disorder.

Method: A retrospective chart review was conducted on 439 outpatients receiving antipsychotic drugs at the University of Rochester Department of Psychiatry. Diagnosis of diabetes was established through the presence of documentation in the medical record.

Results: Mean (SD) age of patients was 42.8 (10.8) years, and 56.9% were men. Patients were 61.3% Caucasian, 30.6% African American, 5.2% Hispanic, and 2.7% other. Sixteen percent had a known family history of diabetes. Mean (SD) total lifetime duration of antipsychotic drug exposure was 14.29 (9.5) years. Overall prevalence of diabetes mellitus was 15.3%. Chi-square analysis revealed significant effects of age (χ²=16.514, p < .001), family history of diabetes (χ²=27.128, p < .001), and gender (χ²=14.114, p < .001).

Conclusion: Prevalence of diabetes among outpatients with schizophrenia and schizoaffective disorder receiving antipsychotic drugs is significantly higher than that reported in the general population. Results of this study are limited by the retrospective methodology, which is likely to underestimate the actual prevalence by failing to detect undiagnosed cases.

References:

NR182 Monday, May 19, 3:00 p.m.-5:00 p.m.
Rapid Antimanic Effect of Risperidone Monotherapy: A Three-Week, Multicenter, Randomized, Double-Blind, Placebo-Controlled Trial
Supported by Johnson & Johnson Pharmaceutical Research & Development
Robert M.A. Hirschfeld, M.D., Psychiatry & Behavioral Science, University of Texas Medical Branch, 301 University Boulevard 1.302RSH, Galveston, TX 77555-0188; Paul E. Keck, Jr., M.D., Keith Karcher, M.S., Michelle L. Kramer, M.D., Fred Grossman, D.O.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the efficacy and safety of risperidone monotherapy in the treatment of mania in patients with bipolar disorder.

Summary:
Background: We evaluated the efficacy and tolerability of flexible doses of risperidone in acute bipolar mania.

Methods: For three weeks, 279 patients in an acute manic episode of bipolar I disorder received 1–6 mg/day of risperidone. Efficacy was measured as change from baseline to treatment endpoint in Young Mania Rating Scale (YMRS) scores.

Results: The trial was completed by 56% of the 125 patients in the risperidone group and 42% of the 134 patients in the placebo group. The mean modal dose of risperidone was 4.1 mg/day. Improvements in YMRS scores were significantly greater in the risperidone than placebo group at endpoint (−11.1 ± 0.9 vs −5.0 ± 0.9; P<0.001). Significant between-group differences in change scores were seen as early as three days after start of treatment (risperidone, −6.9 ± 0.6; placebo, −4.3 ± 0.5; P<0.001) and at weeks 1, 2, and 3. The most common adverse event reported among risperidone patients was somnolence (28%).

Conclusion: Risperidone was efficacious and well tolerated in the treatment of patients with acute bipolar mania, with a rapid onset of action seen as early as day 3.

References:

NR183 Monday, May 19, 3:00 p.m.-5:00 p.m.
Use Patterns for Antipsychotics Among Medicaid Beneficiaries
Supported by Janssen Pharmaceutica Products, L.P.
Linda M. Robison, M.S.P.H., Department of Pharmacy, Washington State University, PO Box 646510, Pullman, WA 99164-6510; Tracy L. Skaer, Pharm.D., David A. Sclar, Ph.D., Robert M.A. Hirschfeld, M.D., Psychiatry & Behavioral Science, University of Texas Medical Branch, 301 University Boulevard 1.302RSH, Galveston, TX 77555-0188; Paul E. Keck, Jr., M.D., Keith Karcher, M.S., Michelle L. Kramer, M.D., Fred Grossman, D.O.

Educational Objectives:
For three weeks, 279 patients in an acute manic episode of bipolar I disorder received 1–6 mg/day of risperidone. Efficacy was measured as change from baseline to treatment endpoint in Young Mania Rating Scale (YMRS) scores.

Results: The trial was completed by 56% of the 125 patients in the risperidone group and 42% of the 134 patients in the placebo group. The mean modal dose of risperidone was 4.1 mg/day. Improvements in YMRS scores were significantly greater in the risperidone than placebo group at endpoint (−11.1 ± 0.9 vs −5.0 ± 0.9; P<0.001). Significant between-group differences in change scores were seen as early as three days after start of treatment (risperidone, −6.9 ± 0.6; placebo, −4.3 ± 0.5; P<0.001) and at weeks 1, 2, and 3. The most common adverse event reported among risperidone patients was somnolence (28%).

Conclusion: Risperidone was efficacious and well tolerated in the treatment of patients with acute bipolar mania, with a rapid onset of action seen as early as day 3.

References:
**Educational Objectives:**

At the conclusion of this session, the participant should be able to (1) Recognize the treatment patterns associated with the use of antipsychotic pharmacotherapy for the treatment of schizophrenia, (2) Optimize the selection of antipsychotic pharmacotherapy for the treatment of schizophrenia.

**Summary:**

**Purpose:** This inquiry was designed to discern pharmacologic treatment patterns (switch; augment; both) among Medicaid beneficiaries in the state of South Carolina diagnosed with schizophrenia, and prescribed antipsychotic pharmacotherapy.

**Methods:** Data were abstracted for the time-frame January 1, 1995, through December 31, 2000. Each patient-level record contained extensive information six months prior to, and 12 months post-initiation of antipsychotic pharmacotherapy (n=20,791). Logistic regression was used to derive odds-ratios and 95% confidence intervals for the likelihood of switching, augmentation, or both, and were adjusted for age, sex, race, psychiatric service intensity, and other factors of interest.

**Results:** Patterns of use in the 12 months post-initiation of antipsychotic pharmacotherapy: (1) Switch pattern: 28.3% with conventional; 23.8% with atypicals (clozapine [64.4%]; risperidone [20.0%]; quetiapine [29.9%]; olanzapine [24.7%]); (2) Augmentation pattern: 12.0% with conventional; 15.2% with atypicals (clozapine [65.0%]; risperidone [11.0%]; quetiapine [18.2%]; olanzapine [16.2%]); (3) Switch and Augmentation pattern: 8.5% with conventional; 13.4% with atypicals. Among patients initiating pharmacotherapy with an atypical, use of risperidone resulted in a significantly lower probability [ORs, 95% CIs] of switching, augmentation, or both (p < 0.05).

**Conclusion:** Selection of initial antipsychotic influences the extent of switching, augmentation, or both among patients with schizophrenia.

**References:**


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**NR185 Monday, May 19, 3:00 p.m.-5:00 p.m.**

**Duloxetine in the Treatment of the Pain Associated With Diabetic Neuropathy**

**Supported by Eli Lilly and Company**

David J. Goldstein, M.D., Eli Lilly and Company, Lilly Corporate Center, DC2206, Indianapolis, IN 46285; Yili Lu, Ph.D., Smriti lyengar, Ph.D., Michael J. Detke, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to describe the rule of serotonin and norepinephrine in the mediation of endogenous analgesic mechanisms and understand that duloxetine, a potent and balanced dual reuptake inhibitor of serotonin and norepinephrine, is efficacious in the treatment of pain associated with diabetic neuropathy.

**Summary:**

**Objective:** To examine the efficacy and safety of duloxetine, a balanced dual reuptake inhibitor of pain associated with diabetic neuropathy. Both 5-HT and NE are thought to inhibit pain via spinal chord pathways.

**Methods:** In a 12-week, multicenter, double-blind study, 457 patients with diabetic neuropathy were randomly assigned to treatment with duloxetine 60 mg BID, 60 mg QD, 20 mg QD, or placebo. The primary efficacy measure was the weekly mean score of the 24-Hour Average Pain Severity on the 11-point Likert Scale.

**Results:** Duloxetine 60mg QD and BID demonstrated statistically significant improvement compared with placebo on the 24-Hour Average Pain Severity score, beginning one week after randomization and continuing through the acute phase. Duloxetine also separated from placebo on nearly all of the secondary measures. Safety and tolerability were very good with less than 20% discontinuation due to adverse events.

**Conclusion:** This study provides definitive evidence that duloxetine at 60 mg QD and 60 mg BID was safe and effective in the treatment of pain associated with diabetic neuropathy.

NR186  Monday, May 19, 3:00 p.m.-5:00 p.m.

Does Ziprasidone Use in Children and Adolescents Cause QTc Interval Alteration?

Madhvi P. Richards, M.D., Psychiatry, University of Michigan, 1500 E. Medical Center Drive, Ann Arbor, MI 48109-0390; Fida Hassan, M.D., Paul E. Quinlan, D.O., Norman E. Alessi, M.D.

Educational Objectives:

At the conclusion of this session, the participant should have a better understanding of QTc alterations in children and adolescents taking Ziprasidone in order to help with treatment in this population.

Summary:

Objective: There is no published information about ziprasidone affecting QTc intervals in children and adolescents, a potentially important issue as QT prolongation may have serious cardiac consequences. The study’s objective is to characterize short-term QTc interval alterations in children and adolescents on Ziprasidone.

Method: A retrospective chart review was performed on 16 children and adolescents with psychiatric illnesses treated with Ziprasidone. EKGs were obtained prior to and within four weeks of initiation of ziprasidone to assess QTc interval changes.

Result: The principal diagnoses of this sample were psychosis (NOS autistic disorder, post traumatic stress disorder and impulse disorder), there were 10 males and six females with a mean age of 12.19 ± 3.54 years. The average dose of ziprasidone was 42.5 ± 17.7 mg. The mean baseline QTc was 412.14 ± 12.68ms, and that obtained after starting ziprasidone was 416.37 ± 13.42ms. 56% of subjects showed a significant QTc increase and 44% a significant decrease.

Conclusion: Significant alterations noted in QTc intervals appear to be due to both increase and decrease in its duration. Prospective studies are needed to further explore the effects of Ziprasidone on QTc intervals in the pediatric population and to determine their significance.

References:


NR187  Monday, May 19, 3:00 p.m.-5:00 p.m.

Implication of Citalopram and N-Desmethylcitalopram Blood Levels to Clinical Response in Major Depression

Cristobal Gasto, M.D., Department of Psychiatry, Hospital Clinico, Rosellon 140, Barcelona 0836, Spain; Rosa Catalan, M.D., Nerc Torra, M.D., Andrea Gabilono, M.D., Rafael Penades, Ph.D., Miguel Roodhohns, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the occurrence of injection-site pain and other side effects after injection of long-acting risperidone.

Summary:

Introduction: Medication adherence is essential to optimal outcome in schizophrenia. Conventional depot antipsychotics are advantageous in this regard, but compromised by injection-site reactions secondary to oil-based formulations. Long-acting risperidone, a novel aqueous-based formulation, may present less injection site effects while providing the advantages of an atypical antipsychotic.

Method: Two studies (open-label, 50-week; double-blind 12-week) assessed long-acting risperidone (25–75 mg every two weeks). Patients completed a visual analogue scale for pain (0mm=none, 100mm=unbearable) after each injection. Investigators rated injection-site pain, redness, swelling, and induration as absent, mild, moderate, or severe.

Results: Patient pain ratings were low at all assessments, decreasing from the first to final injection (50-week study: 18.4±0.8

References:

to 10.7±0.6). No effect of prior treatment (oral risperidone, conventional depot) was apparent. Data were similar in the 12-week study with comparable ratings among groups (final injection: placebo 12.7±2.3; 25 mg 9.6±1.3; 50 mg 14.3±2.5; 75 mg 9.7±1.8). In the 12-week study, investigator rated redness, swelling, and induration as absent in 97% to 100% of assessments, and pain as absent in 78% to 100%. No differences were seen between long-acting risperidone and placebo groups.

**Conclusion:** Patient-rated pain was low and investigator ratings of site pain, swelling, induration or redness were infrequent with long-acting risperidone.

**References:**


**NR189**

**Monday, May 19, 3:00 p.m.-5:00 p.m.**

**Effects of Atypicals on the Syndromal Profile in Treatment-Resistant Schizophrenia**

Jean-Pierre Lindenmayer, M.D., Manhattan Psychiatric Center, 600 East 125th Street, New York, NY 10035; Pal Czobor, Ph.D., Jan Volavka, M.D., Jeffrey A. Lieberman, M.D., Leslie L. Citrome, M.D., Brian B. Sheltman, M.D., Joseph P. McEvoy, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to recognize the wider spectrum of action with atypical antipsychotic medications in treatment-resistant schizophrenia.

**Summary:**

**Background:** There has been considerable support for the observation that atypicals have a more expanded pattern of clinical effects than traditional antipsychotics. We are exploring whether this difference can also be seen in patients with treatment-resistant schizophrenia.

**Methods:** The subjects were 157 treatment-resistant inpatients diagnosed with chronic schizophrenia or schizoaffective disorder. They were randomly assigned to treatment with clozapine, olanzapine, risperidone, or haloperidol in a 14-week, double-blind trial and rated with a standard measure of clinical antipsychotic efficacy (PANSS). Factor analysis with principal components at baseline and endpoint together with changes in five PANSS derived factors were examined.

**Results:** At baseline, the excitement factor was followed by the negative, positive, cognitive, and depression/anxiety factors explaining 61% of the total variance. At endpoint, the negative factor was followed by the positive, excitement, cognitive, and depression/anxiety factors explaining 59% of the total variance. The 14-week data indicated statistically significant improvements by time on the positive factor for all three atypicals, but not for haloperidol. The negative factor showed significant improvement on clozapine and olanzapine, with significant worsening for haloperidol. Clozapine, olanzapine, and risperidone were superior to haloperidol on the negative factor, while clozapine was also superior to risperidone. The cognitive factor showed significant improvement on all atypicals, as did the depression/anxiety factor. Only clozapine improved the excitement factor, and was superior to both haloperidol and risperidone.

**Discussion:** Treatment with atypicals did not change the underlying PANSS five factor structure in a significant way. However, antipsychotic treatment with all three atypical medications was associated with significant improvements in four of five syndromal domains (positive, negative, cognitive, and depression/anxiety) of schizophrenia. Only clozapine improved the excitement domain. This confirms that atypicals are associated with improvement of an expanded spectrum of symptoms in treatment-resistant patients.

**References:**


**Nr190**

**Monday, May 19, 3:00 p.m.-5:00 p.m.**

**Clozapine Augmentation Strategies: Evaluation of Effectiveness**

Jean-Pierre Lindenmayer, M.D., Manhattan Psychiatric Center, 600 East 125th Street, New York, NY 10035; Mohan Parak, M.D., Victoria E. Cosgrove, B.A.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to understand the effects of adjunctive medication on a stable regimen of clozapine in patients with treatment refractory schizophrenia.

**Summary:**

**Background:** While clozapine is still the gold standard for treatment refractory schizophrenia, there are 55% to 70% of patients who fail to respond or only partially respond to clozapine after an adequate trial. Through retrospective blinded chart review, we evaluated the efficacy of adding another psychotropic medication to a stable clozapine regimen in patients with treatment refractory schizophrenia who had not responded to clozapine.

**Method:** Based on pharmacy records all inpatients on clozapine during a 24-month period were screened at a large state psychiatric center. Data were obtained from all inpatients with DSM-IV schizophrenia/schizoaffective disorder who were treated with clozapine for at least six months, clozapine-resistant and had received clozapine plus adjunctive treatment with either a second antipsychotic, mood stabilizer, or antidepressant for at least three months. Clinical chart notes were evaluated by blinded and trained raters using the CGI-Severity Scale at the start of the adjunctive medication (baseline) and after three months of treatment (follow up) as well as the CGI-Improvement Scale (CGI-IS) at follow up.

**Results:** Data on 73 clozapine-resistant inpatients treated with adjunctive medication were available. Mean baseline CGI-S was 4.68 (SD=0.8) and mean follow-up CGI-S was 4.32 (SD=0.91, P= 3.90, p<0.004) with 12.33% of patients rated as much improved, 32.88% as minimally improved, 54.79% as no change and none as very much improved or worsened. There was no superiority for any type of adjunctive medication. A significant effect was found for ethnicity (chi-square = 20.11; p<0.003) and a trend effect for chronicity of illness (F = 4.54; p<.04).

**Conclusion:** Adjunctive medication modestly enhanced the effects of clozapine and in only a small group of patients with treatment-resistant schizophrenia (12.3% much improved). No particular adjunctive strategy showed superiority. African-American patients showed better improvement, and there was a non-significant trend for patients with less chronicity of illness to show a better response to the adjunctive regimen.
NR191  Monday, May 19, 3:00 p.m.-5:00 p.m.
Depot-Drugs May Reduce Relapses in Schizophrenic Outpatients: A Meta-Analysis
Claudia C. Mentschel, M.D., Department of Psychiatry, Hillside Hospital, 76-69 263rd Street, Research Building, Glen Oaks, NY 11004; Stefan M. Leucht, M.D., John M. Kane, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the evidence for the effectiveness of depot antipsychotic drugs for relapse prevention in outpatients with schizophrenia.

Summary:
Objective: A recently published summary of Cochrane reviews did not find evidence that depot antipsychotics prevent schizophrenic relapses more effectively than oral antipsychotics. However, this review included a number of inpatient and short-term studies possibly inappropriate to assess the impact of depot antipsychotic drugs.

Methods: Therefore, a sensitivity analysis of the Cochrane reviews was undertaken by including only long-term outpatient studies. Relapse rates and the number of participants leaving the studies early were analyzed in a meta-analysis using a random effects model and relative risks (RR) as an effect size measure.

Results: Eight studies with a total of 615 subjects were included. Fewer participants in the depot groups (88 of 290 (30%)) than in the oral groups (146 of 325 (45%)) relapsed (pooled RR 0.78, 95%CI 0.66-0.91, p=0.002). A similar number of patients in both groups discontinued prematurely (pooled RR 1.26, 95% CI 0.33-1.90, p=0.3).

Conclusion: When only long-term outpatient studies are considered, there is some evidence that depot antipsychotics prevent psychotic relapses more effectively than oral antipsychotics. However, the effect is not robust, and the database is very limited. Large, long-term pragmatic, randomized trials are needed to establish the efficacy of depot antipsychotic drugs.

References:

NR192  Monday, May 19, 3:00 p.m.-5:00 p.m.
Polysomnographically-Monitored Sleep Promoting Properties of Quetiapine in Healthy Subjects Supported by AstraZeneca Pharmaceuticals
Stefan Cohrs, M.D., Psychiatry, University of Goettingen, Von Sieboldstrasse 5, Goettingen 37075, Germany; Andrea Rodenbeck, Ph.D., Zhenhua Guan, Kathrin Pohlmann, Wolfgang Jordan, M.D., Joerg Kinkelbur, M.D., Eckart A. Ruether, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe a series of cases of pancreatitis with atypical antipsychotic quetiapine on sleep in healthy subjects. The implication for further research, and the possible use in different patient groups.

Summary:
Objective: The study aimed to determine the effects of the atypical antipsychotic quetiapine on polysomnographically registered sleep.

Method: Eighteen healthy male subjects were studied in a double-blind, placebo-controlled, randomized, cross-over design three times for three consecutive nights, four days apart. After an adaptation night, the effect of quetiapine was studied during one night under standard sleep laboratory conditions (N1) and the following night under acoustic sleep fragmentation (N2). Placebo, 25 mg or 100 mg were administered orally one hour before standard polysomnography.

Results: Two subjects dropped out of the study due to orthostatic hypotension resulting in brief fainting and total recuperation after the first dose of 100 mg quetiapine, one subject withdrew because of private reasons, one was excluded from N2 due to technical reasons. 25 mg and 100 mg quetiapine significantly improved measures of sleep continuity under both conditions. Pronounced effects were seen during N2. In comparison with placebo, quetiapine (both doses) significantly increased total sleep time, sleep efficiency, percentage sleep stage 2, and significantly decreased sleep latency. REM percentage significantly decreased under quetiapine only during N1. Periodic leg movements increased dose dependently, slightly weaker during N2.

Conclusions: These data demonstrate sleep promoting properties of quetiapine in healthy subjects possibly due to protecting from external stressful stimuli. Further studies investigating the effect of longer application of quetiapine on sleep and side effects in other target groups are needed.

Study results were sold to AstraZeneca, Germany. We thank AstraZeneca for the supply of medication.

References:

NR193  Monday, May 19, 3:00 p.m.-5:00 p.m.
Pancreatitis Associated With Newer Antipsychotics in the U.S.
P. Murali Doraiswamy, M.D., Department of Psychiatry, Duke University, 3350 Hospital South, Box 3018, Durham, NC 27710; Elizabeth A. Koller, M.D., James T. Cross, M.S., Saul N. Malozowski, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe a series of cases of pancreatitis with atypical antipsychotics increase awareness of potential adverse events.

Summary:
We conducted a pharmacovigilance study of patients who developed serious adverse events of pancreatitis associated with clozapine, olanzapine, and risperidone compared to haloperidol. Cases were identified from the FDA’s MedWatch surveillance program and MEDLINE through February 2002. There were a total of 192 cases of pancreatitis of which 40%, 33%, 16%, and...
12% (because of rounding numbers do not total 100%) occurred in patients using clozapine, olanzapine, risperidone, and haloperidol, respectively. Onset in the majority of cases was within 6 months. Ten cases and one death occurred in children aged 10–17 years. There were 21 other deaths with 75% of them linked to clozapine and olanzapine. In 50% of all haloperidol cases, an atypical antipsychotic was listed as a concomitant drug. Valproate was used concomitantly in 23% of cases. Concomitant hyperglycemia and acidosid, although uncommon, occurred for all drugs except haloperidol. Estimated pancreatitis reporting rate, adjusted for total prescriptions, was several fold higher for clozapine, olanzapine, and risperidone (in that order) compared to haloperidol. Our study cannot prove causality, but suggests the need for heightened awareness and more definitive studies of causality.

References:

NR194  Monday, May 19, 3:00 p.m.-5:00 p.m.  
Memory Loss Associated With Statins  
P. Murali Doraiswamy, M.D., Department of Psychiatry, Duke University, 3350 Hospital South, Box 3018, Durham, NC 27710; Leslie R. Wagstaff, Pharm.D., Melinda Mitten, Pharm.D., Beth McLendon Avik, Pharm.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to review the links between statins and cognition/dementia risk; to present a series of cases of statin associated memory loss

Summary:
In addition to their proven cardiovascular benefits, preclinical and observational studies have reported that HMG CoA-reductase inhibitors (or statins) may improve cerebral blood flow and reduce the risk for dementia. However, two randomized controlled studies with cognition as a secondary outcome reported no cognitive benefits for statins. Also, two published cases as well as reports in the lay press and user group forums have linked statins with memory loss. To clarify this further, we searched the FDA MedWatch system between November 1997 and February 2002 for reports cognitive adverse event reports associated with three widely prescribed statins (atorvastatin, pravastatin, and simvastatin). Of approximately 25,000 adverse events reported to the FDA during this time period with all statins, about 2% had a cognitive identifier. We selected and critically reviewed 60 adverse reports of memory loss in patients (mean age 62 years, 45 men) of which 36 were with simvastatin, 23 with atorvastatin and one with pravastatin. 60% of the reports were by consumers. About 50% of cases noted memory impairment within two months of therapy. Fourteen (of 25) cases, with such data, reported improvement when the statin was discontinued. Memory loss recurred in 4 (of 4) cases with rechallenge. None of the 60 reports included any objective cognitive test results. While there reports do not contain sufficient evidence to judge causality, clinicians must be aware of such reports. Prospective controlled studies comparing the short- and long-term effects of various statins on cognition are warranted.

References:

NR195  Monday, May 19, 3:00 p.m.-5:00 p.m.  
Remission Rates in Elderly Depressed Patients Treated With Sertraline  
Supported by Pfizer Inc.
Javaid I. Sheikh, M.D., Department of Psychiatry, Stanford University, 3801 Miramar Avenue, Palo Alto, CA 94304; Tal Burt, M.D., Cathryn M. Clary, M.D.

Educational Objectives:
At the conclusion of this session, the participant should (1) recognize the importance of remission in the management of depression, and (2) familiarize themselves with sertraline remission data in late-life depression.

Summary:
Purpose: Depression in older adults is common, under-diagnosed, disabling, and treatable. Although increasingly recognized as an important indicator of antidepressant efficacy, little data are available on remission rates from placebo-controlled trials in the elderly. We report remission rates based on analyses performed on the largest placebo-controlled trial conducted in elderly patients with depression.
Methods: Outpatients (N=752) 60 years or older (mean age 69.9), with DSM-IV diagnosis of major depression, and a 17-item Hamilton Rating Scale for Depression (HAM-D) total score ≤ 18, who randomized to receive sertraline or placebo for eight weeks. Remission was defined as endpoint HAM-D<10 or CGI-S of 1 or 2 (normal, not at all ill, or borderline mentally ill). Remission rates were calculated using the Cochran-Mantel-Haenszel Test.
Results: There were significantly more remitters in the sertraline group than in the placebo group. HAM-D remitters were 34% on sertraline and 24% on placebo (completers) and 29% on sertraline and 23% on placebo (LOCF at endpoint). CGI-S remitters were 37% on sertraline and 25% on placebo (completers) and 33% on sertraline and 23% on placebo (LOCF at endpoint).
Conclusion: These results suggest that sertraline is effective in achieving complete remission of symptoms in elderly patients with major depression. The eight-week duration of the study should be taken into account when interpreting these findings as longer antidepressant treatment periods, particularly in the elderly, may be associated with higher remission rates. Future studies are needed to confirm these observations.

References:

NR196  Monday, May 19, 3:00 p.m.-5:00 p.m.  
Aripiprazole as an Augmentor of SSRIs in Mood and Anxiety Disorder Patients  
John W. Worthington III, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 815, Boston, MA 02114; Maurizio Fava, M.D., Megan E. Hughes, B.A., Gustavo D. Kinrys, M.D., Christina M. Dording, M.D., Hannah Reese, B.A., Mark H. Pollack, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand new pharmacologic approaches available for treatment refractory and treatment intolerant patients.
Summary:

Objective: Approximately one-third of patients treated with an adequate course of antidepressants are non-responders. Of patients who do start a trial of an antidepressant, over half of them stop their medication within three months. We wanted to examine whether treatment-resistant mood and anxiety disorder patients would be able to respond to and tolerate augmentation with aripiprazole, with its unique pharmacologic profile of dopamine D-2 partial agonism, serotonin 5HT-1A partial agonism and 5HT-2A antagonism.

Method: We report six cases of augmentation in patients with mood and anxiety disorders, who were not full responders to a variety of SSRIs. To our knowledge these are the first reported findings in this type of patient population and we will provide further data as our usage of this medication widens. The primary outcome measure was the Clinical Global Impression of Improvement.

Results: In four out of six subjects in this early cohort, patients were much or very much improved in terms of their mood and anxiety symptoms. Two patients showed an early, as well as sustained, response to augmentation with doses of aripiprazole between 15 to 30 mg/day.

Conclusion: The present preliminary findings suggest that aripiprazole may be effective as an augmentor of SSRIs in patients with mood and anxiety disorders. Since this is a retrospective case review, further prospective studies are needed to confirm these findings.

References:

NR197 Monday, May 19, 3:00 p.m.-5:00 p.m.
Olanzapine Versus Placebo for Relapse Prevention in Bipolar Disorder
Supported by Eli Lilly and Company
Mauricio F. Tohen, M.D., Department of Research, Eli Lilly and Company, One Lilly Corporate Center, Indianapolis, IN 46285; Charles L. Bowden, M.D., Joseph R. Calabrese, M.D., Gary S. Sachs, M.D., Thomas Jacobs, M.A.S., Robert W. Baker, M.D., Angela R. Evans, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the attendee should be able to determine the relative strengths and weaknesses of olanzapine for relapse prevention in bipolar I disorder.

Summary:
Objective: To determine if olanzapine is effective in relapse prevention in patients with bipolar disorder.

Methods: Patients in acute manic or mixed episodes of bipolar I disorder were treated openly with olanzapine for 6–12 weeks. Patients achieving symptomatic remission (YMRS <=8) were randomized to olanzapine (N=225) (5–20 mg/d) or placebo (N=136) for 52 weeks of double-blind treatment.

Results: Olanzapine significantly prolonged time to relapse to any affective episode (YMRS >=15 or HAMD-21 >=15 and/or psychiatric hospitalization) (p<.001). Olanzapine-treated patients who had a significantly lower incidence of manic (16.4% vs 41.2%, p<.001) or depressive relapse (34.7% vs 47.8%, p=.015). Common and significant adverse events for the olanzapine group were weight gain, fatigue, and akathisia. Significantly more olanzapine-treated patients (23.6%) completed the 52-week trial than those on placebo (9.6%, p=.001) with approximately twice as many placebo-treated patients discontinuing due to lack of efficacy (57.4% vs 28.4%, p=.001).

Conclusion: This placebo-controlled study found that olanzapine treatment delays relapse in bipolar disorder, and significantly reduces rates of both manic and depressive episodes.

References:

NR198 Monday, May 19, 3:00 p.m.-5:00 p.m.
Long-Acting Injectable Risperidone: Safety and Efficacy in Stable Patients Switched From Conventional Depot Antipsychotics
Supported by Johnson & Johnson Pharmaceutical Research & Development
Martin Turner, M.D., Department of Psychological Medicine, University of Glasgow, Garsgaber Avenue, Lenzie, Glasgow G66 3UJ, Scotland; Marielle Eerdekens, M.D., Mary Jacko, D.P.M.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the safety and efficacy of long-acting injectable risperidone in patients whose treatment was switched from conventional depot antipsychotics.

Summary:
Objective: Long-acting injectable risperidone (Risperdal Consta™) was evaluated in symptomatically stable patients who had been receiving conventional depot antipsychotics.

Methods: In a 12-week, multicenter, open-label study, after a run-in period that included two cycles of their depot antipsychotic, patients were switched to long-acting risperidone given by intramuscular injection every two weeks.

Results: The mode dose of long-acting risperidone was 25 mg in 86% of the patients and 37.5 mg in 14%. The trial was completed by 92% of the patients. Adverse events were reported in 58% of the 166 patients, the most common being psychosis in 13%, insomnia in 10%, headache in 7%, and rhinitis in 7%. Hyperprolactinemia was reported in 11% of the patients; however, no association between prolactin levels and any signs or symptoms known to be associated with hyperprolactinemia was noted. Adverse events related to extrapyramidal symptoms (EPS) were reported in five patients (3%). Severity of EPS was low at baseline and was further reduced during the trial. At endpoint, significant improvements were seen in mean PANSS total scores and scores on the positive and negative subscales.

Conclusion: Long-acting injectable risperidone was well tolerated and efficacious in patients whose treatment was switched from conventional depot antipsychotics.

References:

NR199 Monday, May 19, 3:00 p.m.-5:00 p.m. Breast-Feeding and Treatment With SSRIs Supported by H. Lundbeck A/S
Jan Berle, M.D., Department of Psychiatry, University of Bergen, Haukeland University Hospital, Box 7800, N-5021 Bergen, Norway; Harald Brellid, M.S.C., Olav Spigset, Ph.D., Trond O. Aamo, M.D., Vidar M. Steen, Ph.D.

Educational Objectives: At the conclusion of this session, the participant should be able to increase knowledge about antidepressants as a treatment option for postpartum depression, especially among breast-feeding mothers.

Summary: Objective: Treatment of postpartum depression with antidepressants is complicated by the possible risk that the drugs may affect the infants during breast-feeding. Clinical data on antidepressants and breast-feeding are limited. Our objective was to determine drug levels in breast milk and in serum from infants and breast-feeding mothers during maternal treatment with antidepressants, together with analysis of genetically-determined variations in drug metabolism.

Methods: The study included 22 breast-feeding women on citalopram (n=9), sertraline (n=5), paroxetine (n=4), fluoxetine (n=1), and venlafaxine (n=3) and their nursing infants. Antidepressant serum levels in mother and infant and antidepressant milk concentrations were monitored by liquid chromatography-mass spectrometry (LC-MS). CYP2D6 and CYP2C19 activity was determined indirectly by PCR-based genotyping of the women and their infants.

Results: The milk/maternal serum concentration ratios were in the range of 0.6-3.6. Although the participating mothers had serum concentrations within the therapeutic range, the infant serum concentrations were typically very low. In one mother-infant pair, both identified as CYP2D6 poor metabolizers, the infant paroxetine level was below the limit of detection.

Conclusions: Nursing infants are exposed to very low amounts of antidepressants through breast milk. Breast-feeding should not be absolutely contraindicated when using these antidepressants.

References:

NR200 Monday, May 19, 03:00 p.m.-05:00 p.m. Role of Temperament in Mixed Depressive and Psychotic Mania
Supported by Sanofi-Synthelabo, Inc.
Hagop S. Akiskal, M.D., Department of Psychiatry, University of California at San Diego, 3350 La Jolla Village Drive, San Diego, CA 92161; Elle G. Hantouche, M.D., Jean-Michel Azorin, M.D., Sylvie Lancrenon, Ph.D., Liliane Chatenet-Duchene, M.D.

Educational Objectives: At the conclusion of this session, the participant should be able to recognize the influence of affective temperaments on the clinical picture of acute mania which includes pure, dysphoric and psychotic sub-types.

Summary: Following the EPIMAN study (Akiskal et al, 1998), a new French study (EPIMAN-ii Thousand) was initiated in December 2000 with the objective of including 1000 patients with acute mania. In this report, data are focused on the influence of affective temperaments on the clinical picture of mania.

Method: “EPIMAN-ii Thousand” is a national multi-site collaborative study dedicated to the clinical sub-types of mania. It involved training 317 French psychiatrists working in different sites representative of France. The study actually succeeded in recruiting 1090 cases admitted for acute mania (DSM-IV criteria). To minimize any “state contamination” the full self-rated version of Affective Temperament Scales (four scales adapted by Hantouche et al, 2001) was filled out by patients after acute mania abated. Mixed Mania was defined by the presence of two depressive symptoms or more.

Results: compared with pure mania, mixed mania was characterized by augmented global scores on: Cyclothymic-T. (12,5 vs 9,1), Depressive-T. (8,9 vs 6,9) and irritable-T. (7,3 vs 5,9) (all p=0,0001). On the contrary, the score on Hypothymic-T. was higher in Pure Mania (13,1 vs 12,0, p=0,001). When separating subgroups according to psychotic features, the highest score on Hypothymic-Temp was obtained in cases with mood-congruent psychotic features (13,5 vs 12,4 in non psychotic mania, p<0,05). The high score on irritable-T. characterized the sub-group with mood-incongruent psychotic features (7,2 vs 6,1 in nonpsychotic mania, p<0,05).

Conclusion: Complex phenomenology of acute mania could be related to the intimate interweaving with affective temperament. Mood-incongruent psychotic features could be best explained by the presence of a high level of long-standing irritable traits.

References:

NR201 Monday, May 19, 3:00 p.m.-5:00 p.m. Reboxetine Attenuates Weight Gain and Increases Dehydroepiandrosterone Levels in Olanzapine Treated Schizophrenia Patients
Michael Poyurovsky, M.D., Research Unit, Tirt Carmel Mental Health Center, 9 Eshkol Street, Tirt Carmel 30200, Israel; Rachel Maayan, D.H.D., Irit Gil-Ad, D.H.D., Abraham Weizman, M.D., Ronit Weizman, M.D.

Educational Objectives: At the conclusion of this presentation, the participant should recognize the attenuating effect of reboxetine on olanzapine treated schizophrenia patients and the role of neurosteroids (DHEA) as a possible mediator of reboxetine’s weight attenuating effect.

Summary: Objective: Dehydroepiandrosterone (DHEA) and its sulfate ester (DHEAS) are neurosteroids, which have been found to possess hypophagic properties and reduce food intake. Clozapine decreases brain DHEA/DHEAS levels, accounting for clozapine’s propensity to induce weight gain. The selective norepinephrine reuptake inhibitor reboxetine attenuated olanzapine-induced weight gain. In the present study, we evaluated the DHEA/DHEAS...
levels in olanzapine-treated patients with and without add-on reboxetine.

Method: In a randomized double-blind designed study, 20 DSM-IV schizophrenia inpatients completed six weeks of olanzapine treatment (10 mg/day) with either reboxetine (4 mg/day, N=10) or placebo (N=10). DHEA/DHEAS levels were evaluated prior to and at completion of the trial using radioimmunoassay method.

Results: A significant between group difference was noted in plasma DHEA levels (olanzapine/reboxetine group: pre-treatment 54.9±23.4 pmol/ml; post treatment 68.4±20.4 pmol/ml) (olanzapine/placebo group: pre-treatment 66.1±22.0 pmol/ml; post treatment 60.5±23.4 pmol/ml) (t=5.4, df=18, p=0.0015). DHEAS levels increased in both groups with no between group differences. The olanzapine/reboxetine group demonstrated a significantly lower increase in body weight (mean = 2.5 ± 2.7kg) than the olanzapine/placebo group (mean = 5.5 ± 3.1 kg) (t = 2.31, df=18, p=0.033).

Conclusion: Add-on reboxetine may attenuate olanzapine-induced weight gain in schizophrenia patients and increased DHEA levels may mediate this effect.

References:

NR202 Monday, May 19, 03:00 p.m.-05:00 p.m.
Reboxetine Attenuates Weight Gain and Increases Dehydroepiandrosterone Levels in Olanzapine-Treated Schizophrenia Patients
Michael Poyurovsky, M.D., Research Unit, Tirit Carmel Mental Health Center, 9 Eshkol Street, Tirit Carmel 30200, Israel; Rachel Maayan, D.H.D., Itt Gil-Ad, D.H.D., Abraham Weizman, M.D., Ronit Weizman, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should recognize the attenuating effect of reboxetine on olanzapine treated schizophrenia patients and the role of neurosteroids (DHLA) as a possible mediator of reboxetine’s weight attenuating effect.

Summary:
Objective: Dehydroepiandrosterone (DHEA) and its sulfate ester (DHEAS) are neurosteroids which have been found to possess hypophagic properties and reduce food intake. Clozapine decreases brain DHEA/DHEAS levels, accounting for clozapine’s propensity to induce weight gain. The selective norepinephrine reuptake inhibitor reboxetine attenuated olanzapine-induced weight gain. In the present study, we evaluated the DHEA/DHEAS levels in olanzapine-treated patients with and without add-on reboxetine.

Method: In a randomized double-blind designed study, 20 DSM-IV schizophrenia inpatients completed 6 weeks of olanzapine treatment (10 mg/day) with either reboxetine (4 mg/day, N=10) or placebo (N=10). DHEA/DHEAS levels were evaluated prior to and at completion of the trial using radioimmunoassay method.

Results: A significant between group difference was noted in plasma DHEA levels (olanzapine/reboxetine group: pre-treatment 54.9±23.4 pmol/ml; post treatment 68.4±20.4 pmol/ml) (olanzapine/placebo group: pre-treatment 66.1±22.0 pmol/ml; post treatment 60.5±23.4 pmol/ml) (t=5.4, df=18, p=0.0015). DHEAS levels increased in both groups with no between group differences. The olanzapine/reboxetine group demonstrated a significantly lower increase in body weight (mean = 2.5 ± 2.7kg) than the olanzapine/placebo group (mean = 5.5 ± 3.1 kg) (t = 2.31, df=18, p=0.033).

Conclusion: Add-on reboxetine may attenuate olanzapine-induced weight gain in schizophrenia patients and increased DHEA levels may mediate this effect.

References:

NR203 Monday, May 19, 03:00 p.m.-05:00 p.m.
Long-Term Use of Topiramate in the Treatment of Binge Eating Disorder
Susan L. McElroy, M.D., Department of Psychiatry, University of Cincinnati College of Medicine, 231 Albert Sabin Way, Cincinnati, OH 45267-0559, Lesley M. Arnold, M.D., Nathan A. Shapiro, M.D., Paul E. Keck, Jr., M.D., Shu-Chen Wu, Ph.D., James I. Hudson, M.D., Julie Capece, B.A., Norman R. Rosenthal, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to review the long-term efficacy and safety of topiramate for binge eating disorder.

Summary:
Objective: Assess efficacy and safety of topiramate (TPM) for treatment of binge-eating disorder (BED) in a 14-week, double-blind (DB), placebo-controlled study with a 42-week, open-label extension (OLE).

Methods: Patients receiving ≥1 dose TPM and providing ≥1 efficacy evaluation during the DB and/or OLE were analyzed. For patients receiving TPM during DB and OLE, the DB baseline was used (GroupA); for patients receiving TPM during OLE only, the end of DB represented baseline (GroupB). TPM was titrated by 25 mg/wk to 600 mg/day or maximum tolerated dose.

Results: Forty-three patients, mean baseline weight 123kg, received TPM for a median duration of 184 days with a median final dose of received mg/day. For GroupA, baseline mean weekly binge frequency, CGI-Severity, and weight declined from 5.0 to 0.6, 4.6 to 1.9, and −5.9kg, respectively, at DB end and to 0.5, 1.8, and −14kg at OLE end. For GroupB, baseline binge frequency, CGI, and weight declined from 4.1 to 0.7, 3.9 to 1.8, and −14kg, respectively, at OLE end. Most common adverse events were paresthesia, dry mouth, cognitive problems, headache.

Conclusions: The durability of our previous double-blind efficacy trial is supported, suggesting that topiramate is effective and safe for long-term treatment of BED.

References:
Venlafaxine Extended Release and Paroxetine in the Short-Term Treatment of Panic Disorder
Supported by Wyeth Research

Mark H. Pollack, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC-812, Boston, MA 02114; Evan Tzanis, B.A., Timothy M. Whitaker, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to compare the efficacy and tolerability of venlafaxine XR compared with placebo and with an SSRI (paroxetine); discuss the efficacy and tolerability of two fixed doses of venlafaxine XR in the treatment of panic disorder.

Summary:
Objective: To compare the efficacy and safety of venlafaxine extended release (XR) and paroxetine with placebo in the short-term treatment of panic disorder.

Methods: In this multicenter study, 664 adult outpatients with DSM-IV panic disorder (with or without agoraphobia) were randomly assigned to receive one of two fixed doses of venlafaxine XR (75 mg/day or 150 mg/day), paroxetine (40 mg/day), or placebo for up to 12 weeks. The primary efficacy measure was the proportion of panic-free patients (PAAS scale). Two key secondary measures were the PDSS and response rate (CGI-I ≤ 2). Remission was defined as panic free and CGI-I = 1.

Results: Venlafaxine XR and paroxetine were associated with significantly greater improvement on all efficacy measures versus placebo. No significant differences between venlafaxine XR and paroxetine emerged. At the final on-therapy evaluation, the percentage of panic-free patients was 54.1%, 61.4%, 60.0%, and 34.4% for venlafaxine XR 75 mg, 150 mg, paroxetine, and placebo, respectively (ITT, all P<0.001 vs placebo). The incidence and severity of adverse events were generally comparable with venlafaxine XR and paroxetine.

Conclusions: These results suggest that venlafaxine XR is safe, effective, and well tolerated in the short-term treatment of panic disorder.

References:

Schizophrenia: Hospitalization and Antipsychotic Therapy in Latin America
Supported by Eli Lilly and Company

Janey Shin, M.S.C., Lilly Research, Eli Lilly Canada, 3650 Danforth Avenue, Scarborough, ON M1N 2E8, Canada; Nicole M. Nitz, M.S., Madhav Namjoshi, Ph.D., Elizabeth Brunner, M.D.

Educational Objectives:
Following this presentation, participants should be able to describe changes in hospitalization rates in Latin America for patients with schizophrenia using different antipsychotic therapies.

Summary:
Objective: To compare psychiatric hospitalizations for Latin American patients with schizophrenia following initiation or change of antipsychotic therapy.

Methods: The Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) study enrolled 2671 patients in Latin America (age, mean±SD=35.8±12.5; 59% male, Chi-square tests compared proportion of patients hospitalized during six months prior to initiation/change of antipsychotic therapy (prebaseline) with proportion hospitalized during six months following antipsychotic change (postbaseline). Multiple logistic regression compared probability of postbaseline hospitalization among patients initiating different antipsychotic therapies, adjusting for baseline CGI total score, age, gender, prebaseline hospitalization, country, and disease duration.

Results: Across Latin America, the proportion of patients hospitalized decreased (32% to 8%) following antipsychotic initiation/change (p<.001). By country, postbaseline hospitalization rates ranged from 2% (Honduras) to 15.2% (Peru). Compared with patients initiating typical monotherapy antipsychotics, patients initiating olanzapine monotherapy were 42% less likely to have been admitted to hospital during the postbaseline period (OR=0.58, 95% CI:0.37,0.9). Postbaseline hospitalization did not differ statistically significantly from typical monotherapy initiators for patients initiating risperidone monotherapy (OR=0.80, 95% CI: 0.33, 1.1) or other atypical monotherapy antipsychotics (OR=0.47, 95% CI: 0.22, 1.0).

Conclusions: Patients initiating olanzapine monotherapy were significantly less likely to have been hospitalized compared with patients initiating typical monotherapy.

References:
Results: The olanzapine patient cohort experienced an overall relapse rate of 30%, whereas the lithium patient cohort experienced an overall relapse rate of 39%. While 14% (n = 31) of the olanzapine patients were admitted to the hospital during the course of the study, 23% (n = 49) of the lithium patients were hospitalized during the same period (p = 0.02). Olanzapine patients had a total of 31 hospital admissions during the study with a mean of 0.14 admissions compared with a total of 51 hospital admissions with a mean of 0.24 admissions for lithium patients (p=0.01).

Conclusion: The results of this study indicate that patients with bipolar disorder treated with olanzapine experience fewer relapses that result in fewer hospitalizations over 12 months compared with patients treated with lithium.

References:

NR207 Monday, May 19, 3:00 p.m.-5:00 p.m.
Long-Term Olanzapine Treatment Versus Haloperidol in First-Episode Psychosis
Supported by Eli Lilly and Company
Joseph P. McEvoy, M.D., Adult Admission Unit, John Umstead Hospital, 1003 12th Street, Building 32, Butner, NC 27509-1695; Jeffrey A. Lieberman, M.D., Diana O. Perkins, M.D., Robert M. Hamer, Ph.D., Tonmoy Sharma, M.D., Robert B. Zipursky, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to delineate differences in long-term efficacy and safety between olanzapine and haloperidol in first episode psychosis.

Summary:
The aim of this study was to compare, in a large and well-controlled clinical trial, the acute and long-term effectiveness of haloperidol and olanzapine in first-episode schizophrenia and schizoaffective disorder patients.

263 first-episode subjects were randomly assigned under double-blind conditions to haloperidol or olanzapine and followed for up to 104 weeks. Domains measured included treatment continuation and adherence, psychopathology, psychosocial measures, neurocognitive function, brain morphology and metabolism.

Both haloperidol and olanzapine were associated with substantial and comparable reductions in symptom severity. At 12 weeks, olanzapine-treated subjects showed significantly greater symptom decreases in mixed-model analysis, lower rates of treatment-emergent Parkinsonism and akathisia, and greater weight gain. Treatment discontinuation rates were high overall with only 47 patients remaining in the study by two years. Retention was greater with olanzapine. Beginning by week 6, there were more dropouts with haloperidol than olanzapine, and this difference in dropout rates widened over the course of the study with 12% of haloperidol subjects and 24% of olanzapine subjects staying in the study at two years. The psychopathology and safety results of through 104 weeks will be presented and discussed.

References:

NR208 Monday, May 19, 3:00 p.m.-5:00 p.m.
Metabolic and Cardiac Changes With Ziprasidone Treatment
Supported by Portland VA Research Service
Thomas E. Hansen, M.D., Department of Psychiatry, VA Medical Center, 3710 SW US Veterans Hospital Road, Portland, OR 97239; Beal G. Essink, M.D., William F. Hoffman, M.D., Daniel E. Casey, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize and manage the metabolic and cardiac side effects that occur in a naturalistic, clinical setting with use of ziprasidone.

Summary:
Introduction: Atypical antipsychotic medications may lead to metabolic and cardiac problems. Data often come from highly controlled industry-sponsored studies. Our objective was to carefully monitor these side effects in a routine clinical population treated with ziprasidone, hypothesizing that ziprasidone would be associated with decreased weight and fasting blood sugar and lipids, but that QTc would not change.

Method: Sample of convenience study with only inclusion criterion being that ziprasidone is indicated. Evaluations (weight, EKG, and fasting glucose, hemoglobin A1c, and lipids) were pretreatment, one week, and one, three, six, and 12 months.

Results: 17 of 42 enrolled patients have at least 3 month evaluations, with decreases in all parameters (weight 236 to 232, hemoglobin A1c 5.8% to 5.6%, LDL cholesterol 126 to 120 mg/ml, and triglycerides 214 to 192 mg/ml, and fasting glucose from 121 to 108 mg/ml). Standard deviations were large for all laboratory variables. QTc values increased by about 5 msec (see poster for data from all time points).

Conclusions/Discussion: Metabolic parameters decreased modestly except for the moderate decrease in glucose. Based on variability for individual patients and high standard deviations, clinicians should consider allowing 3 months treatment for observation of changes, and should repeat abnormal labs. For routine patients, EKG monitoring does not seem to be necessary.

References:

NR209 Monday, May 19, 3:00 p.m.-5:00 p.m.
Risk of Diabetes in Medi-Cal Patients Prescribed Atypical Antipsychotics
Supported by Janssen Pharmaceutica Products, L.P.
Amy L. Grogg, Ph.D., Department of Outcome Research, Janssen Pharmaceutica Products, L.P., 1125 Trenton-
Harbourton, Titusville, NJ 08560; Jeffrey Markowitz, Ph.D., Ramy A. Mahmoud, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to compare rates and risks of new-onset diabetes among patients treated with olanzapine, quetiapine, and risperidone in a Medicaid population as well as understand other independent risk factors for diabetes.

Summary:
Objective: Diabetes and ketoacidosis are a dangerous, growing, and under-investigated concern with atypical psychotropics. Differential label changes have recently been affected in many countries, but not in the U.S. We evaluate relative risk of new-onset diabetes for different serotonin-dopamine antagonists in the largest Medicaid population in the United States.

Methods: Subjects included all California Medicaid patients under age 65 initiating monotherapy with olanzapine, quetiapine, or risperidone after 12/31/98. Patients were followed until disenrollment, new onset diabetes (diagnostic claim or an anti-diabetic prescription), treatment switch/discontinuation, or end of the data. Incidence density rates were computed and independent risk factors were identified by logistic regression.

Results: 18,023 patients were eligible: 8,550 olanzapine, 1,578 quetiapine, and 7,895 risperidone. Incidence of diabetes per year averaged 4.74%, 3.04%, and 3.15% for olanzapine, quetiapine, and risperidone, respectively. Significant independent risk factors were: olanzapine, higher antipsychotic dose, increasing age, hypertension, depression, mood stabilizers, and medium/high number of co-morbid conditions. Compared with risperidone, subjects prescribed olanzapine had a 30% increased risk of developing diabetes (adjusted odds ratio=1.30; 95% Cl=1.05, 1.62).

Discussion: Risk of diabetes was significantly higher for subjects prescribed olanzapine. Diabetes risk was also associated with higher dose, mood stabilizers, and both psychiatric and medical comorbidity.

References:

NR210 Monday, May 19, 3:00 p.m.-5:00 p.m.
A Controlled Trial of Bupropion SR for Smoking Cessation in Patients With Schizophrenia Supported by GlaxoSmithKline
Eden A. Evins, M.D., Department of Psychiatry, Massachusetts General Hospital, 25 Staniford Street, 2nd Floor, Boston, MA 02114; Donald C. Goft, M.D., Casey Olm-Shipman, B.S., Nancy A. Rigotti, M.D., Corinne Cather, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that smoking cessation is a major clinical priority for patients with schizophrenia. Understand that bupropion appears to be an effective treatment for smoking cessation in patients with schizophrenia that is associated with stability of psychiatric symptoms during a smoking cessation attempt.

Summary:
Objective: To determine whether bupropion is safe and effective for smoking cessation treatment in patients with schizophrenia.

Method: Outpatients with schizophrenia who smoked >10 cigarettes/day and wanted to quit smoking were randomly assigned to receive double blind bupropion 300 mg per day or identical placebo for 12 weeks. All subjects received a weekly cognitive behavioral group intervention and set a quit date at week 4.

Results: 62 subjects enrolled and 52 completed the study. Baseline measures of smoking did not differ between groups. Expired air carbon monoxide (CO) was reduced in the entire group from 29.7 (16.5) ppm at baseline to 11.9 (8.7) at the quit date (t=5.5, p<.0001) and to 19.2 (11.0) at week 12 (t=3.6, p<.001). The primary outcome measure was 7 day point prevalence smoking reduction at week 12, defined as >50% reduction from baseline in expired CO. In the bupropion group, 28% achieved significant reduction at week 12 (z=2.98, p=0.01, 95% Cl .09–.48) and in the placebo group 12% achieved significant reduction (z=1.84, p=0.06, 95% Cl –0.007–24.7). 13% of the bupropion group and none in the placebo group achieved continuous abstinence (weeks 4–12), (z=1.94, p=0.05). Psychiatric symptoms remained stable during the smoking cessation attempt.

Conclusions: These data confirm previous findings that bupropion SR is safe and effective for smoking cessation in patients with schizophrenia.

References:

NR211 Monday, May 19, 3:00 p.m.-5:00 p.m.
Impact of Use of Different Atypical Antipsychotics on Nursing Home Center
Shyam D. Karki, Ph.D., Pharmacy Department, Monroe Community Hospital, 435 East Henrietta road, Rochester, NY 14620; William R. Patterson, B.S.

Educational Objectives:
At the conclusion of this session, the participant should recognize different cost factors in the use of atypical antipsychotics.

Summary:
Purpose: To evaluate impact of the use of three atypical antipsychotics (risperidone, olanzapine and quetiapine) on nursing home costs.

Method: Charts of nursing home residents stabilized on fixed doses of risperidone (R), olanzapine (O), and quetiapine (Q) for at least six months were reviewed for dosage and dosage frequency. Time taken in dispensing and administration was determined by monitoring at three different occasions and their costs were calculated.

Results: There were 50 residents on R, 30 on O and 60 on Q. Mean daily dose was 1.2 ± 0.9 mg for R, 4.2 ± 2.3 for O and 240 ± 135 for Q. Dosage frequency was 1.6 ± 0.5 for R, 1.0 for O, and 2.5 ± 0.7 for Q. Nursing costs were $682 for R, $426 for O and $1,065 for Q. Pharmacy cost was $139 for R, $87 for O and $217 for Q.

Discussion: NY State Medicaid program provides additional reimbursement for atypical antipsychotics. However Pharmacy (P) and nursing (N) costs may vary significantly.

Conclusion: P & N costs per therapy year were $821 for R, $513 for O, and $1,282 for Q indicating O as the most cost effective.
atypical antipsychotic in the management of agitation in residents with dementia in N.Y. State nursing homes.

References:

NR212 Monday, May 19, 3:00 p.m.-5:00 p.m.
Medication Adherence and Atypical Antipsychotics National Institute of Mental Health
Dawn I. Velligan, Ph.D., Department of Psychiatry, University of Texas H.S.C., 7703 Floyd Curl Drive, San Antonio, TX 78229-3900; Yui-Wing Lam, Pharm.D., Larry Ereshefsky, Pharm.D., Natalie J.L. Maples, M.A., Margaret A. DiCocco, Desiree A. Castillo, Alexander L. Miller, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate levels of adherence to atypical antipsychotics 3 months after hospital discharge in patients with schizophrenia.

Summary:
Introduction: Atypical antipsychotics with more favorable side-effect profiles than conventional neuroleptics have been expected to improve medication adherence for patients with schizophrenia. We examined rates of adherence to oral atypical antipsychotic medications in a sample of 59 schizophrenia patients recently discharged from a state hospital.

Method: Three blood samples were obtained from the patients immediately after discharge, while medication intake was closely monitored to determine the percentage of days covered (%DC) in plasma-level under ideal conditions. Two random predose blood samples were obtained three months postdischarge and %DC and Cp/dose differences from baseline were used as adherence indicators. Pill counts and self-reports were also collected.

Results: At three months, fewer than 12% of subjects were refusing medication. However, combining %DV and Cp/dose differences to classify patients, we identified 75% of subjects as poorly adherent. Pill counts identified 65% of subjects as poorly adherent and suggested that only 9% of subjects had taken the exact number of pills prescribed.

Conclusion: While there are many benefits to atypical antipsychotics over conventional neuroleptics, major obstacles to medication adherence remain. The development of depot atypical antipsychotic medications may be important in addressing the problem of partial adherence for schizophrenia patients.

References:

NR214 Monday, May 19, 3:00 p.m.-5:00 p.m.
Treatment of Panic Disorder With Venlafaxine Extended Release Supported by Wyeth Research
Jacques Bradwejn, M.D., Department of Psychiatry, University of Ottawa, 1145 Carling Avenue, Ottawa, ON K17 7K4, Canada; Gerard Emilien, Ph.D., Timothy M. Whitaker, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the effects of venlafaxine XR on the symptoms of panic disorder; discuss the use of venlafaxine XR for short-term treatment of panic disorder with or without agoraphobia.

Summary:
Objective: To determine the efficacy and safety of venlafaxine extended release (XR) in short-term treatment of panic disorder.

Methods: In this multicenter, randomized, parallel-group study, 361 adult outpatients with DSM-IV panic disorder (± agoraphobia) were randomly assigned to receive flexible dose venlafaxine XR (75 to 225 mg/day) or placebo for ≤10 weeks. The primary efficacy measure was the proportion of patients free from panic attacks (PAAS scale). Secondary efficacy measures included the propor-
tion of responders (CGI-I ≤ 2) and remitters (panic free and CGI-I = 1), and reduction in panic attack frequency.

Results: At the final on-therapy evaluation, 55% of venlafaxine XR- and 52.4% of placebo-treated patients were panic free (ITT population). Response and remission rates were greater with venlafaxine XR treatment than with placebo (response 68.1% vs 55.4%, P < 0.05; remission: 35.6% vs 24.4%, P < 0.05). Venlafaxine XR was superior to placebo in reducing panic attack frequency (median change from baseline of -5.0 vs -3.7, respectively, P < 0.05). The incidence and severity of adverse events associated with venlafaxine XR treatment were comparable with those observed in patients with depression and generalized anxiety disorder who received venlafaxine XR.

Conclusion: These results suggest that venlafaxine XR is safe, effective, and well tolerated in short-term treatment of panic disorder.

References:

NR215 Monday, May 19, 3:00 p.m.-5:00 p.m.
Risk Factor Profile for Reversibility of Olanzapine Treatment: Emergent Diabetes
Rafael A. Torres, M.D., Department of Mental Health, Veterans Administration Medical Center, 1500 E.W. Wilson Drive, Suite 116A3, Jackson, MS 39216; Henry A. Nasrallah, M.D., Candace L. Perry, B.S., Erica Love, B.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify patient characteristics that favor reversal of Olanzapine treatment-emergent diabetes upon Olanzapine discontinuation and switch to another antipsychotic.

Summary:
Objective: Antipsychotic treatment-emergent hyperglycemia is a clinically important complication of Olanzapine treatment in patients with schizophrenia. The objective of this study was to identify factors that may favor reversal of Olanzapine treatment-emergent diabetes.

Methods: A retrospective chart review was conducted on 11 patients with Olanzapine treatment-emergent diabetes. Patient characteristics, treatment history, laboratory values, and clinical course were recorded.

Results: Five out of 11 patients with Olanzapine treatment-emergent diabetes had reversal of glucose abnormality upon Olanzapine discontinuation. Factors associated with reversal included shorter duration of Olanzapine treatment, lower BMI increase during treatment, and a family history of diabetes.

Conclusion: Identifying factors that favor reversal of Olanzapine treatment-emergent diabetes may help guide treatment decisions in patients with diabetes.

References:

NR216 Monday, May 19, 3:00 p.m.-5:00 p.m.
Is Gabapentin Augmentation to Antidepressants a Viable Option for the Treatment of Resistant Unipolar Recurrent Major Depression?
Rosa Catalán, M.D., Department of Psychiatry, Hospital Clinic, Rosellon 140, Barcelona 08036, Spain; Andrea Gabicondo, M.D., Teresa Plana, M.D., Rafael Penddes, Ph.D., Cristobal Gasto, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the rationale for using gabapentin augmentation in the treatment of antidepressant-resistant recurrent major depression.

Summary:
Forty-eight outpatients with moderate to severe unipolar recurrent major depression were treated with open-label gabapentin augmentation (300–1,600 mg/day) in combination with several classes of antidepressants at least during 8 weeks in a prospective case-series design. The diagnosis of treatment-resistant depression was made according to proposed staging criteria by Thase and Rush (1995). The average age of patients was 47.65 (+12.35) and number of prior episodes was 3.2 (+1.7). Efficacy was based on a Clinical Global Impression Scale as least 8 consecutive weeks with either (CGI score = 1 or 2).

Results: Seventy percent of patients responded to gabapentin augmentation, 85% of patients achieved clinical remission, and 71% of patients were assessed as responders to gabapentin augmentation (mean doses daily 850 mg SD 251.36). There were no significant differences at the baseline level of severity of illness, sex, duration of illness, or the number of prior episodes between responders and nonresponders.

Conclusions: Gabapentin augmentation is a viable option for the treatment of resistant unipolar recurrent major depression.

References:
NR217  Monday, May 19, 3:00 a.m.-5:00 a.m.
Cost-Effectiveness of Atypical Antipsychotics in Acute Bipolar Mania
Supported by Johnson & Johnson Pharmaceutical Research & Development
Lisa J. McGarry, M.P.H., Innovus Research, 10 Cabot Road, Suite 102, Medford, MA 02155; Amy P. Bird, B.S., David Thompson, Ph.D., Philip S. Wang, M.D., Silas C. Martin, B.S., Milton C. Weinstein, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the state-transition approach to modeling acute bipolar disorder and the basic concepts of cost-effectiveness analysis. Participants should be able to use our assessment of the cost-effectiveness of atypical antipsychotics to inform clinical decisions in acute bipolar mania.

Summary:
Objective: To determine if atypical antipsychotics (AA) in combination with mood stabilizers (MS) are cost-effective for treatment of acute bipolar mania.

Methods: We developed a state-transition Markov model to estimate the cost-effectiveness of combination therapy with AA+MS in hospitalized patients with acute mania. Treatment alternatives include: olanzapine+MS, risperidone+MS, haloperidol+MS, or lithium monotherapy. Over the three-week intervals, patients may remain manic, become depressed, die from suicide or other causes, or stabilize and enter the continuation/maintenance phases. While in each state, patients accumulate medical-care costs and utilities (measures of quality of life). Transition probabilities and costs were estimated from published sources; utilities for each state were assessed using the standard gamble method. Cumulative costs and utilities for each treatment were used to estimate incremental cost per quality-adjusted life-year (QUALY) gained.

Results: Haloperidol+MS is the least costly therapy option, while risperidone+MS provides the most QUALYs. Risperidone+MS costs an additional $3,300 per QUALY gained versus haloperidol+MS, and is cost saving versus either olanzapine+MS or lithium monotherapy. Results were sensitive to drug costs, drug efficacy, suicide rate, and rate of tardive dyskinesia.

Conclusions: Combination therapy with the atypical antipsychotic risperidone plus MS provides good value for money in the treatment of acute bipolar mania.

References:

NR218  Monday, May 19, 03:00 p.m.-05:00 p.m.
Conditional Probability of Remission in the Treatment of Depression
Supported by Pfizer Inc.
Maurizio Fava, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC-812, Boston, MA 02114; Tal Burt, M.D., Evan Batzar, M.A., Harold A. Sackeim, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should improve the participant’s understanding of the relationship between early improvement and remission.

Summary:
Objective: To examine the relationship between early improvement and remission in the acute treatment of MDD.

Methods: Data were pooled from two eight-week, double-blind, placebo-controlled studies of sertraline (50-200 mg/d) in outpatients with major depressive disorder (N=556; female, 58%; mean baseline HAM-D, 23). Remission rates were defined as endpoint HAM-D total score ≤7. A conditional probability analysis was performed on eight-week completers (N=359) to quantify the proportion of patients achieving remission given at least minimal early improvement at week 4 (CGI-I ≤3) among study completers (N=345) with valid week 2 data.

Results: Remission rates at week 8 were 53% for sertraline and 32% for placebo. Achievement of CGI-I ≤3 at week 2 was associated with a 59% conditional probability of remission on sertraline, and 40% on placebo. For patients treated with sertraline, use of CGI-I ≤3 at week 2 to predict eight-week remitter status is associated with a sensitivity of 79%, a specificity of 40%, and a positive predictive value (PPV) of 59%.

Conclusion: Early improvement has only modest clinical value as a predictor of remission, with a 60% false negative rate, indicating that acute remission is frequently achieved despite delayed onset of antidepressant effect.

References:

NR219  Monday, May 19, 03:00 p.m.-05:00 p.m.
Topiramate for Bulimia Nervosa: Open-Label Follow-Up of a Controlled Trial
Supported by Ortho-McNeil Pharmaceuticals
Scott P. Hoopes, M.D., Mountain West Clinical Trials, LLC, 315 North Allumbaugh Street, Boise, ID 83704-9208; Dawson W. Hedges, M.D., Frederick W. Reimherr, M.D., Robert E. Strong, D.O., Jim Xiang, Ph.D., Julie Capece, B.A., Norman R. Rosenthal, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to review the long-term efficacy and safety of topiramate for bulimia nervosa.

Summary:
Objective: Assess efficacy and safety of topiramate (TPM) for treatment of bulimia nervosa in a 10-week double-blind (DB) placebo-controlled study with a 40-week open-label extension (OLE).

Methods: Patients receiving ≥1 dose TPM and providing ≥1 efficacy evaluation during the DB and/or OLE were analyzed. For patients receiving TPM during DB and OLE, the DB baseline was used; for patients receiving TPM during OLE only, the end of DB represented baseline. TPM was titrated by 25 mg/wk to 400 mg/day or maximum tolerated dose.

Results: Forty-seven patients received TPM for a median duration of 125 days (range 5–428) and median final dose of 100 mg/day. The primary outcome, mean weekly binge and/or purge days,
declined from a baseline 4.5 to 0.8 at Month 10. 11/14 patients were rated very much or much improved on CGI and PGI scales at Month 10. Eating Disorder Inventory improved for Drive for Thinness, Body Dissatisfaction, and Bulimia; Eating Attitudes Test improved for Dieting and Bulimia/Food Preoccupation. HAM-A fell from 6.2 at baseline to 2.1. Most common adverse events were paresthesia, flu-like symptoms, fatigue, concentration/attention difficulty.

Conclusions: Topiramate appears to be associated with long-term improvement in eating behaviors and attitudes in patients with bulimia nervosa.

References:

NR220 Monday, May 19, 03:00 p.m.–05:00 p.m.
SOHO Study: Six Months of Data on Subjective Well-Being and Social Functioning Supported by Eli Lilly and Company
Ralf W. Dittmann, M.D., Lilly Research, Lilly Deutschland GmbH, Saalburgerstrasse 153, Bad Homburg D-61350, Germany; Anne Karow, M.D., Joerg Czekalla, M.D., Christina Mahl, Thomas Wagner, Frank Langer, Dieter Naber, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe how real-life treatment with antipsychotics improves QoL and social functioning in schizophrenic patients.

Summary:
Introduction: Subjective well-being (SWN) and social functioning were observed in German schizophrenic outpatients treated with antipsychotics.

Methods: Naturalistic observational study planned for 36 months. Decision to initiate, change, or add a new antipsychotic was made prior to observation. Assessment at baseline, three and six months by self-rated SWN scale and social function questionnaire. All comparisons are descriptive and based on ITT.

Results: German sample at six months: N=2,450 (retention 85%), most patients still received the antipsychotic initiated or added at baseline (e.g., clozapine 95.7%, olanzapine 90.5%). Most pronounced improvement of the SWN total score at six months compared with baseline was seen for olanzapine (by 15.1 points) followed by clozapine (14.4), risperidone (12.4), amisulpride (10.8), quetiapine (10.0), and less with oral (8.3) and depot antipsychotics (8.0). Social functioning assessment at 6 months showed marked improvement of patients' social activities, but not for work status, or housing status.

Conclusions: Findings suggest that patients treated with atypical antipsychotics experience strong improvements in QoL as assessed by SWN at 6 months. For the olanzapine cohort, this corroborates clinical trial data (Naber et al., 2001). In this way, atypical antipsychotics such as olanzapine appear to help to move patients' life forward. Assessment of 'social functioning' items will be of particular interest in the long term.

References:

NR221 Monday, May 19, 3:00 p.m.–5:00 p.m.
Overt Aggression and Psychotic Symptoms in Patients With Schizophrenia Treated With Clozapine, Olanzapine, Risperidone, or Haloperidol
Leslie L. Citrome, M.D., Clinical Research/CREF, Nathan Kline Institute for Psych. Research, 140 Old Orangeburg Road, Building 37, Orangeburg, NY 10962-2210; Jan Volavka, M.D., Pal Czobor, Ph.D., Karen Nolan, Ph.D., Jeffrey A. Lieberman, M.D., Jean-Pierre Lindenmayer, M.D., Brian B. Sheltman, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize clozapine has superior antiaggressive effects in treatment-resistant patients; this superiority develops after the patient has been exposed to an adequate dose regimen.

Summary:
Objective: Published studies of antiaggressive treatments are largely uncontrolled and use indirect measures of aggression. We present the effects of four antipsychotics on incidents of overt aggression in a controlled study.

Method: The subjects were 157 treatment-resistant inpatients diagnosed with chronic schizophrenia or schizoaffective disorder. They were randomly assigned to treatment with clozapine, olanzapine, risperidone, or haloperidol in a 14-week double-blind trial. Incidents of overt physical aggression were recorded and their severity scored. A standard measure of clinical antipsychotic efficacy (PANSS) was administered.

Results: Atypical antipsychotics showed an overall superiority over haloperidol, particularly after the first 24 days of the study when dose escalation of clozapine was completed. Once an adequate therapeutic dose of clozapine was reached, it was superior to haloperidol in reducing the number and severity of aggressive incidents. Patients exhibiting persistent aggressive behavior showed less improvement of psychotic symptoms than the other patients. There was an interaction between aggressiveness, medication type, and antipsychotic response: risperidone and olanzapine showed better antipsychotic efficacy in patients exhibiting less aggressive behavior; the opposite was true for clozapine.

Conclusions: Clozapine appears to have superior antiaggressive effects in treatment-resistant patients; this superiority develops after the patient has been exposed to an adequate dose regimen. The interaction between medication, aggressiveness, and treatment response suggests that the information about the level of aggressive behavior is critically important for a choice of treatment: clozapine should be the first-line atypical antipsychotic in patients with schizophrenia showing persistent aggressive behavior.

References:

NR222 Monday, May 19, 3:00 p.m.–5:00 p.m.
Antipsychotic Medication Treatment and New Prescriptions for Insulin and Oral Hypoglycemics
Leslie L. Citrome, M.D., Clinical Research/CREF, Nathan Kline Institute for Psych. Research, 140 Old Orangeburg Road,
Concomitant Use of Mood Stabilizers in Bipolar I Disorder

Supported by GlaxoSmithKline

Charles L. Bowden, M.D., Department of Psychiatry, University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284-7792; Joseph R. Calabrese, M.D., Gary S. Sachs, M.D., Robert A. Leadbetter, M.D., Alan Metz, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss clinical improvements with long-acting risperidone in patients previously receiving oral olanzapine.

Summary:

Introduction: Although atypical antipsychotics have advanced the management of schizophrenia, currently available agents require daily dosing, commonly associated with limitations on adherence, response, and functional outcomes. This analysis examined long-acting risperidone for symptom control and quality of life in patients previously receiving the oral atypical olanzapine.

Methods: A 12-week, placebo-controlled, multicenter, double-blind study assessed patients receiving long-acting risperidone (25, 50, or 75 mg) every two weeks (n=370). Patients receiving prior therapy with oral olanzapine were analyzed (n=16, placebo; n=42 long-acting risperidone).

Results: Baseline PANSS-Total scores and mean prior olanzapine doses were comparable between placebo and long-acting risperidone groups (83.3±9.7, 83.1±2.4; 15.3±1.9 mg/d, 16.0±0.83 mg/day, respectively). At endpoint, PANSS-Total scores worsened in placebo group, while improving significantly...
from prior olanzapine treatment (p=0.027) in the long-acting risperidone group (+4.4 and −6.9, respectively; p=0.05 between groups). Significant improvement (p<0.05) from prior olanzapine treatment was present in the long-acting risperidone group across Positive, Negative and Mood/Anxiety domains. Improvement from prior olanzapine treatment was present in the SF-36 domain social functioning (p=0.053) and the mental health index (p=0.041), following treatment with long-acting risperidone.

Conclusions: These data support potential improvements in symptoms and quality of life with long-acting risperidone in patients previously receiving oral olanzapine.

References:

NR225
Monday, May 19, 3:00 p.m.-5:00 p.m.
Brain Function Correlates of Side Effects in Nondepressed Individuals Randomized to Venlafaxine Versus Placebo
Aimee Hunter, Ph.D., Psychiatry Department, UCLA, 760 Westwood Plaza, Los Angeles, CA 90024; Andrew F. Leuchter, M.D., Melinda Morgan, Ph.D., Ian A. Cook, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify patterns of brain function, as measured by QEEG cordance, that are associated with side effects in normals taking venlafaxine or placebo.

Summary:
Objective: Medication side-effects are a major reason for treatment non-compliance in depression. We characterized severity of side-effects in normal subjects treated with either venlafaxine IR or placebo, and examined brain functional differences between high and low side-effect reporters.

Method: Normal adult subjects underwent 4 weeks' double-blind treatment with venlafaxine IR (n = 16) or placebo (n = 15). Side effects were assessed and brain assessment was performed prior to and during treatment using quantitative electroencephalographic (QEEG) cordance, a measure that has moderately strong associations with cerebral perfusion.

Results: Both venlafaxine and placebo subjects reported a significant increase in side effects during treatment, with venlafaxine subjects showing a significantly greater number than placebo subject. Baseline cordance in the occipital region was strongly associated with side effects in venlafaxine (p = .007) and placebo (p = .006) groups, and changes in cordance in the right parietal region were associated with both placebo- and medication-related side effects (p = .04).

Conclusions: These data suggest that normal subjects who experience side-effects on either medication or placebo exhibit specific brain functional characteristics. Brain function may help explain mechanisms of drug- and placebo-induced side effects.

Funding Sources: Supported by Eli Lilly and Company, National Institute of Mental Health (NIMH), and Wyeth-Ayerst Laboratories.

References:
NR228  Monday, May 19, 3:00 p.m.-5:00 p.m.
Comparison of Venlafaxine Extended Release and Paroxetine in Short-Term Treatment of SAD
Supported by Wyeth Research

Richard Mangano, Ph.D., Wyeth Research, 500 Arcola Road, Collegeville, PA 19426; Michael R. Liebowitz, M.D., Christler Allgulander, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the effects of venlafaxine XR on the symptoms of SAD, and compare the efficacy and tolerability of venlafaxine XR with placebo and an established treatment option (ie, paroxetine).

Summary:

Objective: To report on two studies that investigated the efficacy, safety, and tolerability of venlafaxine extended release (XR) in the treatment of generalized social anxiety disorder (SAD) in comparison with placebo and paroxetine.

Methods: Study 1 (n = 434) and study 2 (n = 429) were double-blind, multicenter studies. Patients were randomly assigned to receive venlafaxine XR (flexible dose: 75 to 225 mg/day), paroxetine (flexible dose: 20 to 50 mg/day), or placebo for ≤12 weeks. The primary efficacy variable was the Liebowitz Social Anxiety Scale total score. Secondary efficacy variables included CGI-S score, Social Phobia Inventory (SPIN), and responder status (CGI ≤ 2).

Results: Both active treatments were associated with significantly greater improvement than placebo on each efficacy measure listed (LOCF analysis). A significant difference between active treatments was observed in study 2, in which SPIN scores with venlafaxine XR were superior to those with paroxetine at weeks 1 and 2. Adverse events were similar in the studies and included nausea, insomnia, somnolence, asthenia, dry mouth, and dizziness.

Conclusion: Venlafaxine XR and paroxetine were effective short-term treatments for generalized SAD, with a potential advantage for venlafaxine XR compared with paroxetine in terms of earlier symptomatic relief.

Funding Source(s): Wyeth Research.

References:

1. Pizzella G, Maslinger-Gehmayr R, Contu A: Treatment of Depression in patients with breast cancer: a comparison between...


NR230 Monday, May 19, 3:00 p.m.-5:00 p.m.
Can Stable Patients With Schizophrenia Improve? The Impact of Partial Compliance Versus Constant Therapy
Supported by Janssen Pharmaceutica Products, L.P.
Courtney Lonchena, Janssen Pharmaceutica Products, L.P., 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Robert A. Lasser, M.D., Cynthia Bossie, Ph.D., Young Zhu, Ph.D., Georges Bharabawi, M.D., Ross J. Baldessarini, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the benefits of long-acting injectable risperidone in apparently stable patients with schizophrenia.

Summary:
Background: Available atypical antipsychotics require daily dosing that is associated with partial adherence and possibly suboptimal treatment response. We tested the hypothesis that further improvement is possible with long-acting risperidone in patients previously considered "stable" with oral risperidone.

Methods: Schizophrenia/schizoaffective disorder patients rated as clinically stable with daily oral risperidone (N=336) were converted to approximately equivalent biweekly injections of long-acting risperidone (25, 50 or 75 mg) for a year.

Results: Extrapyramidal sign (EPS) ratings decreased substantially acting risperidone (25, 50 or 75 mg) for 26 weeks. The primary outcome measure was the proportion of patients experiencing significant weight gain (≥7%) from baseline to endpoint.

Results: In patients remaining on therapy, more olanzapine-treated patients experienced ≥7% weight gain than aripiprazole-treated patients throughout the study. Significant differences in mean weight change were observed at weeks 6 and 26; at week 26, there was a mean weight increase of 4.23 kg with olanzapine and a mean weight loss of 1.37 kg with aripiprazole (P<0.001). Differences favoring aripiprazole were also seen for total cholesterol, HDL, and triglycerides. There was no difference in the rate of clinical response between aripiprazole and olanzapine, either acutely (week 6) or in number of patients remaining in response and on therapy at week 28.

Conclusion: While clinical response was comparable, the incidence of weight gain and dyslipidemias were significantly lower with aripiprazole than with olanzapine. These effects on weight and lipids may lead to more advantageous long-term metabolic profile in patients treated with aripiprazole compared with olanzapine.

References:

NR231 Monday, May 19, 3:00 p.m.-5:00 p.m.
Long-Term Weight Effects of Aripiprazole Versus Olanzapine
Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co, Ltd.
Robert D. McQuade, Ph.D., Bristol-Myers Squibb Company, Route 206 & Province Line Road, Princeton, NJ 08543; Darlene Jody, M.D., Mary J. Kujawa, M.D., William H. Carson, Jr., M.D., Taro Iwamoto, Ph.D., Donald G. Archibald, M.Phil., Elyse G. Stock, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should have a better understanding of the weight effects of aripiprazole compared with olanzapine in patients with acute relapse of schizophrenia.

Summary:
Objectives: To compare long-term weight effects of aripiprazole and olanzapine in patients with acute relapse of schizophrenia.

Methods: In this double-blind, multicenter study, 317 patients were randomized to aripiprazole (15–30 mg/day) or olanzapine (10–20 mg/day) for 26 weeks. The primary outcome measure was the proportion of patients experiencing significant weight gain (≥7%) from baseline to endpoint.

Results: In patients remaining on therapy, more olanzapine-treated patients experienced ≥7% weight gain than aripiprazole-treated patients throughout the study. Significant differences in mean weight change were observed at weeks 6 and 26; at week 26, there was a mean weight increase of 4.23 kg with olanzapine and a mean weight loss of 1.37 kg with aripiprazole (P<0.001). Differences favoring aripiprazole were also seen for total cholesterol, HDL, and triglycerides. There was no difference in the rate of clinical response between aripiprazole and olanzapine, either acutely (week 6) or in number of patients remaining in response and on therapy at week 28.

Conclusion: While clinical response was comparable, the incidence of weight gain and dyslipidemias were significantly lower with aripiprazole than with olanzapine. These effects on weight and lipids may lead to more advantageous long-term metabolic profile in patients treated with aripiprazole compared with olanzapine.

References:
...tween the two groups in an intent-to-treat analysis, either in terms of treatment. No significant differences in outcome were noted between the two groups in an intent-to-treat analysis, either in terms of very early (2-4 weeks) or not so early (5-10 weeks) responses during treatment. Drop-out rates were similar in the paroxetine/olanzapine group vs. the paroxetine/placebo group (29% vs. 36%, p=.5), and paroxetine/olanzapine was well tolerated.

Conclusions: These findings are in contrast to those in panic disorder, where early co-administration of clonazepam with an SSRI has been shown to be efficacious in moderate-to-severely ill patients (Goddard et al., 2001). Despite the limitations of this study (small sample size, low dose of clonazepam), these data argue against routine early co-administration of clonazepam with an SSRI for moderate to severe GSAD. Nevertheless, the role of benzodiazepines in other instances (e.g. for augmenting SSRI partial- or non-response) is deserving of further investigation.

References:

NR233 Monday, May 19, 3:00 p.m.-5:00 p.m.
Early Co-administration of Clonazepam With Paroxetine for Generalized Social Anxiety Disorder
Soraya Seedat, M.D., Department of Psychiatry, University of Stellenbosch, P.O. Box 19063, Cape Town 7505, South Africa; Murray B. Stein, M.D.

Educational Objectives:

At the conclusion of this session, the participant should have some knowledge of the efficacy of pharmacological interventions for generalized social anxiety disorder.

Summary:

Background: Generalized social anxiety disorder (GSAD) is a pervasive form of social anxiety that affects approximately 5% of persons in the community. Among evidence-based pharmacological treatments for the disorder, selective serotonin reuptake inhibitors (SSRIs) have become widely used and are known to be efficacious. Although benzodiazepines have been less well studied, a single randomized controlled trial of clonazepam monotherapy (Davidson et al., 1993) demonstrated clear-cut efficacy compared with placebo. The purpose of the present study was to determine if early co-administration of clonazepam with paroxetine (vs. placebo with paroxetine) would enhance short-term outcomes in patients with GSAD.

Methods: Twenty-eight patients (22 men and 6 women) with generalized social anxiety disorder (GSAD) were included in the study; 23 (82%) met DSM-IV criteria for Avoidant Personality Disorder. Mean age was 31.2 years (SD=7.7) with a mean duration of illness of 12.1 years (SD=5.8). Patients were randomized to receive double-blind clonazepam 0.5-1.0mg b.i.d./day (or placebo) along with open-label paroxetine 20–40mg/day for 10 weeks. A two-week taper of double-blind medication was followed by an additional eight weeks of open-label paroxetine treatment (during which the dose of paroxetine could be increased to a maximum of 50mg/day).

Results: Nineteen (68%) of twenty-eight patients completed treatment. No significant differences in outcome were noted between the two groups in an intent-to-treat analysis, either in terms of very early (2-4 weeks) or not so early (5-10 weeks) responses during treatment. Drop-out rates were similar in the paroxetine/olanzapine group vs. the paroxetine/placebo group (29% vs. 36%, p=.5), and paroxetine/olanzapine was well tolerated.

Conclusions: These findings are in contrast to those in panic disorder, where early co-administration of clonazepam with an SSRI has been shown to be efficacious in moderate-to-severely ill patients (Goddard et al., 2001). Despite the limitations of this study (small sample size, low dose of clonazepam), these data argue against routine early co-administration of clonazepam with an SSRI for moderate to severe GSAD. Nevertheless, the role of benzodiazepines in other instances (e.g. for augmenting SSRI partial- or non-response) is deserving of further investigation.

References:

NR234 Monday, May 19, 3:00 p.m.-5:00 p.m.
Lamotrigine Effect on Depression and Anxiety in Patients With Epilepsy: A Preliminary Study Supported by GlaxoSmithKline
Tomasz Wolanczyk, M.D., Department of Child Psychiatry, Medical University of Warsaw, Marszałkowska 24, Warszawa PL 00-576, Poland; Damian Kaszuba, M.D., Adam Jozwik, Ph.D., Maciej Moskwa, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that lamotrigine in addition to its anticonvulsant effect, may be effective in alleviating depression and anxiety in patients with epilepsy.

Summary:

Objective: Depressive and anxiety symptoms are highly prevalent in patients with epilepsy (PWE). The anti-epileptic drug lamotrigine in addition to its anticonvulsant effect improves general well-being in PWE. This study was designed to assess its effectiveness in alleviating depression and anxiety in PWE.

Method: 731 patients ≥16 years of age were recruited to an open-label, 24-week study. The following assessment was performed at baseline, week 8, 12, and 24: medical history, seizure frequency, serious life events, current treatment, and mood evaluation (Beck Depression Inventory (BDI), Spielberger State and Trait Anxiety Inventory (STAI) and General Health Questionnaire (GHQ-28)). Lamotrigine was used in monotherapy or as add-on treatment.

Results: The preliminary data from 286 patients who attained Visit 3 (week 12) revealed significant reduction in seizure frequency. There was significant decrease in mean values of BDI (from 18.9 to 11.2), State Anxiety in STAI (from 16.4 to 13.0) and Trait Anxiety in STAI (from 26.5 to 21.1) between baseline and Visit 3. There was also significant decrease in all subscales of GHQ-28. There was no correlation between mood scores and epilepsy variables including seizure frequency.

Conclusion: This open-label study provides preliminary evidence that lamotrigine may have positive effect on mood and anxiety in PWE.

References:
NR235  Monday, May 19, 3:00 p.m.-5:00 p.m.

Olanzapine/Fluoxetine Combination and Quality of Life in Rapid-Cycling Bipolar Depression
Supported by Eli Lilly and Company

Lizheng Shi, Ph.D., Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46255; Carlos Vallarino, Ph.D., Madhav Namjoshi, Ph.D., Mauricio F. Tohen, M.D.

Educational Objectives:
At the conclusion of this presentation, the attendee should be able to recognize the effects of olanzapine/fluoxetine combination and olanzapine alone on patient-reported HRQoL outcomes in treating patients with bipolar depression (with rapid-cycling or non-rapid cycling feature).

Summary:
Objective: To examine effects of olanzapine (Olz) and olanzapine/fluoxetine combination (OFC) versus placebo (Pla) on health-related quality of life (HRQoL) in patients with rapid-cycling or non-rapid-cycling bipolar depression.

Methods: In an eight-week, double-blind, randomized study, 833 patients with bipolar depression (baseline MADRS total score >20) were randomized to olanzapine (5–20 mg/day, N=370), OFC (6/25, 6/50, or 12/50 mg/day, N=86), and placebo (N=377). Rapid-cycling histories were determined based on SCID. HRQoL outcomes (measured by the SF-36 and the QLDS) were analyzed in two subsets: 258 rapid cyclers (Olz; n=105; OFC; n=28; Pla; n=125) and 335 nonrapid cyclers (Olz; n=145; OFC; n=30; Pla; n=160).

Results: In OFC-Pla comparisons, OFC exhibited greater improvement in several SF-36 domains and QLDS total score (rapid cyclers: general health [p=0.006], mental health [p=0.015], social functioning [p=0.018], and QLDS-total [p=0.028]; nonrapid cyclers: bodily pain [p=0.004], general health [p=0.005], mental health [p=0.001], role-emotional [p<0.01], social functioning [p=0.008], vitality [p=0.007], and QLDS-total [p<0.001]). Similar results were found in OFC-Olz comparisons. Olanzapine was found to improve HRQoL better than placebo only in nonrapid cyclers.

Conclusion: OFC-treated subjects (both rapid cyclers and nonrapid cyclers) experienced greater HRQoL improvement than olanzapine- or placebo-treated subjects. Olanzapine alone effectively improved HRQoL in nonrapid cyclers.

References:

NR236  Monday, May 19, 3:00 p.m.-5:00 p.m.

Does Constant Therapy Infer Optimal Efficacy in Schizophrenia? Moving to an Advanced Pharmacotherapeutic Option
Supported by Janssen Pharmaceutica Products, L.P.

Ronald Urioste, Janssen Pharmaceutica Products, L.P., 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Cynthia Bossie, Ph.D., Robert A. Lasser, M.D., Georges Gharabawi, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the use of long-acting risperidone in patients with schizophrenia or schizoaffective disorder previously stable on conventional depot antipsychotics.

Summary:
Objective: To assess the efficacy and safety of long-acting risperidone in patients previously stable on conventional depot antipsychotics.

Method: Open-label study in 725 stable patients with schizophrenia or schizoaffective disorder. Patients were assigned to receive 25, 50, or 75 mg of long-acting injectable risperidone every two weeks for 50 weeks.

Results: Conventional depot antipsychotics had been received by 188 patients. After patients were switched to long-acting risperidone, mean Positive and Negative Syndrome Scale (PANSS) total scores improved significantly throughout the 50 weeks. Although patients were judged clinically stable at study entry, 51.5% demonstrated clinical improvement, defined as ≥20% PANSS total score reduction, and 15.6% had a ≥60% PANSS total score reduction. The Extrapyramidal Symptom Rating Scale subjective rating and physician rating of parkinsonism decreased significantly at each time point and at endpoint (P<.001). The most common adverse events were anxiety (28.7%), psychosis (19.2%), headache (18.1%), and insomnia (17.6%).

Conclusions: Stable patients previously receiving conventional depot antipsychotics showed significant symptom improvement and decreased severity of extrapyramidal symptoms when switched to long-acting risperidone. These results challenge the concept that constant treatment with conventional depot phecantarticdrugs provides optimal efficacy for schizophrenia and support the use of a long-acting atypical antipsychotic.

References:

NR237  Monday, May 19, 03:00 p.m.-05:00 p.m.

Clinical Predictors of Response to Maintenance Treatment in Bipolar I Disorder
Supported by GlaxoSmithKline

Terence A. Ketter, M.D., Department of Psychiatry, Stanford University School of Medicine, 401 Quarry Road, Room 2124, Stanford, CA 94305-5723; Charles L. Bowden, M.D., Joseph F. Calabrese, M.D., Joseph F. Goldberg, M.D., Patricia Suppes, M.D.

Educational Objectives:
At the conclusion of this session, the participant will be able to identify patient and clinical characteristics that may be predictive of response to maintenance therapy in bipolar I disorder.

Summary:
Objective: To examine predictors of response to maintenance treatment in bipolar I disorder.

Methods: 638 patients were randomized to 18 months of double-blind monotherapy with lamotrigine (n=280; 50–400mg/day fixed and flexible dose), lithium (n=167; 0.4–1.1mEq) or placebo (n=191). The effects of the total number of episodes and the number of manic or depressive episodes in the one and three years prior to treatment, early onset of illness, attempted suicide, time to
randomization, and gender were examined against time to inter-
vention for a mood episode using a Cox Proportional Hazard
Model. Analyses were controlled by index mood and treatment.

Results: Overall, <3 depressive episodes in the previous three
years, later onset of illness, shorter time to stabilization, and lack
of previous psychiatric hospitalization were predictive (p<0.05) of
treatment response. Lithium response was associated with a late
onset of illness (> age 20 years), lamotrigine response was associ-
ated with <3 depressive episodes in the previous three years,
and placebo response was associated with <3 manic episodes in
the previous three years.

Conclusion: Response to maintenance treatment in bipolar I
order appears related to severity of illness; response differs by
treatment. These results may facilitate clinical decision-making in
bipolar disorder.

References:
1. AC Swann, CL Bowden, JR Calabrese, SC Dilisaver, DD Morris:
Pattern of response to divalproex, lithium, or placebo in four
naturalistic subtypes of mania. Neuropsychopharmacol 2002;
26:530–536.
2. GV Obrocea, RM Dunn, MA Frye, TA Ketter, DA Luckenbaugh,
GS Leverich, AM Speer, EA Osuch, K Jajodia, RM Post: Cli-
cal predictors of response to lamotrigine and gabapentin mo-
notherapy in refractory affective disorders. Biol Psychiatry

NR238
Monday, May 19, 03:00 p.m.-05:00 p.m.
Adjuvant Ziprasidone in Treatment-Resistant
Depression: A Pilot Study
Supported by Pfizer Inc.

David L. Dunner, M.D., Department of Psychiatry, University of
Washington, 4225 Roosevelt Way NE, 306C, Seattle, WA
98105-6099; Jay D. Amsterdam, M.D., Richard C. Shelton,
M.D., Howard A. Hassman, D.O., Murray Rosenthal, D.O.,
Steven J. Romano, M.D.

Educational Objectives:
At the conclusion of this session, participants will be able to
discuss the findings of this pilot study showing efficacy of the
antipsychotic agent ziprasidone when used adjuvantly with
sertraline in patients with treatment-resistant depression without
psychotic features.

Summary:
Objective: To evaluate the efficacy of ziprasidone as adjunctive
therapy in treatment-resistant depression without psychotic
features.

Methods: Patients had a history of failure to respond to at least
four weeks’ adequate antidepressant therapy with ≥1 non-SSRI
or an SSRI only. After a one-week screening period, 64 patients
entered a six-week open-trial of sertraline 100-200 mg/day. Nonre-
spenders (<30 percent improvement on MADRS, CGI-S score ≥4,
and meeting of DSM-IV major depression criteria) were random-
ized to eight weeks of open treatment with sertraline monotherapy
(n=20) or combination therapy with ziprasidone 40 mg or 80 mg
BID (n=40).

Results: At endpoint, patients with a history of non-SSRI treat-
ment resistance who received combination therapy (n=26) demon-
strated significantly greater improvement versus those patients
who received monotherapy (n=13) in MADRS, the primary efficacy
variable (P<.05), and in HAM-D 17 (P<.05), CGI-S (P<.01), and
CGI-I (P=.05). Among patients with a history of SSRI resistance
only, improvement with combination therapy (n=14) did not reach
significance versus sertraline monotherapy (n=7). No specific
safety concerns were observed with combination therapy.

Conclusions: In patients with major depression and a history of
non-SSRI treatment failure, combination therapy with ziprasidone
and sertraline demonstrated greater efficacy than sertraline mo-
notherapy.

References:
1. Thase ME, Rush AJ. Treatment-resistant depression. In Bloom
FE, Dupfler DJ, eds. Psychopharmacology: the Fourth Genera-
2. Shelton RC, Tolleson GD, Tohen M, Stahl S, Gannon KS,
Jacobs TG, Buras WR, Bymaster FP, Zhang W, Spencer KA,
Feldman PD, Meitzer HY: A novel augmentation strategy for
treating resistant major depression. Am J Psychiatry 2001;
158:131–134.

NR239 Monday, May 19, 03:00 p.m.-05:00 p.m.
Olanzapine-Induced Reduction in Frontal Lobe
Lactate in FE Psychosis
Supported by Eli Lilly and Company

Perry F. Renshaw, M.D., Brain Imaging, McLean Hospital, 115
Mill Street, Belmont, MA 02178; Deborah Yurgelun-Todd,
Ph.D., Hank Wei, Ph.D., Cecil Charles, Ph.D., Gary D.
Tollefson, M.D., Jeffrey A. Lieberman, M.D.

Educational Objectives:
At the conclusion of this session, participants will be able to
discuss differences associated with olanzapine and haloperidol
treatment on brain lactate levels and resulting correlations with
improved clinical status, in patients with first-episode psychosis.

Summary:
Lactate is a neurochemical marker that increases with mitochon-
drial dysfunction and can be detected using proton magnetic reso-
nance spectroscopy (1H-MRS). Subjects with first-episode psy-
chosis (N=263) were randomized in a multisite, double-blind trial
to olanzapine or haloperidol. Single voxel, 6 cm3, 1H-MR spectra
of left frontal lobe (FC), basal ganglia (BG), and hippocampal (HC)
regions were acquired before and following 12 weeks of treatment
(n=156). An acceptable fit of the lactate resonance was obtained
for 81 subjects. After 12 weeks, mean lactate reductions in FC,
BG, and HC were 12%, 18%, and 13% for the olanzapine cohort;
1%, 3%, and 8% for haloperidol (n.s.d.).

Reductions in FC lactate were strongly correlated with reduc-
tions in PANSs (r=0.347, p=0.0011) and BPRS scores (r=0.344,
p=0.0017) for the entire subject population, and the olanzapine
cohort (r=0.441, p=0.0353 and r=0.367, p=0.017, respectively; N=
42). These correlations were weaker in the haloperidol cohort (r=
0.225, p=0.17 and r=0.326, p=0.043, respectively; N=39).

Reductions in FC lactate during olanzapine treatment appear
associated with resolution of psychotic symptoms. This relation-
ship is numerically weaker with haloperidol, which has been asso-
ciated with inhibition of mitochondrial complex 1. Strategies to
reduce brain lactate levels may present novel therapeutic opportu-
nities for schizophrenia treatment.

References:
1. Maurer I, Zierz S, Moller H: Evidence for a mitochondrial oxida-
tive phosphorylation defect in brains from patients with schizo-
2. Magistretti PJ, Pellerin L: Cellular mechanisms of brain energy
metabolism and their relevance to functional brain imaging.
NR240  Monday, May 19, 3:00 p.m.-5:00 p.m.
Gingko Biloba Has No Effect on Cytochrome P-450 2D6 and Marginal Effects on 3A4 Activity in Normal Volunteers Supported by Novartis Pharmaceuticals Corporation
John S. Markowitz, Pharm.D., Department of Pharmaceutics, Novartis, 67 President Street, Room 246N, Charleston, SC 29425; Jennifer L. Donovan, Ph.D., C. Lindsay DeVane, Ph.D., Laura Sipkes, B.S., Kenneth D. Chavin, M.D.

Educational Objectives:
- At the conclusion of this presentation, the participant should be able to understand the apparent lack of significant risk of botanical-drug interactions of gingko biloba with medications metabolized by CYP 2D6 and/or CYP 3A4.

Summary:
- **Background:** Gingko biloba (GB) extracts are purported to exert positive neurocognitive effects and may also be used in the treatment of a variety of vascular and other disorders.
- **Objectives:** This study was to assess, in normal volunteers (n=12), the influence of standardized GB (EGb 761) on the activity of CYP 2D6 and 3A4 enzymes.
- **Methods:** Probe substrates dextromethorphan (CYP2D6) and alprazolam (CYP3A4) were administered at baseline, and following treatment with GB for 14 days. Urinary concentrations of dextromethorphan and dextrorphan were quantified and dextromethorphan metabolic ratios (DMRs) were calculated. ALPZ plasma samples were also collected for pharmacokinetic analysis at baseline and after GB.
- **Results:** No statistically significant differences were found between pre- and post-GB treatment DMRs indicating a lack of effect on CYP 2D6. For ALPZ a small but significant decrease in the area under the plasma concentration versus time curve (AUC); was observed (P<0.05). When a sex-specific analysis was done, male subjects demonstrated a significant reduction in maximum plasma concentrations (p<0.05) and in the AUC: (P<0.01) suggesting a slight inductive effect of GB on CYP3A4.
- **Conclusions:** Standardized GB at recommended doses, is unlikely to significantly alter the disposition of drugs primarily dependent on the CYP2D6 or CYP3A4 pathways for elimination.

References:

NR241  Monday, May 19, 3:00 p.m.-5:00 p.m.
Patterns of Family Relationships in Pediatric Psychiatric Disorders
Anthony J. Giuliani, Ph.D., Department of Child Outpatients, McLean Hospital, 115 Mill Street, East House, Belmont, MA 02478-9106; Vamsi K. Koneru, B.A., Jean A. Frazier, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to recognize that inclusion of a measure of family functioning in diagnostic interviews will help to identify those families at greatest risk for ongoing difficulties. Family socioenvironmental factors likely influence the specific course and characteristics of a childhood mental illness and the results that can be achieved with pharmacological and psychosocial treatments.

Summary:
- **Objective:** The prevalence of global sexual dysfunction among patients treated with antidepressants ranges from 22% to 43% depending on specific medication. This study examines sexual dysfunction among patients who do not exhibit global dysfunction.
- **Methods:** 6,297 adult outpatients (72% women) receiving antidepressant monotherapy were consecutively recruited from 1,101 primary care clinics. Global and subscale sexual dysfunction scores were obtained using the Changes in Sexual Functioning Questionnaire (CSFQ). The five subscales of the CSFQ assess sexual dysfunction in three phases of the sexual response cycle (desire, arousal, orgasm), and sexual pleasure.
- **Results:** Among the 3,916 patients who did not meet CSFQ criteria for global sexual dysfunction, defined as total CSFQ score...
below threshold, 94.8% of women and 96.9% of men exhibited impairment on at least one subscale. Males were more likely than females to experience dysfunction in the desire phase (89% vs. 77%; $\chi^2=72.9, df=1, p<.001$), and orgasmic dysfunction (83% vs. 43%; $\chi^2=514.9, df=1, p<.001$), while females were more likely to experience dysfunction in the arousal phase (82% vs. 70%; $\chi^2=64.3, df=1, p<.001$). Fluoxetine was the medication most likely to be associated with sexual dysfunction in all three phases of the response cycle ($\chi^2=23.9-43.7, df=8, p<.001$). Bupropion SR and IR were least likely to cause sexual dysfunction with no sub-threshold scores on any subscale at 9% and 15% respectively.

**Conclusions:** Among patients who do not experience clinically significant global sexual dysfunction on antidepressant monotherapy, dysfunction in at least one phase of the sexual response cycle and/or sexual pleasure may reduce sexual health-related quality of life.

**References:**


**NR244**

**Monday, May 19, 3:00 p.m.-5:00 p.m.**

**Which Drug for Which Patient? The Fluoxetine Bupropion Assessment Scale**

Dwight S. Bell, M.D., 150 North Santa Anita Avenue, Suite 300, Arcadia, CA 91006-3113; Mark Shipman, M.D., Angela M. Reiersen, Maria Castelli, N.P., Jill Siegelman, M.F.T., Mario Cleves, Ph.D.

**Summary:**

**Objective:** The authors believe that a certain premorbid personality type-hard driving, achievement oriented, often exercise-oriented individuals-correlates with bupropion response; conversely, patients without these premorbid traits and whose depression is marked by mood swings, irritability, and rumination are likely fluoxetine responders.

The authors developed a 10-question, self-administered rating scale (FBAS) to assess these traits, and hypothesized its use would improve outcomes.

**Methods:** An MFT and an RN/NP reviewed 72 charts from one psychiatrist’s office for two time periods: before (#33) and after (#39) the psychiatrist utilized the questionnaire to guide antidepressant selection.

Raters were blinded to the theory and to the time period when treatment was rendered. Utilizing Clinical Global Impressions scale measurements, charts were reviewed on patients with BDI $\geq$17, not on either drug at time of intake, and who were prescribed fluoxetine or bupropion.

**Results:** The data were in the direction of better results in the FBAS-guided group, particularly after adjusting for age, gender and marital status differences (efficacy $p=0.087$) and when global improvement was grouped (1–2, 3–4, 5–7), $p=0.047$. At p=0.009 level, one particular fluoxetine-oriented question (interpersonal needs not being met) seemed particularly associated with global improvement.

**Conclusion:** A larger, randomized study appears indicated.

**NR245**

**Monday, May 19, 3:00 p.m.-5:00 p.m.**

**Topiramate Experience in a Psychiatric Clinic Weight Management Program**

Renu Kotwal, M.D., 13 Burning Tree Lane, Butte, MT 59701; Susan L. McElroy, M.D., Shishuka Malhotra, M.D., Karen King, R.N., Anna Guerdjikova, B.A., Shu-Chen Wu, Ph.D., Katie Harding, B.S., Julie Capece, B.A., Norman R. Rosenthal, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to review the long-term efficacy and safety of topiramate for weight management at a psychiatric clinic.
Objective: Assess long-term effectiveness of topiramate (TPM) in a psychiatric weight management program.

Methods: Naturalistic review of all patients seen for weight management between 2000 and 2002 who were assessed by structured clinical interview for eating and/or mood disorders and treated with TPM as primary/adjunctive therapy. Topiramate was titrated by 25 mg/wk to median daily dose of 200 mg. Efficacy was assessed by mean weekly binge episodes, CGI-Severity, and weight/BMI.

Results: A total of 148 patients (100% BED ± mood disorders; 56% adjunctive TPM therapy), mean age 45 ± 10 years and mean baseline weight/BMI 110 ± 28 kg and 40 kg/m², were followed for a median treatment duration of 110 days (range 1-688). Patients on topiramate experienced significant reductions in mean weekly binge frequency to 1.2 binges/week, a 49% change from baseline. Shift analysis of CGI-Severity showed 37% of patients at final visit improved to a normal or borderline-normal rating compared to 0.7% at baseline. Patients lost an average of 4.7 kg and BMI decreased 1.7 kg/m². Correlations with associated mood disorders will be shown. Most common adverse events included paresthesia, fatigue, dry mouth, and taste perversion.

Conclusions: Topiramate appeared effective for outpatient weight management in patients with obesity associated with eating/mood disorders.

References:

NR246 Monday, May 19, 3:00 p.m.–5:00 p.m.
Oxcarbazepine Efficacy and Safety in Bipolar Disorder: Review of 249 Patients
Supported by Novartis Pharmaceuticals Corporation

Daniel A. Deutschman, M.D., Department of Psychiatry, Case Western Reserve University, 18051 Jefferson Park Road, Cleveland, OH 44130; Douglas H. Deutschman, Ph.D., John S. Chalekian, M.S.

Educational Objectives:
- At the conclusion of this session, the participant should understand the possible role for oxcarbazepine in the treatment of bipolar disorder. Weigh the risk benefit ratio for this agent in children, adolescents and adults in regards symptom reduction, organ damage, weight gain, common adverse events, causes of discontinuation and patient acceptance/adherence.

Summary:
Recent data in the literature suggest that oxcarbazepine may be an effective mood stabilizer with little risk of organ damage or weight gain.

We report on a retrospective review of 249 patients with bipolar disorder I, II or NOS treated in an open-label, naturalistic design with oxcarbazepine during a 22-month period. Age range was five to 85. Two-thirds were female; 98% were Caucasian. Dose range was 300mg/d to 2,400mg/d. Duration of treatment ranged from 42 to 484 days (m=137). Symptom severity was tracked on a five-point Likert scale. Symptom severity for each patient’s first visit was compared with his last visit (LOCF).

The three most common symptoms were irritability, mood swings, and hypomania. Symptom severity dropped from 3.48, 3.35 and 2.99 on first visit to 2.78, 2.77 and 2.39 on the last, respectively. The decrease was significant for all three symptoms (p<0.001).

No evidence of organ damage or weight gain was seen. Patient acceptance was high. Nausea and drowsiness were the most frequent side effects.

We will discuss patient selection, comorbidities, concurrent medications, and other confounds. The data suggest a possible role for oxcarbazepine in the treatment of bipolar disorder. Additional placebo-controlled studies are warranted.

References:

NR247 Monday, May 19, 3:00 p.m.–5:00 p.m.
Olanzapine Versus Risperidone for Treatment of Negative Symptoms in Schizophrenia
Supported by Eli Lilly and Company

Saeeduddin Ahmed, M.D., Lilly Research, Eli Lilly & Company, Lilly Corporate Center, DC 4133, Indianapolis, IN 46285; Fan Zhang, Ph.D., Daniel Walker, Ph.D., Leigh Beglinger, Ph.D., Willie R. Earley, M.D., Pierre V. Tran, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to describe the structure of the SANS scale and how it can be used to compare the effectiveness of antipsychotics for treating the negative symptoms of schizophrenia.

Summary:
Objective: To compare the effectiveness of olanzapine and risperidone in treating negative symptoms in schizophrenia using the Scale for the Assessment of Negative Symptoms (SANS).

Methods: This was a double-blind, 28-week, prospective study of olanzapine (N=172) versus risperidone (N=167) among schizophrenia-spectrum-disorder patients (DSM-IV). SANS (administered at baseline and Weeks 8 and 28) was used to assess Composite and Global scores and evaluate symptoms in the dimensions of affective flattening/blunting, alogia, avolition/apathy, anhedonia/asociability, and attention. The results were analyzed using a repeated-measures analysis of covariance, adjusting for baseline score and anticholinergic use.

Results: Patient demographics and SANS baseline scores were comparable in the two treatment groups. Olanzapine was superior to risperidone on the SANS Composite and Global scores, and on the affective flattening/blunting dimension score at eight and 28 weeks (p<.05). Olanzapine was superior to risperidone on alogia, avolition/apathy, and attention dimension scores at 28 weeks (p<.05). Risperidone was not superior to olanzapine on any dimension score at eight or 28 weeks.

Conclusions: Olanzapine was superior in treating negative symptoms, globally and across 4 of the 5 dimensions. Adequate treatment of negative symptoms helps promote greater social engagement and improves functional outcome.

References:
Ziprasidone Augmentation for Major Depressive Disorder Refractory to SSRIs
Supported by Pfizer Inc.

George I. Papakostas, M.D., Department of Psychiatry, Massachusetts General Hospital, WACC 812, 15 Parkman Street, Boston, MA 02114; Timothy J. Petersen, Ph.D., John W. Worthington III, M.D., Jessica L. Murakami, B.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Maurizio Fava, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the potential role of the atypical antipsychotic agent ziprasidone when used in conjunction with selective serotonin reuptake inhibitors in the treatment of major depressive disorder.

Summary:
Background: Due to their favorable side-effect profile, atypical antipsychotic agents offer important therapeutic advantages in mood disorders. Ziprasidone, due to its unique receptor-affinity profile, may be particularly useful when used in conjunction with standard antidepressants in the treatment of refractory depression. The purpose of this study is to test this hypothesis in depressed patients who had not responded to an adequate trial of selective serotonin reuptake inhibitors (SSRIs).

Methods: Eighteen patients with major depressive disorder (MDD), who had failed to experience a clinical response to an adequate trial of an SSRI were treated with open-label ziprasidone in addition to their SSRI for six weeks. Clinical response was defined as a 50% or greater decrease in depressive symptoms as measures by the 17-item Hamilton Depression rating Scale (HAM-D-17) during the course of the trial (baseline-endpoint).

Results: An intent-to-treat (ITT) analysis resulted in nine (50.0%) patients classified as responders, five (27.8%) as partial responders, and four (22.2%) as nonresponders. The overall proportion of remitters was 5/18 (27.8%).

Conclusions: These results suggest a possible antidepressant role for ziprasidone when used in conjunction with SSRI in refractory MDD.

References:

Treatment of Adults With ADHD Using OROS MPH: A Double-Blind, Placebo-Controlled Study Supported by McNeil Consumer & Specialty Pharmaceuticals
Kenneth W. Steinhoff, M.D., Psychiatry Department, UCI College of Medicine, Building 3, Route 88, 101 City Drive, Orange, CA 92868-3298

Educational Objectives:
At the conclusion of this session, the participant should recognize that once-daily OROS® MPH is an effective and safe treatment option for adults with ADHD, and establish parameters for appropriate dosing in this understudied population.

Summary:
Objective: To evaluate the efficacy, safety, and effective dosing of OROS® MPH administered once daily as compared with placebo in adults with ADHD.

Methods: Thirty adults (18 to 55 years) who met DSM-IV criteria for ADHD were enrolled in this single-center study. Subjects entered a modified rapid titration phase of up to four weeks (36 mg OROS® MPH followed by 18 mg increments; minimum 18 mg, maximum 108 mg). Optimal OROS® MPH treatment dose was defined as the most effective dose (CGI-1) giving: (1) at least 30% reduction in symptoms from baseline on the ADHD Rating Scale (ADHD RS), (2) least side effects. Subjects then entered a four-week, cross-over, within-subjects, two-week, placebo vs. two-week best-dose phase. The primary efficacy endpoint was mean reduction in symptoms from baseline on the ADHD RS. Secondary efficacy analyses included measures of impairment change such as Quality of Life Enjoyment and Satisfaction Questionnaire and Global Assessment of Functioning. Safety and side effects were actively queried and monitored via the Barkley Behavior and Adverse Events Questionnaire-Modified.

Results: Preliminary results suggest that OROS® MPH is effective and safe for treatment of adults with ADHD. Results also provide guidance to clinicians on effective dosing of OROS® MPH in the adult population.

Conclusion: OROS® MPH is an effective and safe treatment option for adults with ADHD and as such, offers a further treatment option for this patient population.

References:
cordance, a measure that has moderately strong associations with cerebral perfusion. Cordance decreased significantly in the right frontotemporal (p=.006) and left parietal regions (p=.034) after 48 hours of treatment in medicated subjects. Decreases were similar to those seen in depressed subjects treated with venlafaxine or fluoxetine. Logistic regression accurately identified treatment condition in 74.2% of normals after 48 hours (two doses).

Conclusions: Results indicate that cordance can detect antidepressant physiologic effects in normal or depressed subjects. It may be possible to utilize cordance to screen putative antidepressant compounds.

Funding: Supported in part by Lilly Research Laboratories and Wyeth-Ayerst Pharmaceuticals.

References:

NR251 Monday, May 19, 3:00 p.m.-5:00 p.m.
Long-Term Treatment of Generalized SAD With Venlafaxine Extended Release Supported by Wyeth Research
Murray B. Stein, M.D., Department of Psychiatry, University of California at San Diego, 8950 Villa La Jolla Drive, Suite 2243, La Jolla, CA 92037; Mark H. Pollack, M.D., Richard Mangano, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss the need for effective long-term treatment options for SAD; discuss the use of venlafaxine XR for long-term treatment of SAD.

Summary:
Objective: To evaluate the efficacy, safety, and tolerability of venlafaxine extended release (XR) in long-term treatment of generalized social anxiety disorder (SAD) in this double-blind, placebo-controlled study.

Methods: Three hundred ninety-five (395) adult outpatients at 19 clinical centers were randomly assigned to receive one of two doses of venlafaxine XR (a fixed dose of 75 mg/day or a flexible dose of 150 to 225 mg/day) or placebo for up to 28 weeks. Efficacy assessments included the Liebowitz Social Anxiety Scale (LSAS) total score (primary), and the Clinical Global Impressions Improvement and Severity scales (CGI-I, CGI-S), Social Phobia Inventory (SPIN), and responder status (CGI score ≤2).

Results: Venlafaxine XR-treated patients demonstrated significantly greater improvement than placebo-treated patients on the CGI-I (weeks 2 through 28) and on the LSAS, CGI-S, and SPIN (weeks 4 through 28; P<0.05). A significantly greater proportion of patients in the venlafaxine XR group than in the placebo group were responders at weeks 4 through 28 (58% vs 33%; R<0.001 at week 28). Venlafaxine treatment was generally well tolerated; adverse events included headache, nausea, nervousness, and somnolence.

Conclusions: These results demonstrate the efficacy and safety of venlafaxine XR in the long-term treatment of generalized SAD.

References:

NR252 Monday, May 19, 3:00 p.m.-5:00 p.m.
Relationship Between Atypical Antipsychotic, Poly Pharmacy, and Concomitant Medication
Douglas Del Paggio, Pharm.D., Office of the Medical Director, Alameda CO BHCS, 2000 Embarcadero Cove, Suite 400, Oakland, CA 94606; Richard P. Singer, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to contrast newer antipsychotic prescribing in regards to dose, polypharmacy and concomitant medication in a large multi-center County mental health system.

Summary:
Methods: In this naturalistic study, data from 750 chronically mentally ill patients treated within a network of 23 County mental health outpatient clinics from 1/1/02-12/31/02 were retrospectively reviewed. Atypical antipsychotic prescribing was analyzed in regards to mean dose, additional anti-psychotic agent, concomitant antidepressant/mood stabilizer and antidysonetic agent.

Results: Over 66% of patients had a diagnosis of a major thought disorder. 26 patients received clozapine, 326 olanzapine, 150 quetiapine, 234 risperidone and 14 ziprasidone. Mean dose: clozapine 445mg, olanzapine 13.8mg,quetiapine 440mg, risperidone 3.2mg, and ziprasidone 90mg. Of these patients, 9% received two or more antipsychotics. While 47% of patients on both quetiapine and risperidone received an additional antidepressant, only 36% of the patients on olanzapine did. In regards to a mood stabilizer, a comparable percentage of each group were prescribed (24–27%) such an agent. Almost 80% of patients receiving risperidone required an antidysonetic agent and had documented adverse effects.

Conclusion: While the mean dose of both olanzapine and risperidone declined, the dose for quetiapine increased over the 12 month study period. Fewer patients receiving olanzapine required an antidepressant. Most patients receiving risperidone also required an antidysonetic agent due to documented EPS.

References:

NR253 Monday, May 19, 3:00 p.m.-5:00 p.m.
Siberian Ginseng (Eleutherococcus Senticosus) Effects on CYP2D6 and CYP3A4 Activity in Normal Volunteers
Jennifer L. Donovan, Ph.D., Department of Psychiatry, Medical University of South Carolina, 67 President Street, Suite 246 North, Charleston, SC 29425; C. Lindsay DeVane, Ph.D., Kenneth D. Chavin, M.D., Robin M. Taylor, B.S., John S. Markowitz, Pharm.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the apparent lack of significant risk of botanical-drug interactions of Siberian ginseng with medications metabolized by CYP 2D6 and/or CYP 3A4.
Summary:

**Background:** Siberian ginseng ([SG]; Eleutherococcus senticosus) is a commonly used herbal preparation with purported “adaptogenic” or anti-stress activity.

**Objectives:** This study assessed in normal volunteers (n=12) the influence of SG on the activity of CYP 2D6 and 3A4.

**Methods:** Probe substrates dextromethorphan (CYP2D6) and alprazolam ([ALPZ], CYP3A4) were co-administered orally at baseline, and again following herbal treatment for 14 days. Urinary concentrations of dextromethorphan and dextrorphan were quantified and dextromethorphan metabolic ratios (DMRs) were determined pre- and post-herbal treatment. Plasma samples were also collected for ALPZ pharmacokinetics pre- and post-herbal treatment.

**Results:** There were no statistically significant differences between pre- and post-SG treatment DMRs or in any ALPZ pharmacokinetic parameter measured.

**Conclusion:** These results indicate that SG at generally recommended doses, is unlikely to interact with medications primarily dependent on the CYP2D6 or CYP3A4 pathways for elimination.

**References:**

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to have a better understanding and compare the long term risk of tardive dyskinesia induced by olanzapine and typical antipsychotics.

**Summary:**

**Objectives:** To assess the risk of tardive dyskinesia among patients with schizophrenia and related disorders undergoing treatment with olanzapine or conventional antipsychotics.

**Method:** This was an open-label, pragmatic, controlled randomized trial that was conducted in three psychiatric hospitals in Brazil. Patients were admitted with a DSM-IV diagnosis of schizophrenia or related disorders with a BPRS score >24, and were randomly assigned to either olanzapine or conventional antipsychotic treatment. After hospital discharge, patients were evaluated using the Positive and Negative Syndrome Scale (PANSS), Clinical Global Impressions Scale (CGI), and Abnormal Involuntary Movement Scale (AIMS), and were then observed for 9 months in a naturalistic setting.

**Results:** The sample comprised 190 patients, with a completion rate of 88.2% for olanzapine-treated patients and 84.9% for patients treated with conventional antipsychotics (p=0.385). The mean differences on the PANSS were in favor of olanzapine. The risk of presenting tardive dyskinesia among patients treated with conventional antipsychotics was 4.1 times higher than that among olanzapine-treated patients (RR=4.1; 95% CI: 1.1–14.9, p<0.002).

**Conclusions:** The results of this open-label, pragmatic, controlled randomized trial showed that olanzapine had a favorable impact on negative symptoms, decreased general psychopathology, and reduced the risk of tardive dyskinesia.

**References:**
therapy in acute bipolar depression and mania, prevention of recurrence and long term maintenance.

Summary:

Olanzapine as monotherapy or add-on therapy has been effective in the treatment of bipolar mood disorder. Long term studies with atypical antipsychotics in treatment of bipolar disorder are limited and beyond one-year duration are scarce. Thirty-seven bipolar I and II patients received open-label, add-on treatment with olanzapine. Thirty-one were depressed and six were hypomanic. Twenty-one females, 16 males with an average age of 45.2, present duration of symptoms 7.9 weeks, mean duration of illness 13.6 years, HAM-D for depression with mean score 21.3, YMRS for mania with mean score 14.3. Patients assessed and followed up to five years. Thirty-three remained in the study until final evaluation. All maintained their stability and have scores less than six HAM-D. Fifteen patients were noncompliant during earlier stage of their treatment but compliance improved over time. Hospitalization days evaluated five years before addition of olanzapine were 43.5 days and post-treatment were 7.2 days for patients due to noncompliance leading to recurrence of their symptoms. All patients received mood stabilizers. Twenty-one patients received antidepressants. Results suggest that olanzapine in combination with existing treatment is effective in treating depression and mania in bipolar disorder. Improvement is sustained and treatment well tolerated over a five-year period.

References:


NR258 Monday, May 19, 3:00 p.m.-5:00 p.m.

Tiagabine as Augmentation Therapy for Anxiety Supported by Cephalon, Inc.

Thomas L. Schwartz, M.D., Department of Psychiatry, SUNY Upstate, 713 Harrison Street, Syracuse, NY 13210; Nouman Azhar, M.D., Juhi Husain, M.D., Nikhil D. Nihalani, M.D., Mihai Simionescu, M.D., Douglas Coovert, M.D., Shefali Jindal, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize the therapeutic potential of tiagabine for the treatment of anxiety.

Summary:

Objective: Gamma-aminobutyric acid (GABA), the main CNS inhibitory neurotransmitter, plays a key role in anxiety and sleep. Tiagabine, a selective GABA reuptake inhibitor (SGRI), enhances normal GABA tone and has been shown to reduce anxiety and improve sleep. This study examined tiagabine as augmentation therapy for anxiety.

Method: This eight-week, open-label study was designed to evaluate 20 patients with anxiety who were stable on current medications (70% taking SSRI s) and still symptomatic. Tiagabine (bid, AM/PM) was initiated at 4 mg/day for days 1–2, increased to 8 mg/day on day 3, and then adjusted for optimum response in 2 mg/3 days (maximum dose 20 mg/day). Assessments included the Hamilton Rating Scale for Anxiety (HAM-A) and Pittsburgh Sleep Quality Index (PSQI).

Results: Fourteen patients entered the study and enrollment is ongoing. Tiagabine significantly improved anxiety (HAM-A±SEM: baseline, 17.6±1.4; endpoint, 8.1±1.6; P<0.0001). Fifty percent of patients receiving tiagabine achieved remission (HAM-A<7). Tiagabine also significantly improved sleep quality (PSQI: baseline, 9.8±1.3; endpoint, 5.5±1.0; P<0.01). Mean tiagabine dose was 12 mg/day (bid) (range: 4–20 mg/day). The most commonly reported adverse events were dizziness (n=3) and insomnia and somnolence (both n=2).

Conclusion: The SGRI tiagabine may be effective augmentation therapy in patients with anxiety who are not adequately treated with current medications.

References:


NR257 Monday, May 19, 3:00 p.m.-5:00 p.m.

Rivastigmine and Galantamine in Neurocognitive Deficits in Bipolar Mood Disorder

Mohammad Z. Hussain, M.D., Prince Albert Health District, Mental Health Centre, 2727 2nd Avenue West, Prince Albert, SK S6V 5E5, Canada; Zubaida A. Chaudhry, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize neurocognitive deficits in bipolar mood disorder and their management with rivastigmine and galantamine and its impact on quality of life and functional recovery.

Summary:

The novel anticonvulsant mood stabilizers, novel neuroleptics, and array of antidepressants have improved the symptomatic recovery for majority of bipolar mood disorder patients but there still remain a considerable number with neurocognitive deficits leading to deficits in social and vocational functioning. The cholinergic hypothesis of Alzheimer’s disease proposes that cognitive deterioration is related to deficits in central cholinergic function and amelioration of the cholinergic deficits leads to improvement. Acetylcholinesterase inhibitors should produce similar improvement in neurocognitive deficits of bipolar mood disorder by improving central cholinergic functioning. Twenty-four patients suffering from bipolar mood disorder with neurocognitive deficits were treated twelve with rivastigmine 3 mg daily and twelve with galantamine 6 mg daily for three months. Fifteen females, nine males, mean age 44.3, mean duration of illness 18.7 years. Nine patients on rivastigmine and eight on Galantamine showed significant improvement in their cognitive functions measured on different neurocognitive tests and have shown improvement in attention, memory, problem-solving, with improved social and vocational functioning. Three showed minimal improvement and four dropped out due to side effects. Acetylcholinesterase inhibitors have beneficial effect on neurocognitive deficits related to bipolar mood disorder.

References:


NR259 Monday, May 19, 3:00 p.m.-5:00 p.m.  
Risperidone Versus Haloperidol in Adult Psychiatric Emergencies  
Supported by Janssen Pharmaceutica Products, L.P.  
Aysegul Yildiz, M.D., Department of Psychiatry, Dokuz Eylul Medical School, Izmir, Turkey, Atilla Turgay, M.D., Manekse Alpay, M.D., Gary S. Sachs, M.D.  

Educational Objectives:  
At the conclusion of this session, the participant should be able to describe the use of antipsychotics in the treatment of agitation and aggression in a variety of adult psychiatric disorders.  

Summary:  
Objective: To provide preliminary data on the effectiveness of risperidone in tablet form in the emergency treatment of agitation.  
Method: Eighteen acutely agitated psychiatric patients who were given either haloperidol (2–5 mg intramuscular-i.m.) or risperidone (1–2 mg tablet) were evaluated hourly using the four different agitation rating scales for two hours. Concomitant use of lorazepam was allowed at the discretion of the acute psychiatry service (APS) physician for both study groups.  
Results: Baseline agitation scores of both groups were comparable. Eighty percent of patients in the haloperidol group in comparison to 12.5% of patients in the risperidone group required the concomitant use of lorazepam during the two hours of study period. Both haloperidol and risperidone were effective in decreasing agitation/aggression in the study population. None of the rating instruments revealed significant differences between haloperidol or risperidone in the control of acute agitation/aggression.  
Conclusions: This pilot study provides preliminary data suggesting that atypical antipsychotics in tablet formulations may be effective in decreasing agitation in emergency settings, as the risperidone group also required significantly less sedation with lorazepam. Further investigations of the use of oral formulations, including the tablet forms, of atypical antipsychotics in the emergency treatment of agitation are warranted.  

References:  

NR260 Monday, May 19, 3:00 p.m.-5:00 p.m.  
Studies on Agitation Management in Adult Psychiatric Emergencies  
Aysegul Yildiz, M.D., Department of Psychiatry, Dokuz Eylul Medical School, Izmir, Turkey, Gary S. Sachs, M.D., Atilla Turgay, M.D.  

Educational Objectives:  
At the conclusion of this session, the participant should be able to describe the comparative effectiveness of typical and atypical antipsychotic use in combination with anti-anxiety medications in psychiatric emergencies presenting with agitation.  

Summary:  
Objective: To provide a systematic analysis of the published studies comparing classical antipsychotics, benzodiazepines, and/or combination of both and the use of atypical antipsychotic medications in controlling agitation and aggressive behavior seen in psychiatric patients in emergency.  
Method: Studies comparing antipsychotics, benzodiazepines, and combination of both and the efficacy trials of atypical antipsychotics, which include an active and/or inactive comparator for the treatment of acute agitation, were identified and reviewed.  
Results: In antipsychotic-benzodiazepine comparisons, 11 trials met the inclusion criteria (N=701). The combination treatment was superior to either agent alone with higher improvement rates and lower incidence of extrapyramidal side effects. In the atypical antipsychotic agents review in agitation treatment, five studies were identified (out of 711 subjects 104 on placebo). Atypical antipsychotics were found to be as effective as typical ones and more advantageous in many aspects.  
Conclusion: Atypical antipsychotics such as risperidone, zypical, and olanzapine with or without benzodiazepines should be considered the primary treatment for acute agitation.  

References:  

NR261 Monday, May 19, 3:00 p.m.-5:00 p.m.  
Survey of Clinician Prescribing Practices in the Treatment of Psychotic Major Depression  
John D. Matthews, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114; Timothy J. Petersen, Ph.D., Christina M. Dording, M.D., Rebecca A. Kornbluh, M.D., Julie L. Ryan, B.A., Mark Bilas, M.D., Maurizio Fava, M.D.  

Educational Objectives:  
At the conclusion of this session, the participant should be able to increase the understanding of clinician prescribing practices in the treatment of psychotic major depression (PMD).  

Summary:  
Background and Significance: Several studies have demonstrated that the course of PMD is more severe than nonpsychotic major depression. Inadequate pharmacological treatment may be a contributing factor to these findings. For example, Mulsant et al. (1997) found that only 4% (2/53) of patients with PMD, referred for ECT, received adequate medication trials; 47% (25/53) PMD patients received either no antipsychotic medication or antipsychotic treatment lasted for less than three weeks.  
Method: 304 of 835 (36%) clinicians (mean age = 50.2 years) attending a psychopharmacology review course in 2000 agreed to respond to nine questions regarding their pharmacological treatment practices of PMD during the acute, continuation, and maintenance phases. Demographic data regarding age, gender, type of practice, location of practice, type of degree, and number of years since training were also obtained.  
Results: Most clinicians (171 or 56.3%) indicated that their preference for the acute treatment of PMD was the combination of an SSRI and an atypical antipsychotic; of the remaining respondents, 100 (33%) preferred using a combination of any antidepressant and any antipsychotic, 17 (6%) preferred using any antipsychotic alone, and 11 (4%) preferred using any antidepressant alone. The order of preference for first-line antidepressants was:
SSRIs (69%), atypical antidepressants (buproprion, venlafaxine, mirtazapine, or nefazadone) (15%), tricyclic antidepressants (3%), and monoamine oxidase inhibitors (1%). The order of preference for first line antipsychotics was: risperidone (45%), olanzapine (37%), any typical antipsychotic (9%), quetiapine (4%), and clozapine (0.3%). After remission of an episode of PMD, most respondents (56%) chose to continue antidepressant treatment, for more than 12 months; whereas only 16% of the respondents chose to continue an antipsychotic for more than 12 months. For continuation of combined treatment, 12% of the respondents chose three months or less, 32% chose 3–6 months, 36% chose 6–12 months, and only 16% chose more than 12 months. Finally, 91% of the respondents discontinue the antipsychotic first, 3% of the respondents discontinue the antidepressant first, and 4% continue combined treatment indefinitely. We, also, found that age, gender, type of practice, type of degree, location of practice, and number of years since training, had no significant relationship with response patterns.

Discussion: Eighty-nine per cent of the respondents report that they appropriately treat the acute phase of PMD. However, respondents preferred to either decrease or discontinue antipsychotic medications much earlier than antidepressants. These results are consistent with recent reports that clinicians may be under-utilizing antipsychotic medications in the long-term management of PMD.

References:

NR263 Monday, May 19, 3:00 p.m.–5:00 p.m.
Venlafaxine and SSRIs: Pooled Remission Analysis Supported by Wyeth Research

Charles B. Nemeroﬀ, M.D., Department of Psychiatry, Emory University School of Medicine, 1639 Pierce Drive, Suite 4000, Atlanta, GA 30322; A. Richard Entsuah, Ph.D., Lauren B. Willard, Ph.D., Mark A. Demitrack, M.D., Michael E. Thase, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss differences in the likelihood of achieving remission with venlafaxine and SSRIs in the treatment of major depression; describe differences in remission rates for venlafaxine and SSRIs based on various remission criteria.

Summary:
Objective: Compare antidepressant efficacy of venlafaxine, SSRIs, and placebo using pooled original data from 33 randomized, double-blind, comparative studies.

Methods: Remission (HAM-D scores ≤7) rates were evaluated in 7,463 depressed patients treated with venlafaxine/venlafaxine XR (n=3,300), SSRIs (n=3,336; 1,673 fluoxetine, 680 paroxetine, 652 sertraline, 197 citalopram, 34 ﬂuvoxamine), or placebo (n=927) for ≥8 weeks. Odds ratios for remission (and 95% conﬁdence intervals) were also calculated for venlafaxine versus the SSRIs.

Results: Overall remission rates were venlafaxine, 41% (1364/3300); SSRIs, 35% (1121/3236); and placebo, 24% (225/927). All comparisons were statistically signiﬁcant for remission and for several of seven alternate measures of antidepressant efﬁcacy (P<0.001). Individual comparisons revealed greater remission rates for venlafaxine versus ﬂuoxetine (42% vs 34%; P<0.001), paroxetine (44% vs 39%; P<0.001), and the other SSRIs (37% vs 32%; P<0.001). The overall odds ratio (OR) for remission was 1.309 (95% CI 1.181–1.451), favoring venlafaxine over SSRIs. Individual ORs were 1.413 (95% CI 1.221–1.635) for venlafaxine versus ﬂuoxetine; 1.203 (95% CI 0.970–1.492) for venlafaxine vs paroxetine; and 1.164 (95% CI 0.925–1.464) for venlafaxine vs sertraline.

Conclusion: These results conﬁrm prior research suggesting the signiﬁcantly greater likelihood of achieving remission of depression with venlafaxine versus ﬂuoxetine and perhaps other SSRIs.
References:

NR264 Monday, May 19, 3:00 p.m.-5:00 p.m.
Galantamine as a Treatment for Mild Neurocognitive Disorder
Julio C. Zarra, M.D., Department of Psychiatry, Hospital Italiano-Neurologia, Calle 51 Entre 29 Y 30, La Plata, BA 1900, Argentina; Luisa C. Schmidt, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate with use galantamine in mild neurocognitive disorder improve cognition, behavioral symptoms, and the general state recognized as mild neurocognitive disorder.

Summary:
Objective: The efficacy, safety, and tolerability of new psychotropic agent galantamine (with a dual mechanism of action on the cholinergic a system) were assessed taking into account the therapeutic response was observed in the group that received 16 and adverse events of the treatment.

Methods: The experience included 252 patients who were enrolled in a prospective, observational, multicenter, and open-label study to receive either 8 mg/day or 16 mg/day of galantamine for 12 months of treatment.

Results: The therapeutic response was measured using the MiniMental State Examination (MMSE) and the Clinical Global Impression Scale (CGI), taking into account the efficacy, safety, and adverse events of the treatment.

Conclusion: The final results of the study showed that galantamine improves cognition, behavioral symptoms, and the general well-being of patients with mild neurocognitive disorder. The best therapeutic response was observed in the group that received 16 mg/day; the incidence of adverse events was not significant and a very good profile of tolerability and safety was observed.

References:

NR265 Monday, May 19, 3:00 p.m.-5:00 p.m.
Direct Medical Treatment Costs for Patients With Bipolar Episodes in the U.K.
Supported by Eli Lilly and Company
Henrik Finnern, Ph.D., Lilly Research, Eli Lilly & Company, Erl Wood Manor, Sunninghill Road, Windlesham GU20 6PH, England; Mickael Lothgren, Ph.D., Gian Gandhi, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the audience will have a better understanding of the drug treatment patterns used for treatment of patients with bipolar disorder in the UK.

Summary:
Objective: To identify the current drug therapies employed in treating patients suffering from bipolar disorder with acute manic episodes in the U.K.

Methods: A retrospective chart review was conducted covering 19 months of observations on a sample of 134 UK patients aged 18 years or over (average age 48.4 years) diagnosed with bipolar disorder.

Results: The most frequently prescribed treatment categories to treatmania in 61 bipolar patients who experienced one or more manic episodes during the study period were mood stabilizers (32%), typical antipsychotics (26%), atypical antipsychotics (22%), and benzodiazepines (15%). Among the most frequently prescribed drug treatment was lithium 54% (n=39), sodium valporate 41% (n=26), haloperidol 34% (n=21), lorazepam 34% (n=21), olanzapine 31% (n=19), and risperidone 18% (n=11). Patients receiving haloperidol received on average 2.9 mg/day of olanzapine received on average 1.4 mg/day and those on risperidone received 3.9 different doses. The average drug dose for haloperidol was ranging from 5.8 mg to 11 mg, for olanzapine from 7.2 mg to 13.6 mg and for risperidone from 1.3 mg to 4 mg.

References:

NR266 Monday, May 19, 3:00 p.m.-5:00 p.m.
Drug Treatment Patterns for Manic Patients in the United Kingdom
Supported by Eli Lilly and Company
Henrik Finnern, Ph.D., Lilly Research, Eli Lilly & Company, Erl Wood Manor, Sunninghill Road, Windlesham GU20 6PH, England; Mickael Lothgren, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the audience will have a better understanding of the drug treatment patterns used for treatment of patients with bipolar disorder in the UK.

Summary:
Objective: To estimate resource use and direct medical costs associated with treatment of Bipolar I Disorder (BPDI) and Bipolar II Disorder (BPDII) episodes in the UK.

Methods: A retrospective chart review was conducted covering 19 months of observations on a sample of 134 U.K. patients aged over 18 years (average age 48.4 years) diagnosed with bipolar disorder.

Results: The yearly average direct cost for patients who experienced at least one episode during the study period was £7,714 for BPDI patients (n=68) and £2,980 for BPDII patients (n=25). Hospitalizations accounted for the major component of total treatment costs with a yearly average hospitalization cost of £6,280 for BPDI patients and £1,636 for BPDII patients. The average yearly drug cost for BPDI patients was £383 (5% of total cost) and £194 (6.5% of total cost) for BPDII patients. The average length of hospital stay was 65 days for manic, 46 days for mixed, and 36 days for depressive episodes.

Conclusions: The average treatment cost of a BPDI patient was found to be more than twice the cost of a BPDII patient due to more frequent hospitalizations and a longer length of hospital stay for manic episodes compared with mixed or depressive Episodes.

References:
Anxiolytic Profile of Levetiracetam in the Elevated Plus-Maze Test in Rats

NR267  Monday, May 19, 3:00 p.m.-5:00 p.m.

Objective: the antiepileptic drug levetiracetam (LEV) has been shown to reverse the anxiogenic effect of benzodiazepine withdrawal in mice in a plus-maze without altering behaviour of normal mice in this model (Lamberty et al., 2002a). This suggested that the anxiolytic effect of LEV was dependent upon stress/anxiety level of the animals. This study evaluated LEV further in the rat using the plus-maze test.

Method: two procedures were used: in the 'standard' protocol (Pellow and File, 1986), Sprague-Dawley rats were placed in an elevated plus-maze for a session of four minutes. In a modified protocol, drug-free animals were pre-exposed to the elevated plus-maze 24 hours before being tested using the standard protocol. This was done to induce a state of 'anticipatory anxiety' in the animals. LEV, 5.4 to 54 mg/kg, and chlordiazepoxide (CDP) 5 mg/kg were administered intraperitoneally, 60 minutes before the test.

Results: LEV had no effect in the standard procedure. In contrast, animals pre-exposed to the test situation presented a significant decreased number of ambulation on open arms, which was prevented by LEV. CDP was active in both procedures.

Conclusions: these results indicate that LEV contrasts CDP by only revealing an effect in "anxious" animals. This suggests that LEV may be useful in anxious people.

References:
patients with schizophrenia in the regions of Asia, Central and Eastern Europe, Latin America, and the Middle East and North Africa.

Summary:

Objective: To compare psychiatric hospitalizations following initiation or change of antipsychotic therapy for patients with schizophrenia.

Methods: The Intercontinental Schizophrenia Outpatient Health Outcomes (IC-SOHO) study enrolled 7,655 patients (age, mean ± SD=35.8±12; 55.4% male). Chi-square tests compared proportion of patients hospitalized during six months prior to initiation/change of antipsychotic therapy (prebaseline) with proportion hospitalized during six months following initiation/change (postbaseline). Multiple logistic regression compared probability of postbaseline hospitalization among patients initiating different antipsychotics, adjusting for baseline CGI total score, age, gender, prebaseline hospitalization, geographic region, and disease duration.

Results: The proportion of patients hospitalized decreased from 30.5% prebaseline to 8.3% postbaseline (p<.001); all geographic regions experienced similar decreases (all p<.001). Compared with patients initiating typical monotherapy antipsychotics, patients initiating olanzapine monotherapy were less likely to have been admitted to hospital during the postbaseline period (OR=0.62, 95% CI: 0.46,0.85). Postbaseline hospitalization did not differ from typical monotherapy initiators for patients initiating risperidone monotherapy (OR=0.77, 95% CI: 0.53, 1.2), other atypical monotherapy (OR=1.21, 95% CI: 0.81, 1.83) or polytherapy antipsychotics (OR=0.80, 95% CI: 0.57, 1.1). Conclusions: Patients initiating olanzapine monotherapy were substantially less likely to be hospitalized post-initiation compared with patients initiating typical monotherapy; initiators of risperidone or other atypicals had results similar to typical antipsychotics.

References:

NR271 Monday, May 19, 3:00 p.m.-5:00 p.m.

Quetiapine Versus Risperidone in Treatment of Anxiety/Panic Disorder

Aleksas Ten, M.D., Psychiatry, Beth Israel Medical Center, First Avenue at 16th Street, Room 6K40, New York, NY 10003; Liliya Malaya, Ph.D., Celena Dancourt, M.D., Alice John, M.D., Soenke Boettger, M.D., Lilian Belman, M.D., Igor I. Galynker, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that low doses of quetiapine or risperidone are effective well-tolerated treatment for anxiety/panic disorders.

Summary:
Background: An open-label, pilot study is being conducted to assess efficacy of quetiapine and risperidone in treatment of patients with anxiety symptoms with and without comorbid depression.

Methods: In the course of the ongoing open-label trial of quetiapine and risperidone for treatment of anxiety symptoms, male and female subjects (ages 30–79) were assessed by HAM-A and HAM-D. Treatment was response-based flexible-dose, initiated at 25 mg QHS, increased by 25 mg/d to 100 mg and by 50 mg/d to 300 mg for quetiapine and at 0.125 mg/d QHS, increased by 0.125 mg/d to 0.25 mg and by 0.25 mg/day to 1.5 mg for risperidone.

Results: The interim analysis of the ongoing study (n=18) showed that quetiapine and risperidone were associated with marked improvement from baseline in HAM-A and HAM-D scores. Mean HAM-A was 24.909, SD 5.4673 at baseline and 6, SD 4.75 after risperidone trial and 23.167, SD 6.08 at baseline and 3.33, SD 2.66 after risperidone trial. Mean HAM-D was 19.545, SD 4.75 at baseline and 11.18, SD 3.19 after quetiapine trial and 25.167, SD 3.533 at baseline and 3.33, SD 3.02 after risperidone trial. Mean dose were quetiapine 115.9 mg and risperidone 0.825 mg. Quetiapine produced more sedation than risperidone, there was no noticeable EPS in either group.

Conclusion: Low doses of quetiapine or risperidone are effective and well-tolerated treatment for anxiety.

References:

NR272  Monday, May 19, 3:00 p.m.-5:00 p.m.
The Use of Trimethobenzamide With Rivastigmine Supported by Novartis Pharmaceuticals Corporation
Keith Edwards, M.D., Research Department, Alzheimers Diagnostic Center, 140 Hospital Drive Suite 210, Bennington, VT 05201; Pramod Sethi, M.D., Judy O’Connor, B.S., Michael Dreyer, M.B., Michele Benke, L.P.N., Carol Gorman, L.P.N., Judy Norton, R.N.

Educational Objectives:
To evaluate the usefulness of trimethobenzamide (TMB) with rivastigmine in patients with Alzheimer’s disease (AD).

Summary:
Objective: To ascertain effects of TMB in treating side effects from rivastigmine.

Methods: A 20-week study of TMB in patients receiving rivastigmine. There were 3 groups of patients: TMB 250 mg bid (group 1), TMB prn (group 2) and a no TMB (group 3). Outcome measures included adverse advents (AE’s), discontinuation of rivastigmine, highest tolerated dose (HTD), Mini-Mental State Exam (MMSE), Clinicians Global Impression of Change (CGIC), tolerance to TMB.

Results: 50 patients were enrolled. Results at 20 weeks indicated a 56% AE rate, group 1; 81%, group 2 and 50%, group 3. There was a 67% completion rate with HTD of 9 mg/d, group 1; a 65% completion with HTD of 6.6 mg/d, group 2; a 50% completion with HTD of 6.6 mg/d, group 3. Other measures were not different from baseline.

Conclusions: TMB use on a 250 mg bid dosing regimen for the first 3 days of each rivastigmine dose increase is efficacious to increase HTD and increase the likelihood of continuing rivastigmine therapy.

References:

NR273  Monday, May 19, 3:00 p.m.-5:00 p.m.
Risk Factors for Diabetes During Clinical Trials of Antipsychotics Supported by Eli Lilly and Company
Margaret O. Sowell, M.D., Lilly Research, Eli Lilly & Company, Lilly Corporate Center, DC 6314, Indianapolis, IN 46285; Eva Marquez, Ph.D., Patrizia A. Cavazzoni, M.D., Alan F. Breier, M.D., Nita Mukhopadhyay, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize major lipid risk factors for coronary heart disease, and recognize that chronic treatment with olanzapine is associated with higher TG levels and qualitative differences in LDL particles compared with risperidone, but that cholesterol levels are not significantly different.

Summary:
Objective: To examine fasting lipid levels in patients with schizophrenia.

Methods: Cross-sectional measurement of fasting lipid profiles in normoglycemic (FBS < 110 mg/dL) patients with schizophrenia treated continuously for >1 year with olanzapine (N=67), risperidone (N=65), or typical (N=52) antipsychotics.

Results: Overall, the three treatment groups were well matched in number of normoglycemic patients completing the protocol as well as for physical, psychiatric, and historical characteristics. No significant differences were seen in mean total cholesterol, LDL cholesterol, LDL particle size, HDL cholesterol levels, or total cholesterol/HDL ratio among patients matched for gender, BMI, duration, and severity of psychiatric illness in the three treatment groups. LDL particle concentration, apolipoprotein B, and fasting (natural log transformed) triglyceride levels were significantly different.
higher in the olanzapine group compared with risperidone but not compared with typicals. The HOMA-IR (insulin sensitivity) and predicted 10-year coronary heart disease risk (Framingham model) were also not significantly different among therapy groups.

**Conclusions:** No significant differences in cholesterol levels, insulin sensitivity, or predicted 10-year CHD risk were seen among treatment groups. Chronic treatment with olanzapine was associated with higher triglyceride levels and some qualitative differences in the LDL subfraction compared with matched patients receiving risperidone.

**References:**


**NR275**  
**Monday, May 19, 3:00 p.m.-5:00 p.m.**

**Reduced Serum Prolactin Levels Following Long-Acting Treatment With Risperidone**  
**Supported by Janssen Pharmaceutical Products, L.P.**

Carla M. Canuso, M.D., Janssen Pharmaceutical Products, L.P., 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Cynthia Bossie, Ph.D., Robert Lasser, M.D., Georges Gharabawi, M.D.

**Educational Objectives:**

- At the conclusion of this session, the participant should be able to discuss the significant reduction in serum prolactin levels following treatment with long-acting risperidone.

**Summary:**

**Introduction:** Prolactin elevation observed with antipsychotic medication use results from pituitary dopamine D2 receptor antagonism. The magnitude and duration of such elevations may vary due to dosing regimens, patient characteristics, and collection bias. Moreover, the relationship and relevance of prolactin levels to presumed clinical sequelae is being increasingly challenged, with less robust relationships being reported than previously believed. Long-acting risperidone, with its reduced peak-trough fluctuations of active drug, may offer insight into some factors contributing to the reported variance of prolactin levels.

**Method:** Data were derived from a randomized, double-blind study of patients with schizophrenia/schizoaffective disorder receiving risperidone or olanzapine (12-week, adult study; eight-week, elderly study). HAM-D 21 scores were obtained at baseline and endpoint (n=358 adults; n=153 elderly). Subjects with at least moderate baseline depressive symptoms (high HAM-D scores, >15) (range: adults 16–37, elderly 16–27), and those with mild ratings (low HAM-D scores, ≤15) were assessed.

**Results:** In both studies, HAM-D total scores were significantly reduced with both risperidone and olanzapine (p<0.05). In the adult study, both treatments significantly reduced HAM-D scores in subjects with both high and low HAM-D baseline scores (p<0.01). In the elderly study, both treatments significantly reduced HAM-D scores in subjects with high HAM-D baseline scores (p<0.05). Risperidone, but not olanzapine, also significantly reduced scores in subjects with low HAM-D baseline scores (p=0.04).

**Conclusion:** These data confirm that these agents improve depressive symptoms in schizophrenia/schizoaffective disorder irrespective of age or symptom severity.

**References:**


**NR277**  
**Monday, May 19, 3:00 p.m.-5:00 p.m.**

**Retrospective Analysis of the Metabolic Effects of Divalproex**  
**Supported by Abbott Laboratories**

Jonathan M. Meyer, M.D., Psychiatry, VA SDH S, 3350 La Jolla Village Dr, 116-A, San Diego, CA 92161; Susan Leckband, R.Ph., Catherine Loh, Ph.D.

**Educational Objectives:**

- At the conclusion of this session, the participant should recognize that therapy with divalproex sodium in adults may not be
associated with adverse effects on serum lipids or glucose despite
the known effect on weight.

Summary:
Background: Increasingly clinicians are concerned about the
metabolic consequences of therapy with psychotropic agents, es-
pecially the impact on weight, serum lipids, and glucose. Dival-
proex has achieved wide use for the management of bipolar disor-
der, and adjunctively for schizophrenia and dementia. While
associated with weight gain, preliminary data suggest that this
agent may not have a significant impact on fasting serum lipids
or glucose.

Method: Employing the VA computerized database, 2000 pa-
tient charts were retrospectively selected from 1999–2002 from
those who received divalproex therapy for a minimum of one year,
with baseline and follow-up measurements of parameters noted
above, excluding those receiving drugs for hyperlipidemia or dia-
abetes mellitus at baseline, and those on agents with known effects
on serum lipids or glucose or which may impact serum divalproex
levels.

Results: Among 37 records with adequate data for analysis, no
significant changes in weight, glucose or lipid parameters were
noted in patients on divalproex for average of 14 months. Although
not statistically significant, a trend toward a decrease in total serum
cholesterol (−7.4 mg/dl) and LDL (−8.4 mg/dl) was observed.

Conclusions: Long term therapy using divalproex is not associ-
ated with significant changes in glucose or lipid parameters, de-
spite known effects on weight.

References:
on plasma lipoprotein (a) and other lipid levels in childhood. J
vs. olanzapine for the treatment of mania in bipolar disorder:
effects on body weight change and related outcome. Poster
presented at American College of Neuropharmacology 2000.

NR279 Monday, May 19, 3:00 p.m.–5:00 p.m.
Extended Release Mixed Amphetamine Salts in
ADHD: Growth Parameter Analysis
Supported by Shire Pharmaceutical Development, Inc.

Joseph Biederman, M.D., Department of Pediatric Psychiatry,
Massachusetts General Hospital, 15 Parkman Street, ACC-725,
Boston, MA 02114; Stephen V. Farace, Ph.D., Thomas J.
Spencer, M.D.

Educational Objectives:
After reviewing this poster, the participant should be able to
discuss the impact of long-term treatment with extended-release
mixed amphetamine salts on growth parameters in children with
ADHD.

Summary:
Objective: To analyze growth parameters of subjects with ADHD
enrolled in a 24-month, multicenter, open-label extension study
of an extended-release formulation of mixed amphetamine salts
(MAS XR).

Methods: We analyzed data from 132 subjects (6–12 yr) who
had not received drug therapy for ADHD before treatment with
MAS XR (titrated to a clinically optimal dose). The number of days
on study ranged from 64 to 821. Height, weight, and body mass
index (BMI) percentiles and Z-scores were calculated.

Results: Subjects were slightly taller and heavier than average
for their age at baseline (mean height, weight, and BMI percentiles
were 57, 65, and 66, respectively). The mean change in growth
percentiles from baseline to last visit was fairly small for height
(−9%) and larger for both weight (−21%) and BMI (−23%). Average
mg/kg dose was significantly correlated with changes in height
(r=−.27, p=.002) and weight (r=−.19, p=.03) percentiles. We found
no significant increase in the number of very short patients (defined
as being at or below 5th percentile of CDC norms) from baseline
(4.8%) to follow-up (1.9%, p=.037 by McNemar's exact test).
There was a significant increase in the proportion of very light
patients from baseline (3.8%) to follow-up (12.9%, p=.0004).

Conclusion: The observed changes in growth parameters do
not appear to be clinically significant.

References:
1. Spencer T, Biederman J, Wilens T: Growth deficits in children
with attention deficit hyperactivity disorder. Pediatrics 1998;
2. Sund AM, Zeiner P: Does extended medication with amphe-
tamina or methylphenidate reduce growth in hyperactive chil-
**NR280**

**Monday, May 19, 3:00 p.m.-5:00 p.m.**

**Extended Release Mixed Amphetamine Salts in ADHD: Growth Parameter Analysis**

**Supported by Shire Pharmaceutical Development, Inc.**

Joseph Biederman, M.D., Department of Pediatric Psychiatry, Massachusetts General Hospital, 15 Parkman Street, ACC-725, Boston, MA 02114; Stephen V. Faraone, Ph.D., Thomas J. Spencer, M.D.

**Educational Objectives:**

After reviewing this poster, the participant should be able to discuss the impact of long-term treatment with extended-release mixed amphetamine salts on growth parameters in children with ADHD.

**Summary:**

**Objective:** To analyze growth parameters of subjects with ADHD enrolled in a 24-month, multicenter, open-label extension study of an extended-release formulation of mixed amphetamine salts (MAS XR).

**Methods:** We analyzed data from 132 subjects (6–12 yr) who had not received drug therapy for ADHD before treatment with MAS XR (titrated to a clinically optimal dose). The number of days on study ranged from 64 to 821. Height, weight, and body mass index (BMI) percentiles and Z-scores were calculated.

**Results:** Subjects were slightly taller and heavier than average for their age at baseline (mean height, weight, and BMI percentiles were 57, 65, and 66, respectively). The mean change in growth percentiles from baseline to last visit was fairly small for height (-9%) and larger for both weight (-21%) and BMI (-23%). Average mg/kg dose was significantly correlated with changes in height (r=-.27, p=.002) and weight (r=-.19, p=.03) percentiles. We found no significant increase in the number of very short patients (defined as being at or below 5th percentile of CDC norms) from baseline (4.8%) to follow-up (2.4%, p=0.375 by McNemar’s exact test). There was a significant increase in the proportion of very light patients from baseline (3.8%) to follow-up (12.9%, p=.0004).

**Conclusion:** The observed changes in growth parameters do not appear to be clinically significant.

**References:**


**NR281**

**Monday, May 19, 3:00 p.m.-5:00 p.m.**

**Does Anticholinergic Burden Differ in Elderly Patients With Dementia Receiving Risperidone or Olanzapine?**

**Supported by Janssen Pharmaceutica Products, L.P.**

Benoit H. Mulsant, M.D., Department of Psychiatry, University of Pittsburgh, 3811 O’Hara Street, Room 3-809, Pittsburgh, PA 15213-2593; Georges Gharabawi, M.D., Cynthia Bossie, Ph.D., Lian Mao, M.S., Bruce G. Pollock, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to evaluate the anticholinergic burden in elderly demented patients treated with risperidone or olanzapine.

**Summary:**

**Introduction:** Reduction in anticholinergic burden in the elderly is associated with improved behavioral and cognitive function. In vitro, some antipsychotics have high, while others have little or no affinity for muscarinic receptors. Their increasing use in older patients mandates studies to ensure their safety in this sensitive population.

**Methods:** Subjects were ≥55 years old with dementia, MMSE score 7–26, and hallucinations/delusions disruptive to care. They were randomized to risperidone (0.75–1.5 mg/d) or olanzapine (5–10 mg/d) for six weeks. Anticholinergic activity (pmol/mL atropine equivalents by radioreceptor assay) was measured at baseline, after three and six weeks of treatment.

**Results:** Anticholinergic activity data were available for 48 (n=23 risperidone; n=25 olanzapine) of 86 randomized subjects (75.0% females; mean±SD age, 84.5±7.18). There was no significant change in mean anticholinergic activity at any time point in the risperidone group (3.32 at baseline, 4.16 at week 3, 3.91 at endpoint, p=0.230); it increased significantly at all time points in the olanzapine group (2.23 at baseline, 3.59 at week 3, 3.64 at endpoint, p=0.003). Between-group differences were not significant (0.05 levels).

**Conclusions:** These results are consistent with in vitro binding studies. Next steps include studying the impact of cholinergic burden on clinical and functional outcomes.

**References:**


of the venlafaxine/venlafaxine XR group; 32% (1032/3176) of SSRIs-treated patients; and 25% (231/927) of placebo patients. All comparisons were statistically significant (P<0.001).

Conclusion: These results demonstrate that treatment with venlafaxine/venlafaxine XR is significantly more effective than SSRIs in complete resolution of somatic symptoms of depression.

References:

NR284 Monday, May 19, 3:00 p.m.-5:00 p.m.
Symptomatic Improvement in Remission: Venlafaxine Versus SSRIs
Supported by Wyeth Research
A. Richard Entsuah, Ph.D., Clinical Research and Development, Wyeth-Ayerst Research, 500 Arcola Road, Collegeville, PA 19426; Lauren B. Willard, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the effects of venlafaxine and SSRIs on individual symptoms of depression, based on HAM-D item score improvement; and compare rates of complete symptom relief observed with venlafaxine and with SSRIs.

Summary:
Objective: To evaluate changes in specific depressive symptoms with venlafaxine, selective serotonin reuptake inhibitors (SSRIs), and placebo.
Methods: Data from eight randomized, double-blind comparison studies were pooled to evaluate remission rates in 2,045 patients with depression treated with venlafaxine/venlafaxine extended release XR (n=851), SSRIs (n=749), or placebo (n=446) for up to eight weeks. Baseline symptoms were categorized as mild, moderate, or severe, and improvement in severity was assessed. Relative rates of complete symptom relief (HAM-D item = 0) on individual HAM-D items were evaluated and compared, with the difference expressed as percentage improvement.

Results: Results demonstrated a significant advantage for venlafaxine compared with SSRIs (P<0.05) and placebo (P<0.001) in agitation, feelings of guilt, somatic general, psychic anxiety, depressed mood, and work/activity impairment, and over placebo for suicidal ideation. SSRIs performed significantly better than placebo (P<0.05) on the same items, with the exception of the somatic general item. Venlafaxine treatment was associated with significant improvement on mild, moderate, and severe symptoms.

Conclusion: These results suggest that the higher remission rates associated with venlafaxine compared with SSRIs are not due to improvements in a limited number of symptoms. Venlafaxine is broadly effective in ameliorating both psychic and somatic symptoms of depression.

References:

NR285 Monday, May 19, 3:00 p.m.-5:00 p.m.
Olanzapine Plasma Concentrations in Patients With Schizophrenia
Supported by Wyeth Research
Niels Bergemann, M.D., Department of Psychiatry, University of Heidelberg, Voss-Str. 4, D-69115 Heidelberg, Germany; Alex Frick, M.D., Peter Parzer, M.S., Juergen Kopolitz, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to better understand new research findings in the field of psychopharmacology and apply an advanced treatment strategy using therapeutic drug monitoring.
NR286

Antipsychotic-Induced Amenorrhea Reported by Psychiatric Patients

Bun Hee Lee, Psychiatry, Korea University, 516 Kochan-Dong Ansan-si, Kyoungki 425-070, South Korea; Chang Su Han, Yong Koo Kim

Summary:

Objective: Some antipsychotic drugs were reported to have relationships with hyperprolactinemia, which can make women suffer from menstruation difficulties or galactorrhea. The purpose of this study was to find out a safe regimen that can relieve irregular menstruation or amenorrhea by antipsychotic drugs.

Methods: A total of 18 schizophrenic, premenopausal women who took risperidone for more than six months reported symptoms of amenorrhea. Their amenorrhea symptoms were prospectively followed during next three months.

Results: During the three month period, dosages of risperidone of nine subjects were reduced and antipsychotics of nine subjects were replaced by olanzapine or quetiapine. Only three subjects had taken less than 4mg risperidone.

Conclusion: This study suggests that amenorrhea symptoms in the patients administered more than 4mg of risperidone as maintenance dosage can not be relieved by reducing dosage of risperidone, but by changing antipsychotic drugs.

References:


NR287

Monday, May 19, 3:00 p.m.-5:00 p.m.

Effectiveness of Quetiapine Treatment of Aggressive Psychosis in the Emergency Psychiatric Setting: A Naturalistic Pilot Study

Supported by AstraZeneca Pharmaceuticals

Dan Bilsker, Ph.D., Psychiatry, Vancouver Hospital, P.A.U. JPN-G 855 West 12th Avenue, Vancouver, BC V5Z 1M9, Canada; Soma Ganesan, M.D., Mark Levy, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to select an appropriate medication for the management of aggressive psychosis with increased knowledge of the utility of quetiapine as one possible tool for this purpose.

Summary:

Objective: Although consensus-based guidelines in emergency psychiatry recommend the use of atypical antipsychotics for management of aggressive psychosis, there is little empirical data demonstrating their effectiveness for this purpose. This (ongoing) uncontrolled study has examined the effectiveness of quetiapine for management of aggressive psychosis.

Method: The setting is an emergency psychiatric unit in a general hospital. Study participants meet thresholds on scales of psychosis and aggression and do not meet exclusion criteria such as hypotension. Although study implementation spans five days, data are included for all patients with at least one day of valid data. Patients are treated with quetiapine (clinicians set dosages within broad limits) but no other antipsychotic medications. Outcome measures are the Overt Aggression Scale and a psychosis index from the Brief Psychiatric Rating Scale.

Results: Based on the initial 27 patients (anticipated total N=50), treatment with quetiapine resulted in a significant decrease in the OAS [p<.0001] and in the BPRS psychosis index [p<.05].

Conclusion: Results of this study give preliminary support for the use of quetiapine in managing aggressive psychosis. After completing this pilot study, the next step will be a randomized, controlled trial.

References:


NR288

Monday, May 19, 3:00 p.m.-5:00 p.m.

Clinical Study of Valproate in the Maintenance Treatment of BPD

Shih-Ku Lin, M.D., Taipei City Psychiatric Center, 309 Sung-Te Road, Taipei 110, Taiwan; Chunj-Hung Pan, I-Ning Yeh, Kun-Po Chen
Educational Objectives:

At the conclusion of this session, the participant should recognize the clinical efficacy and side effects, dose, and plasma concentration of valproate in bipolar patients.

Summary:

One hundred and one (50 men and 51 women, mean age: 44.3 ± 13.0 years) patients with bipolar disorder treated with valproate as maintenance therapy were analyzed by a retrospective, chart-review method. The mean age of onset was 25.5 ± 9.4 years; mean duration of valproate use was 4.3 ± 1.9 years; mean daily dosage of valproate was 999.4 ± 268.6 mg (16.4 ± 4.6 mg/kg by body weight), mean plasma level of valproate was 75.6 ± 20.1 µg/ml. There were 30 (29.7%) patients who concomitantly used lithium or carbamazepine for maintenance treatment. The side effects of valproate included alopecia (2.0%), nausea/vomiting (2.0%), diarrhea (2.0%), body weight gain (21.8%), drowsiness (4.0%), dizziness (3.0%), tremor (3%) and others (6%). The mean admission frequency before valproate use was 0.28 times per year, and 0.19 times per year after valproate use (p < 0.001). Valproate appears to have efficacy in maintenance treatment of bipolar disorder. The side effects of valproate were mild and tolerable in most patients.

NR289

Monday, May 19, 3:00 p.m.-5:00 p.m.

Efficacy of Duloxetine in Models of Persistent Pain: Comparison With Other 5HT and NE Reuptake Inhibitors

Supported by Eli Lilly and Company

Smriti Iyengar, Ph.D., Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Frank P. Bymaster, M.S., Amy A. Webster, Rosa Maria A. Simmons, Susan Hemrick-Luecke

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the evidence that duloxetine, a potent and balanced dual reuptake inhibitor of serotonin and norepinephrine, is efficacious in reducing persistent pain in animal models.

Summary:

Objective: Serotonin (5-HT) and norepinephrine (NE) mediate endogenous analgesic mechanisms via descending inhibitory pain pathways in the brain and spinal cord. The effects of duloxetine and other uptake inhibitors were studied in vivo models of uptake inhibition and in models of persistent pain in rats.

Methods: Inhibition of the transporters in vivo was determined by blockade of PCA-induced depletion of 5HT and a-MMT-induced depletion of NE in rat brain. Extracellular levels of 5HT and NE were measured by in vivo microdialysis. Additionally, drugs were tested in the formalin model of persistent pain and the L5/L6 spinal nerve ligation model of neuropathic pain.

Results: Duloxetine showed potent and selective 5-HT and NE reuptake inhibition in brain, significantly reduced formalin-induced pain behavior and mechanical allodynia behavior in L5/L6 spinal nerve ligated rats and was more potent than mianserin and venlafaxine in the models tested. Low doses of paroxetine and thioridoxetine alone did not have an effect in the formalin model but when combined, showed significant effects.

Conclusions: 5-HT and NE reuptake inhibition by duloxetine may offer a highly effective and safe alternative for treatment of persistent pain states in man.

References:


NR290

Tuesday, May 20, 12:00 p.m.-2:00 p.m.

Immune and Psychological Research on HIV in Spain

David Busse, Ph.D., DIS BARCELONA, CSMA MJ-SAT, PG Luis Companys, Num 8, Sta Coloma Gramenet, Catalonia 08921, Spain; Tomas De Flores, Jose Catalan, Dora D. Cohen, M.D., Rafel Torrubia

Educational Objectives:

At the conclusion of this session, the participant should be able to explain to the American psychiatrists’ Community what is going in AIDS & HIV related disorders in Europe. We demonstrate some psychoneuroimmunological basis of stress related factors with HIV serology. Common sense will elucidates its impact on society, human behavior, CNS and immunity.

Summary:

Introduction: This multi-centric research has recently been awarded by the Spanish Biological Psychiatric Society with the 2002 PhD’s prize. It evaluates the effect of HIV serology communication in cellular lymphocytic and humoral immune changes, and its association with emotional variables.

Objectives: To study the correlation between immune and psychological responses to acute distress.

Methods: 81 prisoners with or without risk were tested for HIV and their response to lymphoblastic stimulation with PHA, CD4/CD8 and WBC were checked before, following disclosure on first, fourth, and eighth week. Psychopathological and psychological parameters on mood, anxiety, perceived distress and personality variables were correlated with the immune changes. Statistic support was by SPSS.

Results: 89% were caucasion & 24.69% were immigrants. 45.46% were single. Heterosexual orientation was declared in 87.34%, 71.60% admitted unprotected sex risky factors and about 1/3 share needles. Approximately 3/4 reported drug use: However, only half of them believe they were not at risk of HIV infection. 17.28% were HIV +.

The rates of anxiety (STAI), depression (BDI) and AIDS Locus of Control were abnormally high from the beginning as well as the acute lymphoblastic and cellular immune response, declining these rates when the results were “good news” (HIV-), the perceived risk and neuroticism (EPO) were low. (EPO). Conclusions: Testing on HIV relates with emotional changes and immunological tests for distress. The results of HIV display 2 different adjustment patterns with an slowed recovery in seropositives, neurotic (EPO), mentally vulnerable (GHQ), hostile and punishment susceptible cases. Today there are several new paradigms in the on-going research AIDS’ Psychiatry in Europe, which are elucidated.

References:


NR291 Tuesday, May 20, 12:00 p.m.-2:00 p.m.

Trauma and PTSD in HIV Positive Incarcerated Women

Catherine F. Lewis, M.D., Department of Psychiatry, University of Connecticut, 263 Farmington Avenue, Farmington, CT 06030-2103;

Educational Objectives:
At the conclusion of this session, the participant should be able to identify Axis I and Axis II diagnoses associated with lifetime PTSD in HIV+ incarcerated women and recognize the importance of childhood sexual and physical abuse as related to PTSD and adult sexual victimization.

Summary:

Objective: To examine the prevalence of exposure to traumatic victimization, post-traumatic stress disorder (PTSD) and comorbidity in HIV+ incarcerated women.

Method: Eighty-one HIV+ incarcerated women (ages 22-54 years; 51% black, 30% white, 16% Hispanic) were interviewed using the Traumatic Events Interview, Clinician Administered PTSD Scale, Structured Clinical Interview for DSM-IV, and Addiction Severity Index.

Results: A history of childhood sexual abuse (CSA; 62%) or physical abuse (CPA; 40%), and of rape in adulthood (47%) was prevalent. Moebi (74.1%) of the women had lifetime PTSD. Lifetime PTSD was associated with: CSA, CPA, rape in adulthood, less education, marijuana abuse, antisocial and borderline personality disorders, lifetime history of major depression, and past psychiatric outpatient treatment. History of CSA was the sole unique predictor of risk of lifetime PTSD in an omnibus multivariate analysis. History of CSA and CPA each were associated with risk of adult rape, but a history of rape did not appear to mediate the relationship between CSA or CPA and adult PTSD.

Conclusions: Incarcerated HIV+ women are likely to have experienced child abuse, adult rape, and PTSD, often with comorbid Axis I and II disorders. Mental health services for HIV+ incarcerated women optimally should consider trauma history and related impairment.

References:

NR292 Tuesday, May 20, 12:00 p.m.-2:00 p.m.

Improvement of Depression and Anxiety Through a Group Psychotherapy Program for HIV-Infected Patients in a Public Mental Health Setting

Araceil Rousaud, ICPP, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain; Jordi Blanch, M.D., Esteban Martinez, Elisa de Lazzari, Josep-Maria Peri, M.D., Ana Milinkovic, Josep-Maria Gatell, Ph.D.

Educational Objectives:
At conclusion of this presentation, the participant should be able to identify the factors associated to a greater improvement of quality of life due to lipodystrophy syndrome in HIV−1 infected patients receiving highly active antiretroviral therapy (HAART).

Summary:

Introduction: Present antiretroviral therapy has given longer survival for HIV-infected patients, but it has also brought new important problems, such as lipodystrophy (LD) (abnormal body fat redistribution). Few studies have assessed the impact on quality of life of lipodystrophy in HIV-infected patients using standardized questionnaires.

Methods: Consecutive HIV−1 infected outpatients with lipodystrophy were asked about lipodystrophic changes in several parts of the body. They completed a modified version of the Dermatology Life Quality Index (DLQI) to measure the impact of this changes in QoL.

Results: Of 84 included patients 65.5% referred that body changes influenced dressing, 48.8% felt ashamed due to body changes; 27.4% had problems in sexual life. Women, intravenous drug users, patients with abdominal or breast lipoaccumulation, and patients suffering from more non-lipodystrophy-related side effects showed greater impact due to body changes on several

NR293 Tuesday, May 20, 12:00 p.m.-2:00 p.m.

Assessment of the Factors Associated to the Impairment of Quality of Life in HIV-1-Infected Patients With Lipodystrophy

Araceil Rousaud, ICPP, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain; Jordi Blanch, M.D., Esteban Martinez, Elisa de Lazzari, Josep-Maria Peri, M.D., Ana Milinkovic, Josep-Maria Gatell, Ph.D.

Educational Objectives:
At conclusion of this presentation, the participant should be able to identify the factors associated to a greater impairment of quality of life due to lipodystrophy syndrome in HIV−1 infected patients receiving highly active antiretroviral therapy (HAART).

Summary:

Introduction: Present antiretroviral therapy has given longer survival for HIV-infected patients, but it has also brought new important problems, such as lipodystrophy (LD) (abnormal body fat redistribution). Few studies have assessed the impact on quality of life of lipodystrophy in HIV-infected patients using standardized questionnaires.

Methods: Consecutive HIV−1 infected outpatients with lipodystrophy were asked about lipodystrophic changes in several parts of the body. They completed a modified version of the Dermatology Life Quality Index (DLQI) to measure the impact of this changes in QoL.

Results: Of 84 included patients 65.5% referred that body changes influenced dressing, 48.8% felt ashamed due to body changes; 27.4% had problems in sexual life. Women, intravenous drug users, patients with abdominal or breast lipoaccumulation, and patients suffering from more non-lipodystrophy-related side effects showed greater impact due to body changes on several
domains of the DLQI. Using the score of the whole DLQI scale as a dependent variable multivariate proportional odds model analysis showed that non-lipodystrophy-related side effects intensity (β = 0.662; p = 0.008) and suffering from lipodystrophic changes in the breast (β = 1.322; p = 0.001) were associated with greater impairment of psychosocial functioning.

Conclusions: The impact of lipodystrophy on QoL seems to be influenced by patients' characteristics, non-lipodystrophy side effects, and changes in certain parts of the body.

References:

NR294 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Depressive Symptoms and Lymphocyte Subsets Outcome in HIV-Infected Asymptomatic Patients: A Two-Year, Follow-Up Study
Jordi Blanch, M.D., Department of Psychiatry, Hospital Clinic, Rosselló 140, Barcelona 08036, Spain; Felipe Garcia, Ph.D., Esteve Cirera, M.D., Teresa Mejias, Araceli Rousaud, Josep-Maria Gatell, Ph.D., Cristobal Gasto, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate the lack of association between depressive symptoms and changes in CD4+ or CD8+ lymphocyte count in a heterogeneous sample of asymptomatic HIV-infected patients.

Summary:
Introduction: Previous studies about immunological changes associated with HIV activation and progression (CD4 and CD8 cell counts) in depressed HIV-seropositive patients showed contradictory results. Most of these studies were carried out before highly active antiretroviral therapy era, and showed methodological limitations.
Methods: In a two-year period, 65 asymptomatic, HIV-infected patients, who never had taken antiretroviral treatment before, were assessed consecutively at four-month intervals. Depressive symptoms were assessed using the Beck Depression Inventory (BDI), and the outcome measures were the CD4+ and CD8+ lymphocyte counts. Univariate and multivariate random-effect linear regression was used to examine the association between depressive symptoms and lymphocyte counts, controlling for patients' characteristics, data about HIV-infection and its treatment, and time-point of assessment.
Results: HIV transmission through sexual intercourse (β = 1.27; p=0.001), and taking antiretroviral treatment (β = 1.22; p=0.003) were independently associated to CD4 count cell. After the eighth month of follow-up, patients showed a significant increase in CD4+ cell count almost every four months of follow-up. Neither the degree nor the duration of the depressive symptoms was associated with CD4 or CD8 cell count.
Conclusions: Similarly to some previous studies, we found no evidence that depressive symptoms were independently associated to changes in CD4+ or CD8+ lymphocyte count in a heterogeneous sample of asymptomatic HIV-infected patients.

References:

NR295 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Open Trial of Mirtazapine In the Treatment of Major Depression in HIV-1-infected Outpatients Supported by Janssen-Cilag Medical Affairs EMEA
Jordi Blanch, M.D., Department of Psychiatry, Hospital Clinic, Rosselló 140, Barcelona 08036, Spain; Joan De Pablo, M.D., Guillem Masana, Ph.D., Araceli Rousaud, Antonio Minarro, Angel Villarroya, Ph.D., Josep-Maria Gatell, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to show the efficacy and good tolerance of mirtazapine in the treatment of HIV-1 infected outpatients with major depression.

Summary:
Introduction: Mirtazapine, an alpha-2 adrenergic, 5-hydroxytryptamine-2, and 5-hydroxytryptamine-3 antagonist, with low potential for drug interactions, was shown to be tolerated with few adverse effects, and efficient for the treatment of depression in HIV-1 infected patients in a previous small trial.
Methods: In a prospective, longitudinal, open-label, observational study twenty-seven HIV-1 infected outpatients with major depression were assessed at baseline and after one, two, four, eight and 16 weeks of treatment with mirtazapine using Hospital Anxiety and Depression Scale (HADS), Beck Depression Inventory (BDI), and the Global Clinical Impression (GCI). Side effects were recorded. Outcome of completing patients was analysed using univariate repeated-measures analysis of variance (ANCOVA) or Friedman test.
Results: Sixteen patients dropped-out before reaching the last visit, mainly due to somnolence and dizziness (5 patients). Completing patients (41%) showed a significant (p<0.05) improvement in all measures: 58% on GCI, 53% on BDI, and 46% on HADS depression subscale. Most of all the patients improved their insomnia during the first week of treatment. No side-effects on sexual functioning were observed. No significant changes on weight were observed.
Conclusions: Despite the risk of abandonment due to side effects, mirtazapine should be considered in the treatment of depressed HIV-1 infected patients because its rapid improving effect on all measures of depression, especially on sleep disturbances.

References:

NR296 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Validation of the Hospital Anxiety and Depression Scale (HADS) in a Spanish Population
Supported by Janssen-Cilag Medical Affairs EMEA
Jordi Blanch, M.D., Department of Psychiatry, Hospital Clinic, Rosselló 140, Barcelona 08036, Spain; Maria Jesus Herrera, M.D., Xavier Torres, Josep-Maria Peri, M.D., Luis Pintor, M.D., Antoni Bulbena, M.D., Joan De Pablo, M.D.
Educational Objectives:
At the conclusion of this session, the participant should be able to show the validation of the Spanish version of the HADS assessing several psychometric properties of the questionnaire, and to determine the optimal cut-off points and respective specificity and sensitivity of this version of the scale.

Summary:
Introduction: The Hospital Anxiety and Depression Scale (HADS) is a self-report screening scale that was originally developed to indicate the possible presence of anxiety and depression states in the setting of a medical non-psychiatric outpatient clinic. Items referring to symptoms that may have a physical cause are not included in the scale, so it is considered to be unbiased by coexisting general medical. The present study aims to validate the Spanish version of the HADS and to determine the ability of this tool for screening mood and anxiety disorders.

Methods: Psychometric properties of the HADS were assessed in different groups of general medical out-patients (N = 385) attending a General Hospital in Barcelona (Spain). Psychiatric diagnoses were made using DSM-IV criteria.

Results: A two-factor solution corresponding to the original two subscales of the HADS was found. The Spanish version of the HADS was found to have good internal consistency and external validity, with favourable sensitivity and specificity in identifying cases of psychiatric disorder as defined by the Structured Clinical Interview for DSM-IV (SCID-I).

Conclusions: The psychometric properties of the HADS and its shortness make it useful for screening for psychiatric disorders in the medically ill.

References:

NR297 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Effect on Body Weight and Depressive Symptoms of Bupropion Sustained Release in Obese Patients Treated for 50 Weeks
Supported by GlaxoSmithKline
Paul S. Bradley, M.D., Candler Medical Center, 340 Eisenhower Drive, Suite 1200, Savannah, GA 31405; Barbara R. Haight, Pharm.D., Vicki J. Foster, M.S.P.H., Nathalie E. Richard, M.S., Jack G. Modell, M.D.

Educational Objectives:
At the conclusion of this session, the participant should have knowledge of data that demonstrate that bupropion SR has been shown to sustain weight loss and reduce depressive symptoms during a 50-week treatment period in obese subjects with current depressive symptoms.

Summary:
Objective: To evaluate the long-term effects of bupropion SR in reducing weight and depressive symptoms in obese adults with current depressive symptoms.

Methods: Patients completing a double-blind, randomized, 26-week trial comparing bupropion SR to placebo could continue in a 24-week, open-label phase and receive bupropion SR 300-400mg/day. Patients were to adhere to a 500-calorie deficit diet during the 50-week period. Weight and Beck Depression Inventory (BDI) scores were obtained. Results are reported for patients who received bupropion SR during the entire 50-week study.

Results: Of the 121 bupropion SR patients who completed the double-blind phase, 112 entered the open-label phase, and 76 completed 50 weeks of treatment. At the end of the double-blind phase, patients had a mean change in weight from baseline of ~5.9kg (~6.1%). This weight loss was maintained at Week 50, ~5.8kg (~6.3%), and was significantly different from baseline (p<0.001). The percentages of patients who lost >5% and >10% of initial body weight were 51% and 24%, respectively, at Week 50. The number of patients with response of their depressive symptoms (≥50% reduction from baseline BDI) increased from 47% at the end of the double-blind phase to 62% at Week 50.

Conclusions: Bupropion SR facilitated sustained weight loss and continued response of depressive symptoms over a 50-week period.

References:

NR298 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Depression and Pain: Six-Year Outcomes for Near-Elderly Americans Supported by Eli Lilly and Company
Nicholas P. Emptage, B.A., Department of Health, Rand, 1700 Main Street, Santa Monica, CA 90407; Roland Sturm, Ph.D., Rebecca Robinson, M.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to study illustrates how depression and pain among the near-elderly affects their long-term functional and workplace outcomes. Participants will recognize depression with pain in problematic cases and its impact on patients in terms of financial changes and discontinuities in insurance coverage.

Summary:
Objective: To determine 6-year outcomes among a representative cohort of Americans with depression and pain.

Method: 9,825 (ages 50 to 60) were interviewed in 1992 and subsequently in two-year intervals throughout the Health and Retirement Survey. Beginning in 1994, measures included health conditions, depression, healthcare costs, employment, disability, and health insurance. Outcomes were compared across four groups: depression and pain, depression-only, pain-only, and neither condition.

Results: In 1994, 9.4% of respondents had depression + pain. 8.0% had depression-only. 16.0% reported pain-only. Depression + pain respondents had higher medical expenditures and greater continuation of both conditions 6 years later, compared to depression - only. Pain raised the probability of continued depression at two- and six-year waves compared to depression - only. The probability of leaving employment was higher in the depression + pain group at all waves. Among those employed at baseline, 47.3% in the depression + pain group were employed six years later, compared to over 60% in other groups. Among privately insured baseline respondents, the depression + pain group was more likely to be uninsured at two years compared to other groups, and more likely to receive services through a public program over six years.
Conclusions: Depression with pain may more adversely affect patients’ employment status and insurance status than either condition experienced singly.

References:

NR299 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Beta-Adrenergic Receptor Function in Patients With Irritable Bowel Syndrome
Eunho Kang, M.D., Psychiatry Department, SamSung Medical Center, 50 Ilwon-Dong, Kangnam-Ku, Seoul 135-710, Korea; Kyungjung Kim, Hyangsook Lee, B.S.N., Pung-Lyul Rhee, M.D., Bum-Hee Yu, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize irritable bowel syndrome (IBS) is one of the most frequent illnesses in gastroenterologists’ practice. Recently some neurotransmitters are known to be related with the syndrome.

Summary:
Objectives: This study was designed to examine anxiety levels and beta-adrenergic receptor function in patients with irritable bowel syndrome.

Methods: Using the Rome-II criteria, 12 patients were enrolled in the study. Twelve normal control subjects who had no major medical and psychiatric illnesses were matched with the patients for age and sex. All subjects completed the Spielberger state and trait anxiety inventory and Beck depression inventory. We also assessed anxiety and depression levels in all subjects with the Hamilton anxiety (HAM-A) and depression (HAM-D) rating scales. Chronotropic 25 dose (CD$_{25}$) was calculated via isoproterenol stimulation test to measure beta adrenergic receptor function. Mann-Whitney U test and Spearman correlation analysis were used for statistical analyses.

Results: Patients with irritable bowel syndrome showed higher HAM-A scores than normal control subjects (8.27±5.42 vs 4.08±2.54, p<0.05) CD$_{25}$ values in the patient group were significantly lower than those in the control group (2.2±1.2 vs. 4.2±1.7; p<0.01). In addition, HAM-A scores were negatively correlated with CD$_{25}$ values in the patient group (Spearman’s rho=-0.609, p<0.05).

Conclusions: These results suggest that beta-adrenergic receptor function is increased in patients with irritable bowel syndrome and anxiety can affect beta-adrenergic receptor function in patients with irritable bowel syndrome.

References:

NR300 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Use of Venlafaxine for Chronic Pain Associated With Post-Herpetic Neuralgia
Supported by Wyeth Research
Mark A. Demitrack, M.D., Research Department, Wyeth, 555 East Lancaster Avenue, St. Davids, PA 19087; Nadia R. Kunz, Pharm.D., A. Richard Entsuah, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss the clinical evidence of venlafaxine in the treatment of the pain associated with post-herpetic neuralgia, and the corresponding clinical and theoretical implications of these observations.

Summary:
Introduction: Several reports have provided evidence of the use of venlafaxine, a serotonin-norepinephrine reuptake inhibitor, as an analgesic agent in both animal and human experimental pain models and in various clinical conditions. We report here the results of an exploratory, randomized, placebo-controlled clinical trial to further evaluate these attributes of venlafaxine in the treatment of the chronic pain associated with post-herpetic neuralgia.

Methods: A total of 135 patients meeting clinical criteria for chronic pain associated with post-herpetic neuralgia were enrolled for study and provided clinical data for analysis. Patients were randomized to six weeks of treatment with either placebo or venlafaxine extended release capsules (75–225 mg QD). Efficacy was evaluated by measuring pain intensity using the standard technique of visual analog scales (VAS-PI). Safety was assessed by spontaneous adverse events and laboratory measures.

Results: A total of 12 patients withdrew from the study due to adverse events, 10 venlafaxine-treated patients, and two on placebo. VAS-PI scores were examined using LOCF technique and showed a numerical, but not statistically significant advantage for venlafaxine compared with placebo treatment (mean adjusted change from baseline: –15.5 mm vs –14.0 mm).

Conclusions: Combined action of norepinephrine and serotonin have been implicated as key mediating neurotransmitters in the perception of chronic painful events. Several reports have provided evidence of venlafaxine’s clinical analgesic effect consistent with this view.

References:

NR301 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
SSRI Therapy Improves Somatic Pain Associated With Physical Illness
Supported by GlaxoSmithKline
David A. Duff, Ph.D., Psychiatry, GlaxoSmithKline, New Frontiers Science Park, 3rd Avenue, Harlow CM19 5AW, United Kingdom; Prakash S. Masand, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that pain in patients with physical illness, with or without comorbid depression or anxiety, may be improved following paroxetine treatment.
NR302  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Improving Somatic Symptoms Associated With Depression Using SSRI Treatment
Supported by GlaxoSmithKline
Jacquie Christie, Ph.D., Department of Psychiatry, GlaxoSmithKline, New Frontiers Science Park, 3 Roave, Marlow CM19SAW, United Kingdom; Charles B. Nemeroff, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that paroxetine is effective against somatic symptoms (including pain) that are associated with major depression.

Summary:
Objective: To assess the effectiveness of paroxetine against somatic symptoms (including pain) associated with depression as determined by the Hamilton Depression Rating Scale Item 13 (HAM-D-13) score.
Method: Pooled data from 30 short-term, double-blind paroxetine studies in major depressive disorder were analyzed using an ANCOVA model.
Results: 2,932 patients received paroxetine and 1,267 received placebo. Similar proportions of patients in both groups had a baseline HAM-D-13 score of 0 (3-4%), 1 (24-28%), or 2 (73-77%). Mean baseline HAM-D-13 scores were 1.70 for paroxetine and 1.73 for placebo. At endpoint, the mean difference versus placebo was significant for paroxetine (~0.17; p<0.0001). A greater proportion of paroxetine patients had a HAM-D-13 score of 0 (31%) at endpoint compared with placebo (22%). More patients with a HAM-D-13 score ≥2 at baseline and 0 at endpoint were seen with paroxetine (29%) than placebo (20%). The significant association (p<0.0001) between a HAM-D-13 score of 2 at baseline and 0 at endpoint, and a CGI score of 1 or 2 suggests that patients with improvement in somatic symptoms are also responders according to CGI.
Conclusions: Paroxetine has demonstrated efficacy in depression. Data shown here indicate that paroxetine improves somatic symptoms (including pain) associated with depression.

NR303  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Organic Catatonia
Conrad M. Swartz, M.D., Department of Psychiatry, SIU School of Medicine, PO Box 19642, Springfield, IL 62794-9642; Daniel Acosta, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify organic catatonia and how its treatment might differ from other types of catatonia.

Summary:
Background: Because of omissions in DSM-IV specifications, it seems appropriate to declare that autonomous character is an essential difference between organic catatonia and delirium.
Objective: Contrast the course of organic catatonia with functional catatonia.
Methods: Review of all known clinical cases of organic catatonia for differences from functional catatonia.
Results: Each case in the series of four identifiable cases suggests that catatonic disorder due to a chronic neurological condition does not respond as well to ECT as functional catatonia does. Every patient showed incomplete response, rapid relapse, or both. Every case of organic catatonia we could identify in the medical literature showed this same pattern.
Conclusions: This evidence suggests that organic catatonia is intrinsically less responsive to ECT than functional catatonia is. Conversely, catatonia resistant to ECT suggests an underlying medical condition. Finally, these cases reinforce that all catatonia is not the same condition.

References:

NR304  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
ADHD in Adults: A Survey of Current Practice in Psychiatry and Primary Care
Supported by Eli Lilly and Company; National Alliance for the Advancement of ADHD Care
Stephen V. Faroone, Ph.D., Department of Pediatric Psychopharmacology, Harvard Medical School, 4F South Main Street, #301, West Bridgewater, MA 02379; Thomas J. Spencer, M.D., Brendan Mondano, M.D., Joseph Biederman, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the referral paths leading to the treatment of adult ADHD and areas in which the care of adult ADHD patients could improve. Additionally, participants should recognize that patterns of diagnosis/treatment differ between psychiatric and primary care.

Summary:
Objective: To determine the referral paths that lead to a diagnosis of adult ADHD and to determine whether diagnosis and treatment differ between psychiatric and primary care practitioner (PCP) settings.
Method: Chart review by 50 psychiatrists and 50 PCPs who examined a total of 537 and 317 medical records of adults diagnosed with ADHD, respectively. Information on other psychiatric disorders, time of onset, treatment, referrals and drug holidays was recorded.

Conclusions: Paroxetine has demonstrated efficacy in depression. Data shown here indicate that paroxetine improves somatic symptoms (including pain) associated with depression.
Results: Forty-five percent of patient records reviewed by psychiatrists and 65% reviewed by PCPs had a previous ADHD diagnosis. Only 25% of ADHD adults were first diagnosed in childhood or adolescence. A diagnosis of ADHD was the initial cause for referral in 80% of psychiatric patients and 50% of PCP patients.

Primary care practitioners were the least aggressive in diagnosing ADHD; the majority of patients were self-referred. In psychiatric and PCP settings, there was a statistical difference in use of pharmacotherapy (91% vs 78%, respectively) and proportion of patients taking drug holidays (24% vs 17%, respectively). Stimulants were the most common pharmacotherapy used (84% of adult ADHD patients).

Conclusions: Data contained within this chart review suggest that adult ADHD is a substantial source of morbidity in psychiatric and PCP settings.

References:
affect the antidepressant responsiveness. This result might be the candidate markers to predict the antidepressant responsiveness.

**Summary:**

**Objective:** There are limitations to predict the antidepressant responsiveness only from the genetic polymorphism of the 5-HTT, so we investigated the genetic polymorphisms of the biogenic amine transporters in Korean depressed patients.

**Methods:** Two hundred four patients with major depressive disorder and 148 normal controls were analyzed for the polymorphisms of the 5-HTT, norepinephrine transporter (NET), and dopamine transporter (DAT) genes. Treatment response to antidepressant medication was defined as a 50% or greater decrease in the HAM-D score at six weeks after medication.

**Results:** We found significant association between antidepressant responsiveness in depressed patients and allelic variations of 5-HTT gene polymorphisms in intron2 and promoter region (p=0.001, p=0.006, respectively). The odds ratio (OR) of long variant (l,l) of intron2 region, short variant (s,s) of the 5-HTTLPR, and G/G allele of NET-8 on the drug response was 2.12 (p=0.01), and 1.79 (p=0.03), respectively. Combination of Intronic (l,l), promoter (s/s) polymorphism of 5-HTT gene and NET-8 polymorphism (G/G) show high specificity than intronic polymorphism only (0.859, p<0.001). And there was an interaction effect between long variant (l/l) of 5-HTTLPR and short variant (s/s) of the intron2 region on the drug response (p<0.05).

**Conclusion:** Results suggest that several allelic variations of biogenic amine transporter genes affect the antidepressant responsiveness. Though other factors may be implicated, it would be the promising tools to predict the antidepressant responsiveness.

**References:**

2. Ogilvie A, et al: Polymorphism in serotonin transporter gene promoter affects the antidepressant responsiveness. This result might be the candidate markers to predict the antidepressant responsiveness.

**NR309 Tuesday, May 20, 12:00 p.m.-2:00 p.m.**

**5HT Transporter Gene Polymorphisms in Depression: Clinical, Functional, and Ethnic Phenotypic Correlates**

Shinn-Won Lim, M.S., Department of Psychiatry, SamSung Medical Center, 50 Ilwon-Dong, Kangnam-Gu, Seoul 135-710, Korea; Min Young Seo, M.D., Hyeran Kim, M.D., Seonwoo Kim, Ph.D., Yun-Hee Chang, Ph.D., Jong-Won Kim, M.D., Doh Kwon Kim, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to recognize the importance of ethnic variation in the study for the genotypic and phenotypic characteristics in patients.

**Summary:**

**Objective:** Serotonin transporter (5-HTT) gene polymorphisms have been linked with response to selective serotonin reuptake inhibitor (SSRI) drugs in depression. We examined in an Asian population the association of antidepressant response to SSRI drugs with two known polymorphisms of 5-HTT gene, and with the functional expression of 5-HTT in platelets.

**Methods:** A total of 57 patients with major depression and 41 normal controls were classified from genomic DNA for two polymorphisms of the 5-HTT gene, and with the functional expression of 5-HTT in platelets.

**Results:** Treatment responders had significantly higher Vmax and Km values than non-responders. Polymorphisms of the 5-HTT gene affect the phenotypic expression of 5-HTT function in platelets, as well as the phenotypic variation of antidepressant response to SSRI drugs. Regardless of ethnic group, high Vmax predicts antidepressant response to SSRI drugs.

**Conclusions:** These results underscore the importance of study of ethnic variation in the evaluation of candidate functional markers and gene markers as predictors of response to treatment of depression.

**References:**

NR310  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Effects of Antidepressant Treatment on Alpha 2-
Adrenoreceptor Function in Depression

Fabrice Duval, M.D., Department of Psychiatry, Centre Hospitalier, 77 Rue du 4eme RSM, Rouffach 68250, France; Marie-Claude Mokrani, Ph.D., Jose Monreal, M.D., Paul Bailey, M.D., Beatrice Hamel, Ph.D., Jean-Paul Macher, M.D.

Educational Objectives:
At the end of this presentation, the participant should be able to understand that some antidepressants induce subsensitivity of alpha 2-adrenoreceptors.

Summary:
Background: The present study aimed to evaluate the effects of chronic administration of amitriptyline (AMI) and fluoxetine (FLU) on alpha 2-adrenoreceptor function in depressed patients.
Method: We investigated the neuroendocrine responses (growth hormone [GH], prolactin [PRL], adrenocorticotropin, and cortisol) to the alpha 2-adrenoreceptor agonist (CLO) on days 0 (drug-free) and 28 in 31 DSM-IV depressed inpatients. Results were compared with those of 24 hospitalized healthy controls.
Results: Compared with controls, depressed patients at baseline showed lower GH and PRL responses to CLO (both p<0.0001). The clinical efficacy of AMI (n=17) and FLU (n=14) was comparable. There were no significant differences in pretreatment or posttreatment hormonal responses to CLO between the patient groups defined by drug taken. Moreover, no statistically significant changes in CLO test responses were induced by the drugs.
Conclusions: Despite different mechanisms of action, AMI and FLU do not restore clonidine's effect on GH and PRL secretion. Although it is known that some antidepressants induce subsensitivity of alpha 2-adrenoreceptors, these results nonetheless suggest that GH and PRL responses to CLO represent a state-independent correlate of depression.

References:

NR311  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Effects of Chronic Exposure With Ziprasidone Versus Haloperidol on Nerve Growth Factor Levels and Choline-Acetyltransferase Immunoreactivity in Rats: A Controlled Study
Supported by Pfizer Inc.

Henry A. Nasrallah, M.D., Associate Dean, College of Medicine, University of Cincinnati Medical Center, 231 Albert Sabin Way, P.O. Box 670559, Cincinnati, OH 45267-0559; Sahebarao Mahadik, Ph.D., Vinay Parikh, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the neuroprotective effects of the atypical antipsychotic Ziprasidone compared to Haloperidol especially in regions that are critical for cognitive performance.

Summary:
Introduction: Atypical antipsychotics (clozapine, risperidone, olanzapine, quetiapine, ziprasidone, and aripiprazole) have been shown to have broader efficacy on positive, negative, mood, and cognitive symptoms in schizophrenia. Atypicals are also associated with significantly lower hypokinesia or akinesia, which are often associated with cognitive dysfunction. Cholinergic activity in the brain is critical for cognitive performance. Nerve growth factor (NGF) plays a protective role in the regulation of cholinergic activity. We hypothesized that chronic exposure to the typical antipsychotic haloperidol will adversely affect NGF levels and choline-acetyltransferase (ChAT) immunoreactivity in rat brains, while the atypical antipsychotic ziprasidone will not.
Methods: Adult male Wistar rats were given oral treatment of haloperidol (HAL) 2.0 mg/kg/day, N=6, ziprasidone (ZIP) 12.0 mg/kg/day, N=6, or vehicle control N=6, for 45 days. NGF and ChAT expression was measured in hippocampus and cortex by immunohistochemistry. Plasma NGF levels were measured by ELISA.
Results: Chronic treatment with HAL, but not ZIP, was associated with markedly reduced NGF and ChAT immunoreactivity in both hippocampal and cortical tissue. Moreover, plasma NGF levels declined in HAL-treated rats (100 ± 11 pg/ml) compared to controls (142 ± 10 pg/ml) or ZIP-treated rats (138 ± 9 pg/ml) (p<0.01).
Conclusions: These data suggest that the adverse neurological effects of HAL may be related to impaired cholinergic activity and reduced NGF levels. Ziprasidone appears to exert a neuroprotective effect by preserving the expression of NGF in brain regions critical for cognitive performance.

References:
cant asymmetry of the optokinetic nystagmus in schizophrenics was noted. Eye movement abnormalities are trait markers of schizophrenia. In this study, the findings further strengthened the anatomical substrate of this psychiatric disorder. The presence of eye movement abnormality in the healthy siblings of patients indicate their latent vulnerability to schizophrenia.

References:

NR313 Tuesday, May 20, 12:00 p.m.-2:00 p.m. Quantitative and Morphologic Analysis of CSF Cells in Schizophrenia
Annabelle Y. Lao, M.D., Department of Neuropsychiatry, Santo Tomas Hospital, University of Santo Tomas Hospital, Manila 1008, Philippines; Aprilyn S. Reyes, M.D., Bernardo J. Conde, M.D., Alejandro E. Arevalo, M.D.

Educational Objectives:
- It is the aim of this study to perform a quantitative and morphologic analysis of the WBC count in the CSF of patients diagnosed with schizophrenia first onset treatment naive and chronic schizophrenics as compared to healthy subjects.

Summary:
Introduction: Several hypothesis have been proposed to explain the etio pathogenesis of schizophrenia, which includes hereditary factors, neurodevelopmental abnormalities, and imbalance in several neurotransmitter system. Recently, there has been a controversy regarding the possible connection between immunologic alteration and schizophrenia.

Objective: It is the aim of this study to perform a quantitative and morphologic analysis of the WBC count in the CSF of patients diagnosed with schizophrenia, first onset treatment naive an chronic schizophrenic as compared to normal healthy subjects.

Methodology: CSF samples from 16 chronic schizophrenics, 15 first-onset schizophrenics, and 10 healthy subjects were collected and sent to pathology for analysis, presence of activated large lymphocytes and macrophages and small lymphocytes were noted.

Results: The Cytological Profile of CSF cells were significantly different from that of the control population. There was also difference in the mean number of cells among groups, chronic schizophrenics have the most number of large activated lymphocytes as compared to first onset and normal controls. The number of macrophages and neutrophils were not statistically significant.

Conclusion: The findings of large activated lymphocytes in the CSF suggest more clearly that immunologic aberration do occur in schizophrenia and also points to a chronic degenerative process.

References:

NR315 Tuesday, May 20, 12:00 p.m.-2:00 p.m. Asperger’s Disorder as a Negative Symptom Disorder: An Open Trial of Risperidone Supported by Janssen Pharmaceutica Products, L.P.
Donna L. Londoño, M.D., Department of Psychiatry and Health Behavior, Medical College of Georgia, 2434 Persimmon Road, Augusta, GA 30912-3800; Elizabeth Sirota, M.D., Jeffrey L. Rausch, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the potential role of the newer atypical antipsychotics in treating the social deficits seen in Asperger’s disorder.

Summary:
Objective: To assess the efficacy of risperidone on negative symptoms and social interaction in patients with Asperger disorder using standardize rating scales.

Method: 12-week, open-trial, pilot study of risperidone in 12 patients, ages six to 18, diagnosed with Asperger’s disorder according to DSM-IV criteria. Patients were screened using the structured clinical interview for diagnosis and the DSM-IV to exclude individuals with psychotic disorders, cluster A personality disorders, and other autistic disorders. Study design progressed from a fixed-dose to a titrated-dose paradigm. Outcome measures were determined at baseline, week 3, 6, 9, and 12 utilizing the Scale...
for Assessment of Negative Symptoms and several secondary outcome measures. Patients were monitored for safety and adverse events throughout the study.

**Results:** Open results of the primary efficacy measure, the Scale for Assessment of Negative Symptoms (SANS), indicated a significant reduction (50%) in negative symptoms at week 6. The modified Asperger Syndrome Diagnostic Scale (ASDS) was examined as a secondary measure. Improvement was noted in all dimensions with significant improvements noted in social functioning at six to nine weeks of treatment. An initial increase in the Abnormal Involuntary Movement Scale (AIMS) during the first three weeks of the trial abated by week nine.

**Conclusions:** This prospective study suggests that the social impairments seen in Asperger’s disorder may respond to risperidone treatment. This is especially enlightening given prior suggestions that pharmacotherapy was unable to target the core deficits of the disorder. Clearly, additional open-trial studies, as well as double-blind, placebo-controlled studies are indicated to confirm these preliminary findings.

**References:**

**NR316** Tuesday, May 20, 12:00 p.m.-2:00 p.m.
**Verbal Memory Deficits in First-Degree Relatives of Patients With Schizophrenia**

Regione Lombardia

Cesare Turrina, M.D., Psychiatry, University of Brescia, P. le Spedali civil, 1, Brescia, 1 25100, Italy; Francesca Gelpi, M.D., Larry J. Seidman, Ph.D., Anna Benato, M.D., Emilio Sacchetti, M.D., Andrea Cesareni, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should recognize which kind of neuropsychological deficits first-degree relatives of schizophrenic patients may have.

**Summary:**

**Objectives:** To evaluate cognitive performance in first-degree relatives of schizophrenic patients, related to the schizotaxia criteria proposed by Tsuang et al. (2000) and to compare it with controls.

**Method:** A random sample of subjects with a schizophrenic first-degree relative was tested. Inclusion criteria were age between 18 and 30, IQ higher than 70, no previous diagnosis of a psychotic illness or drug and alcohol abuse, no CNS diseases. Three cognitive domains were investigated: attention-vigilance, verbal declarative memory, working memory.

**Results:** Eight relatives and six controls were tested. They were five men and nine women, with a mean age of 25.1 yrs. Relatives and controls were not different in mean age and sex distribution. Cognitive performance was significantly worse in relatives of schizophrenic patients on a subscale of the Wechsler Memory Scale (Logical Memory Delayed: 22.5 vs. 28.5-Student, unpaired -2.43, p-.032) and almost significantly worse in another subscale (Logical Memory Immediate: 25.8 vs. 31.7-Student t, unpaired 2.0, p=.069).

**Conclusions:** Our data report a lower cognitive performance in first-degree relatives of schizophrenic patients in verbal memory consistent with other literature. A larger sample is needed to test the construct of the diagnostic criteria for schizotaxia.

**References:**

**NR317** Tuesday, May 20, 12:00 p.m.-2:00 p.m.
**The Increase of Potency of Antidepressant Drugs With Repetitive Transcranial Magnetic Estimulation (rTMS)**

Marco A. Marcolin, Ph.D., Department of Psychiatry, University of Sao Paulo, Angelica Avenue 2466 Con 1232/234, Sao Paulo, SP 012271-100, Brazil; Demetrio O. Rumi, M.Sc., Sergio P. Rigonatti, Ph.D., Moacir A. Rosa, M.Sc., Felipe Fregni, M.D., Carolina M. Santos, M.D., Jose Gallucci, M.D.

**Summary:**

**Introduction:** Repetitive Transcranial Magnetic Stimulation (rTMS) has been found to exert a substantial antidepressant effect in the majority of prior clinical studies. As effect sizes, stimulation conditions and the concomitant use of antidepressants have varied greatly, controversy persists regarding if rTMS could increase the potency of antidepressant effect of antidepressant psychopharmacotherapy.

**Objective:** In the present double-blind randomized controlled study, we investigated whether the use of rTMS with a fixed dose of amitriptyline (10mg/oad) may result in a decrease of onset time of antidepressant action.

**Methods:** Eighteen patients suffering from a moderate to severe major depressive episode (DSM-IV-TR criteria) were randomly assigned to two treatment groups receiving rTMS at different ways. Nine patients (n=9) received standard sham rTMS with a sham coil reproducing all conditions of true rTMS. The other group with 9 patients underwent 20 sessions of 5 Hz rTMS with 1250 stimuli/day (25 trials of 10 seconds per day with 20 seconds intertrials), over the left dorso lateral prefrontal cortex (DLPFC). All patients were evaluated with a blind psychologist that applied the evaluation scales (HAM-D/17 and MADRS). Patients with a major depressive episode (DSM-TV-TR criteria) were randomly assigned to two treatment groups receiving rTMS at different ways. Nine patients (n=9) received standard sham rTMS with a sham coil reproducing all conditions of true rTMS. The other group with 9 patients underwent 20 sessions of 5 Hz rTMS with 1250 stimuli/day (25 trials of 10 seconds per day with 20 seconds intertrials), over the left dorso lateral prefrontal cortex (DLPFC). All patients were evaluated with a blind psychologist that applied the evaluation scales (HAM-D/17 and MADRS).

**Results and Conclusions:** Clinical response (c=50%HAM-D) of depressive symptoms after true rTMS were performed in 83.3% in comparison to sham group that presented 20% of clinical response (p=0.008). Pondering the remission of symptoms (c= 7 pt. HAM-D) were performed in 50% of the true rTMS and 0% concerning the sham group (p=0.015). All the other sample results will be shown.

**References:**

**NR318** Tuesday, May 20, 12:00 p.m.-2:00 p.m.
**Dopamine Transporter Density of Basal Ganglia With IPT SPET of OCD**

Chan-Hyung Kim, M.D., Department of Psychiatry, Yongdong Severance, 146-92 Dogok-Dong, Gangnam-Gu, Seoul 135-270,
Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate the dopaminergic system of the basal ganglia in patients with OCD plays an important role in the pathophysiological mechanism of OCD.

Summary:

Objective: It has been suggested that dopamine was associated with the pathophysiology of obsessive-compulsive disorder (OCD). In present study, we investigated the DAT density of the basal ganglia using iodine-123 labelled N-(3-iodopropen-2-yl)-2β-carbomethoxy-3β-(4-chlorophenyl) tropamine ([123I]IPT) single-photon emission tomography (SPET) in patients with OCD and evaluated the activity of the presynaptic dopamine function in the patients.

Method: Fifteen patients with OCD and 19 normal controls were included. We performed brain SPET 2 hours after the intravenous administration of [123I]IPT and carried out analyses using the obtained SPET data, which were reconstructed for the assessment of the specific/non-specific DAT binding ratio in the basal ganglia. We then investigated the correlation between the scores of Yale-Brown Obsessive-Compulsive Scale (Y-BOCS) and the DAT binding ratio of the basal ganglia.

Results: Patients with OCD showed a significant increased specific/non-specific DAT binding ratio in right and left basal ganglia compared with normal controls. No significant correlation was found between Y-BOCS scores and the DAT binding ratio of the basal ganglia.

Conclusions: Our findings suggest that the dopaminergic system of the basal ganglia in patients with OCD plays an important role in the pathophysiological mechanism of OCD.

References:


NR319  Tuesday, May 20, 12:00 p.m.-2:00 p.m.

In vivo Dopamine D2 Receptor Occupancy With Risperidone Microspheres

Supported by Janssen Pharmaceutica Products, L.P.

Johannes Tauscher, M.D., Gen. Psychiatry, Univ. of Vienna, Waehringr Guertel 18-20, Vienna A-1030, Austria; Georg Weisegger, M.D., Nikolaus Klein, M.D., Susanne Asenbaum, M.D., Siegfried Kasper, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to appreciate effects of typical and atypical neuroleptics on brain areas salient to schizophrenia in adolescents

Summary:

Objective: Risperidone is the first atypical antipsychotic available as injectable depot formulation. This may represent a major improvement of maintenance treatment in schizophrenia. However, up to now there is no published in vivo PET or SPECT study investigating D2 receptor occupancy after i.m. application of risperidone depot. This is of particular interest to estimate equipotent doses at the D2 receptor in comparison to oral risperidone.

Methods: We enrolled 10 patients with a DSM-IV diagnosis of schizophrenia to an open-label treatment with risperidone depot in doses of 25, 37.5, or 50 mg i.m. injections every two weeks for at least three cycles. After that, D2 receptor occupancy was determined by means of [123I]IBZM SPECT.

Results: A preliminary analysis of five patients on 25 mg risperidone depot every 14 days revealed a mean D2 occupancy of 60%.

Conclusions: In previously published neuroreceptor imaging studies, doses of 2–4 mg risperidone daily in first-episode patients, or up to 6 mg/d in chronic patients induced adequate D2 occupancy >65% to treat schizophrenia. These preliminary data suggest that 25 mg risperidone depot every 14 days is equipotent at the D2 receptor to approximately 2 mg/d risperidone administered orally.

References:


NR320  Tuesday, May 20, 12:00 p.m.-2:00 p.m.

FDG-PET and MRI in Never-Previously-Medicated Psychotic Adolescents

Supported by Eli Lilly and Company

Monte S. Buchsbaum, M.D., Department of Psychiatry, Mt. Sinai Medical Center, One Gustave Levy Place, Box 1230, New York, NY 10029; M. Mehmet Haznedar, M.D., Erin A. Hazlett, Ph.D., Jonathan Aronowitz, Jesse Brand, Randall Newmark, Rachel Bloom, B.S.

Educational Objectives:

At the conclusion of this session, the participant should be able to appreciate effects of typical and atypical neuroleptics on brain areas salient to schizophrenia in adolescents

Summary:

Objectives: We test the hypothesis that never-previouslly medicated adolescent schizophrenics might show an improvement in frontal lobe metabolic rate with neuroleptic treatment, a response not yet observed in older, previously medicated patients or with typical neuroleptics.

Methods: We acquired FDG-PET and anatomical MRI in 30 never-previouslly medicated psychotic adolescents (ages 13–20) and 24 age- and sex-matched normal controls. Position emission tomography with 18-F-deoxyglucose was obtained at baseline and after 12 weeks of a randomized double-blind trial of either olanzapine or haloperidol. PET scans were coregistered with the spoiled gradient for accurate anatomical identification of regions of interest traced on the MRI. Brodmann area analysis of MRI and PET used the Perry atlas. Talairach and Tournoux coordinates of striatum and thalamus were selected and the metabolic rate at the center of these structures recorded.

Results: Individuals treated with olanzapine increased relative metabolic rates in the frontal lobe more than the occipital lobe while patients treated with haloperidol did not show an anteroposterior gradient in medication response. These locations were assessed
in the standardized brain and the relative metabolic rate obtained. Ventral caudate increases in relative metabolic rate on haloperidol and shows a small decrease on olanzapine, consistent with lesser D2 effect. Region of the medial dorsal nucleus of the thalamus shows increase in younger patients with both haloperidol and olanzapine but no such increase in older patients.

Conclusions: Adolescent patients may show metabolic normalization with atypical neuroleptics and may show normalization of thalamic metabolism not shown in older patients.

References:
2. Byne W, Buchsbaum MS, Kemether E, Hazlett EA, Shinwari A, Mitropoulou V, Siever LJ: Magnetic resonance imaging of the thalamic mediodorsal nucleus and pulvinar in schizophrenia and schizotypal personality disorder Arch Gen Psychiatry 2001; 58:133–40.

NR321 Tuesday, May 20, 12:00 p.m.–2:00 p.m.
An MRI and PET Study of Stroop's Test in Patients With Major Depression Supported by Lundbeck Pharmaceuticals
Poul Videbech, M.D., Department of Biological Psychology, Psychiatric Hospital, Skovagervej 2, Riskøv 8240, Denmark; Barbara Ravnikilde, Ph.D., Raben Rosenberg, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should understand that the internal capsules may be implicated in the neurobiology of schizophrenia and functional outcome.

Summary:
Objective: The Stroop test (ST) tests the integrity of prefrontal and cingulate functioning. Patients with major depression perform poorly on ST, which points to disturbed prefrontal function in depression.

Methods: Forty-one patients with major depression and 46 age and gender-matched controls were PET scanned during neuropsychological activation with ST. MRIs were used for coregistration and for description of the localization of white matter lesions (WML). The differences between the cerebral blood flow (CBF) of the two scans were mapped for each of the two study groups, and inter-group differences in the activation pattern were calculated on a voxel-by-voxel basis. The patients were followed three to five years to ensure diagnostic stability.

Results: As expected, the patients performed significantly slower on the test and made more errors. The control group activated the left anterior cingulate regions, prefrontal cortices, insula, thalamus, and the cerebellum. No significant differences were found comparing the two study groups. The performance was, however, correlated to the number of white matter lesions (WML) in the frontal lobes and adjacent to the basal ganglia, whereas WML in other locations did not influence the performance.

Conclusions: The results underline the importance of combining PET with MRI when studying depression. Despite poor performance of the patients during ST, the cerebral activation was not significantly altered. The poor performance was explained partly by an increased frequency of WML in fronto-striatal pathways in the depressed patients blocking neurotransmission.

References:

NR322 Tuesday, May 20, 12:00 p.m.–2:00 p.m.
Morphometric Analysis of the Anterior Internal Capsule in Schizophrenia Supported by the Department of Veterans Affairs
Adam M. Brickman, B.A., Department of Psychiatry, Mt. Sinai, One Gustave Levy Place, Box 1505, New York, NY 10029; Zlatin S. Ivanov, M.D., Lina S. Shihabuddin, M.D., Monte S. Buchsbaum, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand that the internal capsules may be implicated in the neurobiology of schizophrenia and functional outcome.

Summary:
Studies that have examined brain morphology in schizophrenia have reliably demonstrated structural deficits in several regions. Three areas in particular—frontal lobe, striatum, and thalampus—have been implicated in the underlying pathophysiology of the disease. However, most structural imaging studies that examine these regions do so in isolation and/or without consideration of their interconnecting white matter. The purpose of this study was to comprehensively examine the morphology of the anterior internal capsule to determine the nature of a possible circuitry abnormality in schizophrenia. Structural 1.5 Tesla MR images were acquired on 146 schizophrenia patients and 42 age- and sex-matched normal controls. Schizophrenia patients were divided into good-outcome (n=54) and poor-outcome (n=52) based on longitudinal assessment of self-care needs. The left and right anterior internal capsules were manually traced in the axial plane on five equidistant slices (dorsal to ventral) by placing 4 landmarks defined by striatal anatomy. Data were analyzed with mixed factorial analysis of variance, with Diagnosis (3: good-outcome, poor-outcome, normal controls) as a between subjects factor, and Slice (5: dorsalmost to ventralmost) and Hemisphere (2: left, right) as within subjects factors. A significant main effect of Diagnosis, F (2, 145)=6.25 p=0.002, revealed that poor-outcome patients had significantly smaller internal capsule size compared to normal controls and good-outcome patients, who were similar to each other. This effect was modified by a significant Diagnosis by Slice interaction, F(2, 580)=2.20 p=0.026, indicating that poor-outcome patients had particularly reduced internal capsule size at more ventral levels than dorsal levels. The findings suggest that cortical-striatal-thalamic connectivity abnormalities, particularly at ventral levels, may be implicated in the pathophysiology of schizophrenia and of functional outcome.

References:

NR323 Tuesday, May 20, 12:00 p.m.–2:00 p.m.
Basal Ganglia and Thalamus Volumes in Bipolar Spectrum Illnesses
M. Mehmet Haznedar, M.D., Department of Psychiatry, Mount Sinai Hospital, One Gustave Levy Place, Box 1505, New York,
Educational Objectives:
At the conclusion of this presentation, the participant will have furthered his knowledge about structural alterations of the basal ganglia and thalamus in bipolar spectrum illnesses, and their clinical implications.

Summary:
Neurons in the basal ganglia innervate areas of cerebral cortex involved in higher cognitive functions, and this connection occurs via the thalamus. In patients with bipolar disorder while functional neuroimaging studies reported alterations in the metabolic activity of the basal ganglia, specifically in caudate nucleus, the structural imaging findings were inconclusive. In the current study, we measured the basal ganglia and thalamus volumes on the MRI scans of 41 patients with bipolar spectrum (BS) illnesses (bipolar type I=17, bipolar type II=7, cyclothymia=16) and 36 sex- and age-matched control subjects. MRI axial acquisitions were done with a 1.5 Tesla GE Signa 5x system (3D volume-gradient recalled acquisition in steady state [spoiled GRASS, TR24, TE5, flip angle 40 degrees, contiguous 1.2-mm slices]). Two researchers, without knowledge of diagnosis, outlined the caudate, putamen and the thalamus on contiguous axial MRI slices. BS patients as a single group did not differ from controls in any of the structure volumes. However, subgroups of BS patients had volumetric changes in the thalamus and basal ganglia compared to controls (ANOVA, GroupxHemispherexRegion, F=2.29, df=6.00, 144.00, p=0.038). The clinical implications of these findings will be discussed.

References:

NR324 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Hippocampus Volume and 3-D Metabolic Mapping in Drug-Naive Schizophrenia Patients
M. Mehmet Haznedar, M.D., Department of Psychiatry, Mount Sinai Hospital, One Gustave Levy Place, Box 1505, New York, NY 10029-6574; Ingrid Vasilii, M.D., Erin A. Hazlett, Ph.D., Elizabeth Licalzi, B.A., Monte S. Buchsbaum, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will have furthered his knowledge of hippocampus dysfunction in schizophrenia and its clinical implications.

Summary:
The hippocampus is involved in the memory and emotion and is implicated in schizophrenia. Compared with controls MRI studies show reduction in the volume of hippocampus in patients with schizophrenia, while functional imaging studies report hypometabolism. In the current study, we examined changes in the volume and glucose metabolic rate in the hippocampus of 24 never-medicated patients with schizophrenia (mean age=25.1) and 24 controls (mean age=27.2). MRI axial acquisitions were done with a 1.5 Tesla GE Signa 5x system (3D volume-gradient recalled acquisition in steady state [spoiled GRASS, TR24, TE5, flip angle 40 degrees, contiguous 1.2-mm slices]). Two researchers, without knowledge of diagnosis, outlined the hippocampus on contiguous MRI slices (intertracer interclass correlation coefficient=0.82). Both left and right hippocampus volumes were significantly reduced in the drug naive patients (t=5.88, df=38.2, p<0.01, t=6.48, df=46, p<0.01, respectively). After co-registration with position emission tomography, significance probability mapping was employed for group comparison on relative glucose metabolic rate (rGMR). The drug naive schizophrenia patients had lower rGMR in the right hippocampus compared with controls (one tailed t=1.68, p<0.05). Clinical correlations of metabolic and structural findings will be discussed.

References:

NR325 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Cingulate Gyrus Gray and White Matter Volumes in Drug Naive Schizophrenia Patients
M. Mehmet Haznedar, M.D., Department of Psychiatry, Mount Sinai Hospital, One Gustave Levy Place, Box 1505, New York, NY 10029-6574; Ingrid Vasilii, M.D., Erin A. Hazlett, Ph.D., Elizabeth Licalzi, B.A., Monte S. Buchsbaum, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will have furthered his knowledge of cingulate gyrus dysfunction in schizophrenia and its clinical implications.

Summary:
The cingulate gyrus is involved in the expression and decoding of affect, attention, memory, higher executive functions. Postmortem studies of patients with schizophrenia report cytoarchitectural changes in the anterior cingulate gyrus and functional imaging studies show hypometabolism. In the current study, we examined the volumetric changes in the cingulate gyrus of 20 never-medicated patients with schizophrenia (mean age=24.4) and 24 controls (mean age=26.7). MRI axial acquisitions were done with a 1.5 Tesla GE Signa 5x system (3D volume-gradient recalled acquisition in steady state [spoiled GRASS, TR24, TE5, flip angle 40 degrees, contiguous 1.2-mm slices]). Two researchers, without knowledge of diagnosis, outlined the cingulate gyrus on contiguous axial MRI slices (intertracer interclass correlation coefficient=0.87). We obtained a threshold for gray-white matter differentiation from histograms on the MRI’s of each subject and calculated the gray-white matter volumes separately. For the size comparison we divided the cingulate gyrus into five Brodmann areas (23, 24, 24’, 23, and 29) following Devinsky, et al. A significant ANCOVA (brain volume as co-variate) GroupxRegionxGray–White–Matter interaction was observed (p=0.006). Patients with schizophrenia had a reduction in the gray matter volume of the left and right anterior cingulate 24’ (t=2.20, df=42, p=0.033, t=3.19, df=42, p=0.003, respectively).

References:
NR326  Tuesday, May 20, 12:00 p.m.-2:00 p.m.

fMRI Response to Negative Pictures in Depression Before and After Treatment Imaging
Supported by Indiana University School of Medicine, the 21st Century Fund for Excellence in Brain

Amit Anand, M.D., Department of Psychiatry, Indiana University, UH 3124 University Boulevard, 550N, Indianapolis, IN 46202; Mark J. Lowe, Ph.D., Yang Wang, M.D., Lubna Bukhari, M.D., Vincent P. Mathews, M.D.

Educational Objectives:
At the conclusion of this session, the participant should learn about pathophysiology and treatment of major depression

Summary:
Objective: We investigated the differential fMRI response to negatively valenced pictures, in depressed patients before and after treatment and in healthy control subjects.

Methods: Patients satisfying DSM-IV criteria for Major Depression, 25-item HAM-D score > 18 and healthy subjects underwent a functional Magnetic Resonance Imaging (fMRI) (1.5 T) session in which they were shown alternate blocks of negative and neutral pictures derived from the International Affective Picture System (IAPS). Patients were scanned again, after 6 weeks of treatment with sertaline up to 200 mg po qd, with a second set of pictures. Analysis of imaging data: Brain areas that were activated were inspected with particular emphasis on the putative limbic-cortical-thalamic-striatal mood regulating circuit (MRC).

Results: Preliminary data from four patients (1M, 3F), 25±4 yrs, 25-item HAM-D scores: 34±9 before and 9±4 after treatment, and four healthy subjects (2M, 2F), 28±4 yrs, has been analyzed. Depressed subjects before treatment showed increased activation in the anterior cingulate cortex (ACC), striatum and amygdala compared to healthy subjects. After treatment, patients had decreased activation of the MRC compared with both depressed as well as healthy subjects.

Conclusion: fMRI showed increased activation of the MRC in depressed subjects compared to healthy subjects in response to negative pictures. After successful treatment the MRC areas were less activated in response to negative visual stimulus.

References:

NR327  Tuesday, May 20, 12:00 p.m.-2:00 p.m.

Blood Flow in the Ventrolateral Prefrontal Cortex in Patients With SAD Positively Correlates With Mood Improvement After One Week of Light Treatment Supported by the National Institute of Mental Health, the National Institute of Health, and the Department of Health and Human Services

Teodor T. Postolache, M.D., SBR, NIH/NIMH/NHI, 10 Center Drive, Room 35231, Bethesda, MD 20892; Jeffrey R. Mathews, M.D., Brenda E. Benson, M.S., Erick H. Turner, M.D., Alvaro Guzman, M.D., Norman R. Rosenthal, M.D., Wayne C. Drevets, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the classification of functional neuroimaging findings in affective disorders as contributory and compensatory, be sensitized to the possibility that certain PET findings might predict antidepressant response.

Summary:
Objective: We previously reported that bright-light treatment, an effective antidepressant in seasonal affective disorder (SAD), acutely activates the ventrolateral prefrontal cortex (VLPFC). We now hypothesized that mood improvement with light treatment will correlate with baseline physiological activity in the VLPFC.

Methods: Cerebral blood flow (CBF) was measured using O water and PET with arterial input functions in 15 SAD subjects (age 45.8±9.1, 10 females and five males), clinically depressed. Three scans were performed at baseline (dim light) at 12-minute intervals. First treatment was administered with a light device suspended above the scanner and delivering in average 8,200 lux at the level of the eye (total exposure of one hour). Afterwards, light treatment consisted of 10,000 lux for 45 minutes bid. SIGH-SAD ratings were repeated after the first session of light treatment and after one week of light treatment. We performed simple correlations between average rCBF in the VLPFC (divided by global CBF) and change in depression scores at one hour and one week.

Results: Changes in SIGH-SAD scores after one week, but not after one hour, of bright-light treatment, positively correlated with baseline rCBF in the VLPFC (p<0.001).

Conclusions: Baseline rCBF in VLPFC, brain region involved in modulation of the emotional and behavioral expression of depression, could represent a clinical predictor of the antidepressant effect of bright-light.

References:

NR328  Tuesday, May 20, 12:00 p.m.-2:00 p.m.

Differences in Brain Blood Flow Between High and Average Creative Subjects

Rosa A. Chavez, M.D., Psiquiatría, Instituto Nacional, Calz Mexico-Xochimilco 101, Mexico City De, DF 14370, Mexico; Ariel Graff-Guerrero, M.S.C., Juan C. García-Reyna, M.D., Victor Vaugier, M.Sc., Walfred Rueda, M.D., Carlos Cruz, Ph.D., Jonathan Eakle, M.Ed.

Educational Objectives:
At the conclusion of this session, the participant should be able to compare the brain blood flow between individuals with high and average creativity index during the performance of the Torrance Test (verbal) of Creative Thinking.

Summary:
Objective: To compare the cerebral blood flow (CBF) between subjects with "high" and "average" creativity indexes (CI) during administration of the Torrance Test of Creative Thinking (TTCT).

Method: Two groups (n = 6 respectively) were formed from an adult cohort using CI as the selection criteria. Two TTCT verbal tasks were used. The first task was a warm-up activity, whereas the second was administered after intravenous injection of the radiotracer Tc99m-ECD. CBF images were obtained by SPECT. Contrast between groups were made by ANCOVA. The significant threshold for a priori regions (fronto-temporal) was Z > 3.25; clusters formed by >10 voxels were analyzed with SPM99.

Results: Significant CBF differences between groups were found. Highly creative subjects had increased activation in: (a) right and
left middle temporal gyrus, Brodmann areas 20 and 21, (b) right uncus, Brodmann area 36, (c) left and right cerebellum, culmen, (d) left parahippocampal gyrus, (e) hypothalamus, and (f) left anterior cingulated.

Conclusions: Creative thinking involves greater activity in right and left temporal lobes, confirming interhemispheric interactions previously found. Furthermore, this study points out the relevant participation of right and left cerebellum and limbic system structures that have been associated with memory processes and subjective difficulty.

Acknowledgments: To CONACyT, and to the Program of Incubation of Talents FUNSALUD.

References:

**NR329**

**Tuesday, May 20, 12:00 p.m.-2:00 p.m.**

**Brain Processing of Visual Affective Cues in Schizophrenia: An fMRI Study**

**Supported by Pfizer Inc.**

William H. Wilson, M.D., Department of Psychiatry, OR Health and Science University, UHN-79, 3181 SW Sam Jackson Pk. Road, Portland, OR 97239; Douglas A. Bigelow, Ph.D.

**Educational Objectives:**
- At the conclusion of this session, the participant should recognize patterns of brain metabolic activity that are associated with viewing pleasant and unpleasant pictures by individuals with schizophrenia and by normal control subjects and discuss the relevance of this to clinical symptoms of anhedonia, affective blunting, and social withdrawal.

**Summary:**

**Background:** Symptoms of schizophrenia such as affective blunting and anhedonia are associated with abnormal response to affective stimuli, and may be due to anomalous neuronal processing of these stimuli. This study compares brain metabolic activity during the experience of pleasant and unpleasant pictures in subjects with schizophrenia and normal controls.

**Methods:** Five young adults with schizophrenia and five matched controls were scanned using Blood Oxygen Level Dependent (BOLD) fMRI while observing pleasant, unpleasant, and neutral pictures and rating the pleasantness of the pictures. Analysis includes within-subject comparisons of brain activity while viewing pleasant and unpleasant pictures and between-subject comparisons for subjects with schizophrenia and controls.

**Results:** Subjects with schizophrenia rated the pleasantness of the pictures with more variance from population norms than did controls. Subjects with schizophrenia and controls had statistically significant differences in brain activation of cortical and subcortical areas when viewing pleasant compared with unpleasant pictures. There appear to be differences in patterns of activation between subjects with schizophrenia and controls. Statistical analysis and brain maps will be presented.

**Conclusion:** fMRI is a viable means for investigating affective stimulus processing in schizophrenia. Future studies will focus on effects of pharmacological treatment in processing affective stimuli.

**References:**

**NR330**

**Tuesday, May 20, 12:00 p.m.-2:00 p.m.**

**Quality of Life Post-MI: Influence of Depression and Effect of Sertraline Treatment**

**Supported by Pfizer Inc.**

J. Robert Swenson, M.D., Dept of Psych, Ottawa General Hosp, 501 Smyth Rd, Ottawa, ON K1H 8L6, Canada; Alexander H. Glassman, M.D., Karl Swedberg, M.D., David Barton, M.D., Louis T. van Zyl, M.D., Les M. Forman, M.D., Christopher O’Connor, M.D.

**Educational Objectives:**
- At the conclusion of this session, the participant should have increased the knowledge about the impact of depression on QOL and functioning in patients with MI.

**Summary:**

**Objective:** To evaluate the efficacy of sertraline in improving QoL and functioning, in a sample (n=369) of patients hospitalized with acute coronary syndrome (ACS) and diagnosed with major depression.

**Method:** After a two-week, single-blind, placebo lead-in, patients were randomized to 24 weeks of double-blind, placebo-controlled treatment with flexible doses of sertraline. Depression status was assessed by HAM-D and CGI-I, and quality of life and functional status were assessed using the Quality of Life, Enjoyment, and Satisfaction Scale (Q-LES-Q), and the SF-36. Severe depression was defined as HAM-D>18 and two or more episodes of major depression.

**Results:** Severe baseline impairment was found in Q-LES-Q and SF-36 scores for the total sample. A multivariate regression analysis identified depression as the strongest predictor of baseline QoL impairment (partial r, –0.37; p = 0.001). In the more severely depressed subgroup, sertraline showed a significant advantage over placebo on improvement from baseline in the SF-36 Mental Component Summary score and on the Q-LES-Q overall life satisfaction and medication items, and a trend on the total Q-LES-Q score.

**Conclusion:** Depression has a substantial negative impact on QoL and functioning in patients hospitalized for ACS. Antidepressant treatment with sertraline resulted in improved mood, and was associated with clinically meaningful improvement in multiple domains of QoL in patients with ACS and severe depression.

**References:**

**NR331**

**Tuesday, May 20, 12:00 p.m.-2:00 p.m.**

**New-Onset Psychiatric Symptoms in a Cohort of Inner-City Traumatic Injury Patients**

**Supported by Langeloth Foundation**

Peter J. Weiden, M.D., Department of Psychiatry, SUNY Health Science Center at Brooklyn, 450 Clarkson Avenue, Brooklyn,
The typical PES patient, assess the impact of the frequent user (FU) on the mental health system for many patients and the only source of treatment for some. The latter patients frequently make repeated visits to the PES, constituting a frequent user (FU) population. Previous FU reports have been inconsistent in both prevalence (from 5 to 55% of the PES population) and clinical characteristics.

The objective of this study was to more precisely define and characterize FUs using a prospective, standardized method of data acquisition.

**Methods:** Clinical and demographic data (up to 60 variables) of patients visiting the PES of a large metropolitan hospital were collected prospectively using an electronic database from July 1, 1996 to December 31, 2000. A patient log of eight variables (predating the study) was subsequently added to the database for a total prospective observation time of certain variables of over 15 years.

**Results:** 14,826 patients made 29,577 PES visits during this period. Using 11 visits or more as a FU criteria, 292 patients (making 6080 visits) were so identified. The majority made between 11 and 29 visits, with only two patients making over a 100 visits during the 15-year period. Compared with the typical PES patient, FUs were more likely female and more likely to have a primary diagnosis of chronic psychosis. No marked differences in personality disorders or substance abuse diagnoses were found between the two groups. Other clinical/demographic variables and FU patterns of PES use will be presented. A comparison with data obtained in three other PESs, where simultaneous data acquisition has been underway since September 02 will be discussed.

Conclusion: PES-FUs represent a substantial clinical and financial burden to the mental health system. The predominance of chronic psychotic patients within this population suggests avenues whereby a combined pharmacological and psychosocial approach may help alleviate this important phenomenon.

**References:**


**NR332**

**Tuesday, May 20, 12:00 p.m.-2:00 p.m.**

The Frequent User of the Psychiatric Emergency Service: Clinical and Demographic Characteristics Over a 15-Year Observation Period

Yves Chaput, M.D., Reed Pavilion, Douglas Hospital, 6875 Boul. LasSalle, Verdun, Quebec H4H1R3, Canada; Edith Labonte, M.D., Mario Fortier, R.N., Lucie Beaulieu, M.D., Marie-Josee Lebel, R.N.

**Educational Objectives:**

Differentiate the clinical profile of the frequent user from that of the typical PES patient, assess the impact of the frequent user on the mental health system and determine possible clinical solutions to this phenomenon.

**Summary:**

The psychiatric emergency service (PES) is a major point of entry into the mental health system for many patients and the only source of treatment for some. The latter patients frequently make repeated visits to the PES, constituting a frequent user (FU) population. Previous FU reports have been inconsistent in both prevalence (from 5 to 55% of the PES population) and clinical characteristics.

The objective of this study was to more precisely define and characterize FUs using a prospective, standardized method of data acquisition.
References:


NR334 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
A Prospective Trial of Sertraline for Chronic Dizziness With Anxiety Supported by Pfizer Inc.

Jeffrey P. Staab, M.D., Department of Psychiatry, University of Pennsylvania, 3400 Spruce Street, Room F11 015, Philadelphia, PA 19104; Michael J. Ruckenstein, M.D., Jay D. Amsterdam, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to (1) effectively treat dizziness associated with anxiety disorders, and (2) understand the potential benefits of SSRIs for treating a syndrome of chronic dizziness and motion hypersensitivity that may be unrelated to psychiatric disorders.

Summary:
Objectives: We previously found SSRIs to be effective for treating chronic dizziness associated with anxiety and depression. To extend these preliminary findings, we conducted a prospective trial of sertraline in patients with a syndrome of chronic dizziness, motion hypersensitivity, and anxiety.

Methods: Twenty patients with chronic dizziness were enrolled in a 16-week, open-label trial of sertraline. Fifteen had panic, phobic, or generalized anxiety disorders. Five had no DSM-IV Axis I diagnosis. None had active neurologic conditions. Sertraline was started at 25 mg/day, and titrated to optimal benefit (maximum 200 mg/day). Dizziness, functional impairment, and psychological distress were measured with the Dizziness Handicap Inventory (DHI) and Brief Symptom Inventory (BSI-53), psychiatric outcomes with standardized anxiety and depression scales. Treatment effects on the DHI and BSI-53 were examined with a repeated measures, multivariate, analysis of variance (MANOVA), using last observations carried forward, controlling for anxiety and depression.

Results: Twelve patients (60%) completed the trial. Four withdrew for adverse events. Four were excluded for medical conditions or protocol noncompliance. We observed significant treatment benefits on the DHI and BSI-53, even after controlling for baseline anxiety and depression and changes in these symptoms.

Conclusions: Sertraline reduced chronic dizziness and psychological distress in this patient population. Its benefits extended beyond expected improvements in anxiety and depression.

References:

NR335 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Weight Gain and Antipsychotics: Focusing on the 5-HT2C Receptor

Daniel J. Mueller, M.D., Psychiatry, CAMH, 250 College Street, Neurogenetics R30, Toronto, ON M5T 1R8, Canada; Vincenzo De Luca, M.D., Pal Czobor, Ph.D., Jan Volavka, M.D., Jeffrey A. Lieberman, M.D., Vincenzo S. Basile, B.Sc., James L. Kennedy, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to assess the potential role of 5-HT2C gene polymorphisms related to antipsychotic induced weight gain in genetically susceptible individuals. The study on the serotonin 5-HT2C gene may serve as good example to illustrate benefits and pitfalls in pharmacogenetic studies.

Summary:
Introduction: The 5-HT2C receptors have been hypothesized to represent important modulators in feeding behaviour. Evidence was based on the observation that knock-out mice for the 5-HT2C receptor gene develop obesity and that many atypical antipsychotics with potent 5-HT2C antagonism may induce weight gain in susceptible individuals. Pharmacogenetic studies focusing either on the Cys23Ser polymorphism or on the 759C/T promoter polymorphism of the X-linked 5-HT2C receptor gene revealed mainly negative or controversial results.

Methods: We analyzed both polymorphisms in 59 inpatients who participated in the ‘CHOR’ study. Subjects were either treated with clozapine, haloperidol, olanzapine, or risperidone. Weight gain was assessed over a time course of 14 weeks.

Results: Patients gained an average of 4.4 kg (SD=6.2kg). ANOVA analysis revealed a significant association between weight gain and the wild-type allele of the Cys23Ser polymorphism (F[2,51]=3.92, p=.026) but no significant association for the −759C/T polymorphism (F[1,57]=1.87, p=.17). The observed effect of the Cys23Ser polymorphism was exclusively driven by females (F[2,8]=12.66, p=.003; males: F[1,41]=.21, p=.64).

Conclusion: These findings suggest that the Cys23Ser polymorphism may predict weight gain in females treated with antipsychotics. However, due to our limited sample size, these findings should be interpreted as preliminary. Replication studies in larger samples are encouraged.

References:

NR336 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Neuropsychiatric Characteristics of SHE in Patients With Liver Cirrhosis

Seung-Ho Ryu, M.D., Psychiatry, Konkuk University Hospital, 1 Hwayang-dong, Gwanjin-gu, Seoul 143-814, Korea; So-Young Lee, M.D., Jin-Se Kim, M.D., In-Kwa Jung, M.D.

Educational Objectives:
This study aimed for the early diagnosis and management of subclinical hepatic encephalopathy in patients with liver cirrhosis.

Summary:
This study was designed to elucidate the psychiatric characteristics, nature of the neuropsychological deficits, and the role of somatosensory-evoked potentials (SEP) associated with subclinical hepatic encephalopathy (SHE) in patients with non-alcoholic liver cirrhosis.

Beck Depression Inventory (BDI), State Trait Anxiety Inventory (STAI), and Health-related Quality of Life Questionnaire (HQLQ) were administered to the 41 non-encephalopathic liver cirrhosis...
patients (NELC) group and 31 carefully matched normal controls. A short, but comprehensive, cognitive test was also conducted. After the NELC group was divided into two groups, SHE group and non-SHE, median nerve evoked cortical responses were recorded for latencies of N13, P16, N20, P25, N30, P45, N65, and P95. Also responses for N13–N20 interpeak latency (IPL) and N20–N65 IPL were recorded.

There were significant differences between the NELC group and normal controls on BDI, trait anxiety scales in STAI, and almost all HQLQ (p<0.05). The NELC group exhibited poor performance in DSST, TMT A, and TMT B compared with normal controls (p<0.05). As 17 NELC patients had abnormal cognitive test results, 41.5% of cirrhotic patients had SHE. In SEP assessment, NELC group with SHE and without SHE had higher N20–N65 IPL, and only NELC group with SHE had higher N65 latency compared with normal controls (p<0.05).

This study suggests that the patients with liver cirrhosis exhibit relatively selective deficits in complex attentional and fine motor skills, with preservation of general intellectual ability, memory, language, and visuospatial perception. And DSST, TMT A, and TMT B are useful screening tests for the detection of SHE. It is expected that late components and N20–N65 IPLs of SEP are helpful in the assessment of SHE.

References:

NR337 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Psychological Evaluation of Patients With a Thyroid Nodule and Surgery
Vladimir M. Diligenski, M.D., Department of Psychiatry, KBC Dr Dragisa Mišovic, NH Milana Tepica 1, Belgrad, YU 11000, Yugoslavia; Zorica N. Caparevic, Ph.D., Nada S. Kostic, Ph.D., Gradimir Bojkovic, M.D., Dragos S. Stoanovic, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the therapeutic potential of tiagabine for the treatment of GAD.

Summary:
Objective: Gamma-aminobutyric acid (GABA), the main CNS inhibitory neurotransmitter, plays a key role in anxiety and sleep. Tiagabine, a selective GABA reuptake inhibitor (SGRI), enhances normal GABA tone and has been shown to reduce anxiety and improve sleep quality in preliminary reports. This study evaluated tiagabine in patients with generalized anxiety disorder (GAD).
Method: This 10-week, open-label, positive-controlled, blinded-rater study randomized patients to tiagabine or paroxetine. Tiagabine was initiated at 4 mg/day bid (AM/PM) and paroxetine at 20 mg (evening) during Week 1. Doses were increased for optimum rater study randomized patients to tiagabine or paroxetine. Tiagabine and paroxetine significantly reduced anxiety (endpoint: HAM-A, both P<0.0001; and P<0.001, respectively) compared with baseline. Tiagabine and paroxetine were well tolerated. Few patients discontinued due to adverse events (n=1, tiagabine; n=2, paroxetine).

Conclusion: Tiagabine and paroxetine improved GAD and sleep quality. Tiagabine may represent a therapeutic option in the treatment of anxiety.

References:

NR338 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Mental Disorders in Long-Term Survivors of Testicular Cancer
Supported by the Norwegian Cancer Society, Norwegian Foundation for Health and Rehabilitation, and Aker University Hospital
Carl F. Haaland, M.D., Department of Psychiatry, Aker Hospital, Sognsunnvseien 21, Oslo 0320, Norway; Alv A. Dahl, M.D., Sophie D. Fossa, Ph.D.

Educational Objectives:
Prevalences of mental disorders in long-term survivors of testicular cancer are generally low, and mostly lower than prevalences in the population. The most prevalent disorder is depression. Screening tests for anxiety, depression and impact of event, will catch a high proportion of these cases.

Summary:
Introduction: Testicular cancer (TC) is the most frequent malignant disease in young men, and due to improved treatment, 95% survive. There is no systematic knowledge about the prevalences of mental disorders in long-term survivors.
Hypothesis: Increased prevalence of mental disorders in men who have survived a life-threatening illness.
Method: Of a national, consecutive sample, 1,405 of 1,838 survivors took part in the study. Mean age at follow-up was 44.7 years, and mean follow-up time was 11.0 years (range 5–21 years). Questionnaires for anxiety, depression, and impact of event were used for screening of possible cases with mental disorders. Those positive were invited to a psychiatric examination.
Results: A total of 213 survivors (15%) showed positive screening for mental disorders. Among the 172 who met for examination, the MINI interview found that 134 survivors (9.5%) had at least one mental disorder, a depressive disorder was observed in 100 (7%), an anxiety disorder in 77 (5.4%), and a substance use disorder in 45 (3.2%).
Discussion: Except for depression, these prevalences were lower than found in the population. These results did not support our hypothesis about the mental effects of life-threatening illness. Some of the prevalence differences observed might be due to issues of methodology.

References:
NR339  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Quality of Life in Patients With BDD
Supported by the National Institute of Mental Health
Katharine A. Phillips, M.D., Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI 02906, William Menard, B.A.

Educational Objectives:

At the conclusion of this presentation, the participant should be familiar with quality of life in patients with body dysmorphic disorder.

Summary:

Introduction: Only one study has examined quality of life (QOL) in BDD. That study (n=62) used the SF-36 and assessed primarily subjects in a pharmacotherapy trial. No study has used other QOL measures or assessed a more broadly representative sample of individuals with BDD.

Methods: 97 consecutive subjects with current DSM-IV BDD (74% female, mean age=32.7 ± 11.5) participating in a study of the course of BDD completed the SF-36; 59 of these subjects also completed the Short and Long Forms of the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q). These scales are reliable, valid, and widely used self-report measures of QOL. The Q-LES-Q Short Form has a total score, whereas the Long Form and SF-36 each have eight individual domain scores. Scores were compared with norms for nonclinical community samples for the Q-LES-Q and SF-36, and to norms for clinical depression for the SF-36.

Results: On the Q-LES-Q Short Form, BDD subjects had a mean converted score of 49.9% ± 17.5%, which was 2.1 standard deviation units lower (poorer) than the community sample score of 78.1% ± 13.7%. 96% of community subjects scored better than the mean BDD score. On the Q-LES-Q Long Form, scores across all domains were a mean of 2.1 (range 1.4–3.0) standard deviation units poorer than community norms. SF-36 mental health-related QOL scores were approximately 1.8 standard deviation units lower (poorer) than U.S. population norms and .4 units poorer than norms for depression. SF-36 physical health-related QOL scores were approximately .4 standard deviation units poorer than U.S. population norms and .3 units better than norms for depression. More severe BDD symptoms were significantly associated (p<.01) with poorer QOL for the Q-LES-Q Short Form (r=-.40, p=.004), for five Q-LES-Q Long Form domains, and for all SF-36 mental health domains.

Conclusion: Individuals with BDD have markedly poor quality of life.

References:

NR340  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Survey of Cardiologists About Relationship of CAD and Mood Conditions
Supported by Pfizer Inc.
Michael Blumenfeld, M.D., Department of Psychiatry, New York Medical College, RMN314 Behavioral Health Center, Valhalla, NY 10595; Robert Feinstein, M.D., Barbara Orlowski, Ph.D., William Frishman, M.D.

Educational Objectives:

After reviewing this poster the participant would better understand the beliefs and practices of cardiologists in regard to the relationship between CAD and mood conditions such as depression and anxiety as well as their preferred choices for CME on this subject

Summary:

Introduction/Hypothesis: Research suggests relationship between CAD and mood conditions. Do cardiologists understand this relationship and demonstrate it in their practice? What is preferred CME choice?

Method: 2,045 NYS cardiologists were sent a six-page questionnaire.

Results: 337 (18%) replied, predominantly male, not rural with those practicing 15+ years responding 2–3x other age groups. Cardiologists practicing 5–10 years are less likely to believe depression is independent variable for CAD although most thought it was. Over 6x as many cardiologists don’t refer more than 10% of patients with resting chest pain for psychological care than those that do. Most cardiologists are comfortable making diagnosis of depression but don’t use DSM or other tools. Most treat depression and anxiety. Men, suburban, older and voluntary academics are more like to do so. (all statistically significant) Sertraline was first choice antidepressant of 40% of 201 who treat paroxetine (26%), fluoxetine (16%), citalopram (11%), bupropion (6.5%) and venlafaxine(4%). Grand Rounds is preferred CME choice followed by annual meetings and CD-ROM which were more popular than audiotape, reports, handouts, internet or videotape. Pharmaceutical reps were last choice. The same preference order occurred when looking at first and second choices combined.

Graphic elaboration of this and additional data will be presented.

References:

NR341  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Sexual Side Effects During Antipsychotic Treatment for Schizophrenia
Supported by Eli Lilly and Company
Martin Dossaenbach, M.D., Lilly Research, Eli Lilly GESEMBH, Barngasse 40–42, Vienna A-1030, Austria; Linda Levitt, Ph.D., Rafael Baez, M.D., Jason M. Boland, B.Sc., Nestor Andrade, M.D., Jose Cabrejes, M.D., Humberto Molinello, M.D.

Educational Objectives:

Sexual dysfunction in patients treated with antipsychotic medication is a common but widely under-diagnosed problem. A lack of recognition of sexual problems may in part be due to doctors who do not routinely enquire about them and also due to the reluctance of patients to talk about.

Summary:

Objective: Report side effects associated with sexual functioning in patients with schizophrenia following six months of antipsychotic treatment.

Method: Three-year, prospective observational study of health outcomes associated with antipsychotic medication in outpatients treated for schizophrenia. Patients were enrolled if they initiated or changed antipsychotic medication.

Results: At baseline, 51% of patients reported sexual dysfunction (27% some problems, 24% unable to perform sexually) while 42% reported sexual dysfunction at six months (25% some problems, 17% unable). There was a significant difference (p<0.001)
in the frequency of patient-reported sexual dysfunction compared with psychiatric-reported events related to sexual function. The percentage of patients experiencing impotence/sexual dysfunction, loss of libido, amenorrhea, galactorrhea, and gynecomasia was significantly less (<p>0.0001) in patients prescribed prolactin-sparing compared with prolactinelevating antipsychotics. In particular, patients prescribed olanzapine had a significantly (p>0.0001) lower incidence of impotence/sexual dysfunction, loss of libido, and amenorrhea compared with risperidone or haloperidol-treated patients.

**Conclusion:** Problems related to sexual functioning are common in patients receiving antipsychotics. Patients suffer from sexual dysfunction more frequently than diagnosed by psychiatrists. Olanzapine is superior to risperidone and haloperidol in terms of sexual function side effects and may offer an alternative therapy for patients receiving antipsychotic treatment who present with these symptoms.

**References:**


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**NR343**

**Tuesday, May 20, 12:00 p.m.-2:00 p.m.**

**Quality of Life and Psychiatric Diagnosis in Grade III Obesity**

*Flavia C. Campos, R.F., Psychiatric Institute, Fed University of Rio De Janeiro, Visconde de Piraja 407/702 Ipanema, Rio de Janeiro, RJ 22410-003, Brazil; Jose C. Appolinario, M.D., Antonio E. Nardi, M.D.*

**Educational Objectives:**

At the end of this session, the participant should be able to recognize that grade III obesity patients displayed a high prevalence of psychiatric diagnosis especially major depression.

**Summary:**

**Objective:** To assess the psychiatric diagnosis and quality of life in a sample of patients with grade III obesity from a Brazilian Medical Center of Obesity in Rio de Janeiro.

**Methods:** Fifty patients with grade III obesity (body mass index (BMI) = weight (kg)/height (m^2) > 40) who were in their first visit to the clinic and agreed to participate in our investigation, were sequentially selected to a psychiatric interview. The scales and a diagnostic interview instrument were applied before beginning any specific treatment for obesity. The following instruments were used: (1) International Neuropsychiatric Interview 4.4 MINI; (2) World Health Organization Quality of Life—WHOQOL; (3) The Body Shape Questionnaire—BSQ to evaluate body image disturbances; (4) Binge Eating Scale—BES to evaluate binge eating behavior.

**Results:** 19 (38.0%) patients displayed an axis I DSM—IV diagnosis. Major depression was the most common psychiatric condition (12 patients, 24.0%), followed by generalized anxiety disorder (six patients—12%). We found a significant correlation between WHOQOL and BES (r=0.34, p = 0.015).

**Conclusion:** Patients in our sample presented a high rate of psychiatric morbidity and a disturbed eating behavior that was associated with low quality-of-life scores.

**References:**


NR344  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Comparison of Emergency Physicians and Psychiatrist Laboratory Assessment for the Medical Clearance of Psychiatric Patients
Leslie Zun, M.D., Emergency YD EPT, Mount Sinai Hospital, 1500 S California, Chicago, IL 60608; Roma Hernandez, Randy L. Thompson, M.D., Lavonne Downey, Ph.D.

Educational Objectives:
Emergency physicians frequently transfer psychiatric patients to psychiatric hospitals with the approval and acceptance of a psychiatrist. Emergency physicians and psychiatrists have unknown set of testing routines and requirements that are used to determine medical clearance of the psychiatric patient. The purpose of this study was to compare the routine and required testing performed emergency physicians as compared to psychiatrists.

Summary:
The purpose of this study was to compare the routine and required testing performed by emergency physicians as compared to psychiatrists.

A survey of routine and required test ordering for the medical clearance of patients presenting with psychiatric complaints by emergency physician and psychiatrist was developed. The survey was distributed to all of the 1,055 of the emergency physicians in the state of Illinois using ACER database and all of the 117 psychiatrists at state operated psychiatric facilities in the state of Illinois. The surveys were mailed and re-mailed to the non-responders in both groups. The study results comparing the emergency physicians with the psychiatrists were performed using the Fisher exact testing.

The survey was returned by 507 (48.1%) of the emergency physicians and 65 (55.6%) of the psychiatrists. 37.0% of EPs responded who were mostly 31-40 years old (187/506), male (347/469), board certified (348/477). The psychiatrists were mostly 51-60 years old (36/56), male (34/57), board certified (95/57). The most frequent routine and required tests ordered by EPs and Psych were a UDS (routine 378/507, 45/66 and required 381/507, 31/66), alcohol (348/507, 33/66 & 348/507, 33/66) and CBC (270/ 507, 53/66 & 334/507, 34/66) and least frequently EEG (0/507, 2/66 & 1/507, 0/66), CT scan (6/507, 3/66 & 2/507, 0/66) and lumbar puncture (1/507, 2/66 & 0/507, 0/66) respectively, at a most frequent estimated cost of required testing of $101-200 for EPs (102/507) and $201-300 for psychiatrists (13/66). There were 10 of 16 differences in routine test ordering and three of 16 required tests performed by emergency physicians compared with psychiatrists.

Although the number of sets required by both groups were different, the tests required by psychiatrists and emergency physicians for medical clearance of the psychiatric patients were found to be similar.

References:

NR345  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
First-Episode Neuroleptic Naïve Outpatients With Schizophrenia
Supported by Eli Lilly and Company
Amanda J. Lowry, B.Sc., Eli Lilly Australia, 112 Wharf Road West Ryde, Sydney, NSW 2114, Australia; Martin Dossenbach, M.D., Jason M. Boland, B.Sc., M. Hadhoud, M.D., Mohand el Mahloud Kessaci, M.D., Jung S. Ahn, M.D., Cesar H. Gonzales, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss the comparative efficacy and side-effect profile of olanzapine, risperidone and haloperidol in treating the clinical and functional symptomatology of schizophrenia in never-medicated, first episode Intercountry outpatients.

Summary:
Objective: Evaluate the clinical/functional status of patients recently diagnosed with schizophrenia and prescribed antipsychotics for the first time.

Methods: This is a subgroup analysis (n=501) from the three-year Intercountry schizophrenia outpatient-health outcomes (IC-SOHO) observational study. Symptomatology, concomitant medications, quality of life, adverse effects, and weight were compared for patients prescribed primarily olanzapine, risperidone or haloperidol after six months treatment.

Results: Improvement in negative symptoms was greatest for patients prescribed olanzapine. Depressive symptoms decreased more for patients prescribed olanzapine and risperidone compared to haloperidol. The incidence of treatment-emergent extra-pyramidal symptoms (baseline EPS 10% overall) was lower (p<0.001) for patients prescribed olanzapine (4%) than those prescribed risperidone (21%) or haloperidol (65%). Tardive dyskinesia (2% overall at baseline) was largely unaffected by atypical antipsychotics, however haloperidol was associated with an increase to 21%. At baseline, 26% of all patients reported loss of libido and 21% impotence/sexual dysfunction. More risperidone (19%) and haloperidol (30%) patients developed impotence/sexual dysfunction compared to olanzapine (3%). At six months, use of anticholinergics (p<0.001) was lower for olanzapine-treated patients than for risperidone and haloperidol. Mean body weight increased irrespective of antipsychotic.

Conclusions: Atypical antipsychotics may provide efficacious control of symptoms with minimal side effects for first-episode patients.

References:

NR346  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Patients Subjective Perception of the Association Between Stress Secondary to Adverse Life Events and the Onset and Activity of Their Inflammatory Bowel Disease
Esther Gomez-Gil, M.D., Department of Psychiatry; Hospital Clinic, Villarroel 170, Barcelona 08036, Spain; Angela Vidal, M.D., Julian Panes, M.D., Jesus Jaen, M.D., Emilio Fernandez-Egea, M.D., Josep-Maria Peri, M.D., Manuel Valdes-Miyar, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss the subjective perception that there is a relationship between stress secondary to adverse life events and the onset and activity of their illness.
Introduction: Several studies have examined the topic of an association between stress secondary to adverse life events (ALE) and inflammatory bowel disease (IBD) and have reported controversial data. Moreover, there are no studies addressing the patients' subjective perception of this association. The aim of this study was to explore the subjective perception in IBD patients. Method: Sixty-one consecutive patients suffering from IBD (35 Crohn's, 26 ulcerative; mean ages 39.28 SD 15.9), were assessed using a self-rating questionnaire related to demographic variables, clinical characteristics, subjective perception of the influence of stress secondary to ALE on the onset and activity of IBD, psychiatric background, and the HAD scale. Results: Thirty-six patients (58%) perceived that there was an influence of ALE with the onset of their disease, 41 (66%) perceived a relation between ALE and the increasing IBD symptoms severity. Forty-five patients (72%) related their ALE with the disease activity. Patients with Crohn's disease were not statistically different from patients with ulcerative colitis. Fourteen of the patients (22%) were visited by a psychiatrist due to the IBD disease. Twenty-one patients (40%) reached a score of 11 or higher on either the depression or anxiety subscales of the HAD, indicating a probable psychological disorder, and 32 (61%) scored over 8, indicating possible psychological disorder. Conclusions: These results suggest that IBD patients perceive a strong relation among having suffered ALE and the onset and activity of the illness. We have observed a high incidence of anxiety and depression symptomatology in these patients. If this observation is confirmed with "objective" measurements, it will be important to take into account psychiatric intervention for these patients.

References:

NR348 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
The Health Psychology in the General Hospital: Data From the Holy House From Sao Paulo, Brazil
Wilze L. Bruscato, D.R., Psychology, Santa Casa, Borges Lagoa 1231 Conj 62, Sao Paulo, SP 04038020, Brazil; Sandra F., Amorim, M.S., Flavia L. Fernandes

Educational Objectives:
At the conclusion of the session, the participant should be able to recognize the importance of mental health services in the general hospital.

Summary:
Introduction: Several studies have shown the benefits of the mental health interventions in the general hospital. Among these benefits are better responses to treatments, improvements in dealing with patients and reduction of recovery periods. Positive reflections, such as decreasing of fall backs and reduction of medical consultations for emotional problems can also be noticed in the hospital as a whole. Objective: Make a quantitative description of the psychology service consultations.

Method: Survey with data from a department record. Results: In a table presenting the full number of consultations of the Unit Consultations in the last five years, we show a total of 3,161 requests. Since each request demands an average of five consultations, there are about 15,000 in the reported period. The specialities that most frequently asked for our intervention were: pediatrics/orthopedical pediatrics, medical clinic, orthopedics, surgical clinic and gynecology/obstetrics. The Liaison Unit, with 4,365 consultations in 2001 had, as main requesters, the Rehabilitation Service, the Morbidly Obese Clinic, the Heart and Lung Unit, the Adolescent Clinic, the Intestine Disease/Intestine and Liver Transplantation Center, Nefrology/ Kidney and Pancreas Transplantation Center, Pediatrics Department, Adolescent Obese Service, Medical Genetics Center and Bodily Pain Therapy Service.

Conclusion: The usage of records in order to compile the data has proved to be an interesting strategy to allow a systematization of information, which leads to the improvement of our intervention as well as the creation of new approach strategies.

References:

NR347 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Double-Blind Study of Venlafaxine in Chronic PainSupported by Wyeth Research
Michael T. Isaac, M.D., PEU, Slam Ladywell Building, Lewisham High Street, London SE13 6LH, United Kingdom; Maria Isaac, M.D.

Summary:
Fifty-three adults suffering from chronic non-malignant pain agreed to take part in a double-blind, randomized, parallel-group trial of venlafaxine-XL versus placebo. We used the Montgomery-Asberg Depression Rating Scale (MADRS) and pain severity to measure response to treatment. We estimated MADRS, Beck Depression Inventory (BDI) and European Quality of Life Measure (EuroQol) at days 0, 7, 14, 28, 42, 56, 84 of the study. We measured the impact of pain using the West Haven-Yale Multidimensional Pain Inventory (WHYMPI) at days 0, 28, and 84. For depressive symptoms, patients were grouped into those with higher levels of pain at day 0 showed statistical differences in EuroQoL at day 28 and 42 of the study. There were statistical differences in onset of action at days 28 and 42.

Conclusions: Venlafaxine-XL had effects on mood and pain.

NR349 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Gender Differences in the Psychiatric Emergency Room
Ronny Bruffaerts, M.A., Department of Psychiatry, University Hospitals Gasthuisberg, Herestraat 49, Leuven 3000, Belgium; Koen Demyttenaere, Ph.D., Remko Huygens, M.D., Paul Enzlin, Jean-Pierre Lepine, Ph.D., Marc Sabbe, Ph.D.

Educational Objectives:
To provide knowledge on epidemiologic pathways and service use of male and female patients with the regard to hospitalization decisions in a psychiatric emergency room. The participants should be able to have an advanced idea of the differential impact
of sociodemographic, clinical, and service use characteristics in male and female patients presenting at the psychiatric emergency room of a university hospital.

Summary:

Objectives: Deinstitutionalization and efforts of cost containment in mental health services lead to an increased number of psychiatric patients living in the community and consulting the psychiatric emergency room. This study aimed to assess gender differences in sociodemographic characteristics, diagnosis, psychiatric history, way of referral, and variables predicting outpatient and hospitalisation in the psychiatric emergency room.

Method: Between March and December 2000, all male (n=462, 44%) and female (n=586, 56%) psychiatric emergency referrals of the University Hospital in Leuven were monitored with regard to sociodemographic characteristics, diagnosis (according to DSM-IV axis 1 criteria), psychiatric history, patterns of referral, and aftercare.

Results: We found no gender differences in sociodemographic characteristics, and psychiatric history. Male patients present mainly with substance use disorders and mood disorder, while female patients present mainly with mood and adjustment disorders. Male patients were more referred by law enforcement while women are more referred by mental health professionals. In male patients being hospitalised before, having psychotic and mood diagnosis increases the probability to be hospitalised. In female patients neurotic diagnosis and living within a family decreases the probability to be hospitalised.

Conclusions: Gender differences concern diagnosis, way of referral, and characteristics predicting hospitalisation and outpatient treatment.

NR350 Tuesday, May 20, 12:00 p.m.-2:00 p.m.

Polymorphisms of Interleukin-Four Promoter and Receptor Gene for Schizophrenia in Korean Population

Tae-Youn Jun, M.D., Department of Psychiatry, St. Mary’s Hospital, 62 Yoido-dong, Youngdeungpo-gu, Seoul 150-713, South Korea; Kyoun-Wh Lee, M.D., Hyuk-Jae Lee, M.D., Jeong-Ho Chae, M.D., Won-Myong Bahk, M.D., Kwang-Soo Kim, M.D.

Summary:

Objectives: We investigated the relationship between exon 1 polymorphism of cytokotoxic T lymphocyte antigen-4 (CTLA-4) gene and bipolar disorder.

Methods: Among the Korean patients diagnosed as bipolar disorder according to DSM-IV, 90 patients without serious medical illness, neurologic illness, hormonal disorder, or concomitant mental illness were selected. Blood was obtained from 149 age- and sex-matched control subjects with no history of autoimmune disease. DNA was extracted from whole blood using proteinase K and the exon 1 region of CTLA-4 gene was amplified by PCR. Gene typing was performed using SSCP.

Results: There were no significant differences in genotype frequencies of CTLA-4 A/G, CTLA-4 G/A, and CTLA-4 A/A between the patients with bipolar disorder and the control group (48.9% vs 48.3%, 44.4% vs 39.6%, and 6.7% vs 14.1%, respectively). There were no significant differences in allele frequencies of CTLA-4 G and CTLA-4 A between the patients with bipolar disorder and the control group (71.1% vs 66.1%, and 28.9% vs 33.9%, respectively).

Conclusions: This study does not show the association of exon 1 polymorphism of CTLA-4 gene with bipolar disorder in Korean population. Further systematic studies according to biological traits would be conducted in future.

References:


NR351 Tuesday, May 20, 12:00 p.m.-2:00 p.m.

Polymorphisms of CTLA-4 for Bipolar Disorder in Korean Population

Tae-Youn Jun, M.D., Department of Psychiatry, St. Mary’s Hospital, 62 Yoido-dong, Youngdeungpo-gu, Seoul 150-713, South Korea; Kyoun-Wh Lee, M.D., Jong-Woo Kim, M.D., Jeong-Ho Chae, M.D., Won-Myong Bahk, M.D., Kwang-Soo Kim, M.D.

Educational Objectives:

At the conclusion of this session, CTLA-4 gene could be a candidate gene for bipolar disorder, but this study does not show the association of exon 1 polymorphism of CTLA-4 gene with bipolar disorder in Korean population.

Summary:

Objectives: We investigated the relationship between exon 1 polymorphism of cytokotoxic T lymphocyte antigen-4 (CTLA-4) gene and bipolar disorder.

Methods: Among the Korean patients diagnosed as bipolar disorder according to DSM-IV, 90 patients without serious medical illness, neurologic illness, hormonal disorder, or concomitant mental illness were selected. Blood was obtained from 149 age- and sex-matched control subjects with no history of autoimmune disease. DNA was extracted from whole blood using proteinase K and the exon 1 region of CTLA-4 gene was amplified by PCR. Gene typing was performed using SSCP.

Results: There were no significant differences in genotype frequencies of CTLA-4 A/G, CTLA-4 G/A, and CTLA-4 A/A between the patients with bipolar disorder and the control group (48.9% vs 48.3%, 44.4% vs 39.6%, and 6.7% vs 14.1%, respectively). There were no significant differences in allele frequencies of CTLA-4 G and CTLA-4 A between the patients with bipolar disorder and the control group (71.1% vs 66.1%, and 28.9% vs 33.9%, respectively).

Conclusions: This study does not show the association of exon 1 polymorphism of CTLA-4 gene with bipolar disorder in Korean population. Further systematic studies according to biological traits would be conducted in future.

References:


Methods: A total of 241 schizophrenic patients and 89 bipolar patients diagnosed by DSM-IV criteria were included as patient groups and data of 125 persons from the Catholic Hemopoietic Stem Cell Information Bank (Seoul, Korea) were used as a control group. DNA was extracted from the whole blood, amplified by polymerase chain reaction, and digested by Ncol. Then the obtained RFLP of two alleles, TNFA*1 with 87bp and 208bp, and TNFA*2 with 107bp were assessed. All data were analyzed by x2 test.

Results: The genotype and allele distributions in patients with bipolar disorder were significantly different from those in the controls. There were no significant differences in genotype frequencies of TNFA*1, TNFA*1/2, and allelic frequencies of TNFA*1, and TNFA*2 between the schizophrenic patient and the controls.

Conclusions: In the present study, we observed a significant association between the TNFA*2 allele with bipolar disorder, but found negative result for the association of the polymorphism of TNF-α gene with schizophrenia. Consecutive further studies including diverse clinical variables would be required.

References:

NR354  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Genetic Association of Clock T3111C Polymorphism in Affective Disorders and Gilles-de-la-Tourette Syndrome
Georg R. Wiesegger, M.D., Department of General Psychiatry, University of Vienna, Laehringer Guertel 18–20, Vienna A 7090, Austria; Ursula Baier, M.D., Friedrich Leisch, Ph.D., Inge Leitner, M.D., Martin Letmaier, M.D., Mara Stanenkovic, M.D., Juergen Stasny

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that there is no association between clock T3111C SNP and affective disorders (poster presentation).

Summary:
Background: Clock gene was hypothesised to be related to susceptibility of affective disorders. Although a lack of studies based on animal models on the function of clock T3111C polymorphism in affective disorders, several suppositions evolved from epidemiology and biological research supporting the impact of the circadian timekeeping system in psychiatric disorders.

Methods: By using DSM-IV criteria we studied affective patients (n = 102) with major depressive disorder and bipolar disorder and with Gilles-de-la-Tourette-Syndrome (GTS) (n = 77). Clock gene is located on chromosome 4q12. By using polymerase chain reaction and restriction fragment length polymorphism we investigated whether the T3111C SNP is associated with affective disorders or GTS compared to healthy controls (n = 103).

Results: No differences were found neither in genotype nor allele frequency distributions of T3111C polymorphism between patients with affective disorders or GTS compared to healthy controls (p<0.2). No deviations from Hardy-Weinberg-Equilibrium were detected neither in both patient groups, nor healthy controls.

Conclusion: Our data suggest that there is no association between the T3111C SNP and affective disorders. Results of our sample are in replication of prior findings of Desan et al. [2000]. In addition, our psychiatric control group of GTS patients did not show different genotype or allele frequency distributions compared to healthy controls.

References:
NR355  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
A Study of Serotonergic Pathway Genes and Personality Traits
Byung-Joo Ham, M.D., Department of Psychiatry, Korea University Hospital, 138-15 Ga Anam Dong, Seoul 136-705, South Korea; M.D. Myung-Jim Chot, Ph.D., Ji-Hyun Cha, M.D., Yum-Kyung Chot, Ph.D., Min-Soo Lee, M.D., Hyum Kim, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the relationship between personality and biological factors such as 5-HTTLPR, 5-HT2A receptor and TPH gene polymorphisms.

Summary:
Serotonergic pathway genes are thought to be an important factor in some personality traits and the etiology of affective disorders. We examined the relationship between personality traits and 5-HTTLPR, 5-HT2A receptor and tryptophan hydroxylase (TPH) gene polymorphisms. The participants included 148 healthy adults with no history of psychiatric disorders and other physical illness during last six months. All participants were tested TCI and genotyped 5-HTTLPR, 5-HT2A receptor polymorphism(A-1438A/G, T102C), and TPH polymorphism(A218C). Genotyping was analysed with PCR(Polymerase Chain Reaction). Differences on TCI dimensions and subscales among three groups were examined by ANOVA. Our result suggests that serotonin transporter gene polymorphism appear to be associated with reward dependence. And our result also indicated a relationship between a 5-HT2A polymorphism and self-determination and self-transcendence within character scales. But there were no significant relationship between TPH polymorphism and personality traits. We found significant associations between some serotonergic pathway genes and the TCI(Temperament and Character Inventory) dimensions. But our results may reflect the false positive results due to the small sample size and low statistical power and require further investigation.

References:

NR356  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
SLC6A4 Haplotype and Platelet 5HT Uptake in Relatives of Autistic Children
Soo-Jeong Kim, M.D., Department of Psychiatry, University of Chicago, 924E 57th Street, KNAPP RO22, Chicago, IL 60637; Jane E. Vandemolen, Ph.D., Nancy J. Cox, Ph.D., Bennett L. Leventhal, M.D., Edwin Cook, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to acknowledge the hypothesis that a haplotype defined by the 5-HTTLPR in conjunction with SNPs in intron 1A may regulate platelet 5-HT uptake.

Summary:
Introduction: Hyperserotonemia in autism has been well-replicated. Previously Cook, et al (1993) studied platelet 5-HT uptake in relatives of children with autism and reported significant difference of platelet 5-HT uptake Vmax between normoseronetic and hyperseronetonic subjects. Lesch et al (1996) reported functional implication of serotonin transporter gene (SLC6A4) promoter polymorphism (5-HTTLPR). We recently investigated SLC6A4 by genotyping several novel polymorphisms as well as 5-HTTLPR and found stronger evidence of transmission disequilibrium at markers other than 5-HTTLPR (Kim et al., 2002).

Method: In this study, we genotyped 5-HTTLPR and SLC6A4 SNPs in 18 relatives of children with autism. Platelet serotonin studies (whole blood 5-HT, [3H]-LSD binding, [3H]-paroxetine binding and 5-HT uptake) were performed and reported previously. We analyzed genotype data to examine if 5-HTTLPR and/or an ancestral haplotype determined by Decay of Haplotype Sharing analysis were related to platelet 5-HT uptake Vmax.

Results: ANOVA and post Hoc test revealed significant difference of platelet 5-HT uptake Vmax, when the subjects were divided into 3 subgroups according to haplotype data of 5-HTTLPR in the promoter and SNPs in intron 1A.

Conclusion: The hypothesis that a haplotype defined by the 5-HTTLPR in conjunction with SNPs in intron 1A regulates platelet 5-HT uptake was supported.

References:

NR357  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Antipsychotic-Induced Weight Gain: Influence of Leptin Gene Polymorphism Supported by Pfizer Inc.
Gavin P. Reynolds, Ph.D., University of Sheffield, Biomedical Science, Western Bank, Sheffield, UK S10 2TN, United Kingdom; Zhijian Yao, M.D., Wen Liu, M.D., Zhijun Zhang, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should understand that genetic factors play an key role in determining drug-induced weight gain, a major and problematic side effect of anti-psychotic drug treatment.

Summary:
Objective: Increased body fat, leading to further morbidity and poor treatment adherence, is a common consequence of treatment with antipsychotic drugs. We have previously found that a common polymorphism of the 5-HT2C receptor gene has a strong influence on drug-induced weight gain. Recent reports show that genetic variants in the leptin gene promoter region are associated with obesity and influence leptin function. We hypothesised that this polymorphism may also affect drug-induced weight gain.

Method: We determined the association of the -2548 A/G leptin gene polymorphism with treatment-induced weight gain in a Chinese population with schizophrenia. Patients (n=159) admitted to hospital following a first psychotic episode were genotyped for the polymorphism; weight was measured before and after ten weeks of drug treatment. Thirty patients also had body fat changes determined by MRI.

References: Patients with GA or GG genotype (n=53) showed less weight gain (mean BMI change 1.04 vs 1.46 kg/m², p<0.05); after removing underweight or obese patients (BMI <17 or >26 kg/m²) the effect became highly significant (n=132, p=0.003). Patients with the AA genotype were more likely to develop substantial (>
7% weight gain (p<0.01; relative risk 1.71). The polymorphism was associated with a significant difference in the increase in subcutaneous fat (p<0.01); the difference in visceral fat deposition did not reach significance (p<0.1).

Conclusion: These findings identify a further genetic factor determining treatment-induced increases in weight in schizophrenia and demonstrate the potential of pharmacogenetics in determining patients' liability to an important antipsychotic drug side effect.

References:

NR358 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
5HTTLPR Polymorphism and Response Time to Sertraline in Elderly Patients
Patrice M. Milos, Ph.D., Pfizer Incorporated, MS 8118D-3011 Eastern Point Road, Groton, CT 06340; Kathryn L. Durham, M.D., Albert B. Seymour, M.D., Hakan Sakul, M.D., Cathryn M. Clary, M.D., John A. Gillespie, M.D.

Educational Objectives:
The presentation should increase participants' understanding of whether speed of response to SSRIs may be related to patients' genetic make-up at a single variant. This also has the potential to influence how physicians think about incorporating genetic variants in the future of medicine.

Summary:
A common polymorphism (5HTTLPLR) within the promoter region of the serotonin transporter gene (SLC6A4) has been shown to influence response time to paroxetine in elderly depressed and overall response to fluoxetine in younger subjects with major depressive disorder (Pollock et al., 2000; Smeraldi et al., 1998). Based on these findings, we hypothesized that a similar effect in response time to sertraline would be observed and that no effect would be seen in a placebo arm. We tested the hypothesis that subjects homozygous for the Long allele (LL) at 5HTTLPR would respond more rapidly to sertraline than subjects carrying one or two copies of the Short allele (SS/SL). LL subjects showed a significant increase in response at week 1 and 2 as assessed by the CGI-I scale compared with SS/SL subjects. No significant difference was observed in the placebo group. These results suggest that genetic variation in the serotonin transporter gene effects the response time to sertraline and provides complementing evidence to previous reports that this polymorphism effects response time to other SSRIs.

References:

NR359 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Factors Associated With Quality of Life Among Older Patients With Schizophrenia Supported by NIGMS
Carl I. Cohen, M.D., Department of Psychiatry, SUNY Health Sciences Center, 450 Clarkson Avenue, Box 1203, Brooklyn, NY 11203; Paul M. Ramirez, Ph.D., Michelle Kehn, M.A., Carol Magai, Ph.D., Ronald Brenner, M.D.

Educational Objectives:
At the conclusion of this session, participants will learn about quality of life (QOL) measures and its importance for older schizophrenic persons; to identify those factors that affect QOL, particularly those that are remediable

Summary:
Objectives: It is expected that the number of older schizophrenic persons will double over the next 30 years; however, researchers and providers have not adequately addressed their needs. This study examines factors that impact on the quality of life of this population.

Methods: Conducted in NYC, we used a stratified sampling technique. 103 persons age 55+ with onset of schizophrenia before age 45 were interviewed using 25 assessment instruments. Age was 61 yrs, 54% were female; 58% were white, 36% black, 6% Latino. Score on the Quality of Life Index (QOLI) was the dependent variable. We used a theoretical model that includes objective and subjective variables that we developed previously.

Results: The M QOLI was 21.4, which was similar to levels reported for medically ill persons. Univariate analysis was used to trim the variables in the model. We then entered 11 variables into a linear regression analysis. Five variables were significant predictors of lower QOLI: financial strain, physical illness, depression, acute stressors, and lower self-esteem.

Conclusion: The results suggest that emotional, social, and physical causes influence QOL, and the most potent of these factors are potentially remediable through improved and targeted medical, psychiatric, and social services. Contrary to what others have proposed, we did not find any association with negative or positive symptoms or level of psychiatric treatment. Comparative judgment scores (of others and one's past) were significant in univariate but not in multivariate analysis.

References:

NR360 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Paranoid Ideation and Psychoses in an Aging Urban Population
Carl I. Cohen, M.D., Department of Psychiatry, SUNY Health Sciences Center, 450 Clarkson Avenue, Box 1203, Brooklyn, NY 11203; Robert Yaffee, Ph.D., Carol Magai, Ph.D., Georges J. Casimir, M.D., Lorna Walcott-Brown, M.A.

Educational Objectives:
At the conclusion of this session participants will learn about the prevalence rates of paranoid ideation (PI) and psychoses (P) in an urban setting, recognize racial differences in rates, consider factors associated with PI and P and the implications of the findings.
NR361    Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Subcortical Cerebrovascular Disease and Psychiatric Symptoms in Elderly Subjects
Supported by the National Institute of Mental Health and NARSAD
Helen Lavretsky, M.D., Department of Psychiatry, UCLA-NPI, 760 Westwood Plaza, Room 37-384, Los Angeles, CA 90095; Wendy Mack, Ph.D., W.J. Jagust, B.R. Reed, M.D., D. Mungas, M.D., J. Kramer, M.D., Helena C. Chui, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the relationship of subcortical cerebrovascular disease to behavioral symptoms in elderly subjects with and without cognitive impairment.

Summary:
Objectives: To examine the impact of subcortical cerebrovascular disease diagnosed by MRI on psychiatric symptoms in subjects with or without cognitive impairment.
Methods: 503 elderly subjects (243 men and 260 women; mean age of 73 years, (SD=8.5), range 54–92 y.o.) were recruited to participate in the multicenter, collaborative study of subcortical ischemic vascular disease (SIVD). They received a comprehensive neuropsychiatric evaluation. All subjects were categorized as normal; cognitively impaired without dementia or with dementia according to the Clinical Dementia Rating score (CDR). Behavioral ratings were based upon clinician ratings using the Psychiatric Evaluation section of the Minimum Uniform Dataset (MUDS-PSY) of the California Alzheimer's Disease Centers Program, DSM-III-R criteria for major depression based on duration and severity, as follows: 0=not present, 1=questionable; 2=present but does not meet the DSM-III-R criteria; 3=present and meets the DSM-III-R criteria; or 9=not determined. All subjects underwent MRI and were classified as having or not having subcortical lacunar infarcts based on the standard quantitative procedures and diagnosis.
Results: 266 subjects had no cognitive impairment while 106 were classified as having cognitive impairment, and 131 subjects were diagnosed with dementia. 157 had lacunar infarctions, and 346 did not. Subjects with dementia had significantly more psychotic symptoms compared to subjects without dementia.

References:

NR362    Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Sex Differences in Brain Structure in Patients With Geriatric Depression
Supported by the National Institute of Mental Health and NARSAD
Helen Lavretsky, M.D., Department of Psychiatry, UCLA-NPI, 760 Westwood Plaza, Room 37-384, Los Angeles, CA 90095; Anand Kumar, M.D., Daniel Pham, Laverne Estanol, Arthur Toga

Educational Objectives:
At the conclusion of this session, the participant should recognize the pattern of sex differences in brain structure in elderly subjects with major depression and normal controls.

Summary:
Objectives: Depressed elderly patients and normal controls age 60 or older were compared to examine gender differences in medical comorbidity and structural brain changes on MRI.
Methods: Patients and controls were closely matched by age and education. They underwent a thorough neuropsychiatric, laboratory, and physical examination and the MRI scans. Measures of the total frontal lobe and the frontal gray and white matter volumes corrected by the intracranial volume were obtained using magnetic resonance imaging (MRI), together with clinical measures of overall medical (CIRS) and cerebrovascular burden (CVRF).
Results: The study samples were comprised of 22 patients with MDD (9 men, 13 women; mean age 71.4 ± 8.1) and 15 controls (4 men and 11 women; mean age 72 ± 6.1). In the univariate analysis, the depressed group had lower MMSE scores (p<0.02); greater severity of medical comorbidity (CIRS scores) (p=0.003) compared to the controls. The depressed group had lower total frontal (p<0.03), left (p<0.03) and right (p<0.05) frontal volumes than the controls (p<0.02). In the depressed group, men had smaller corrected frontal volumes (p<0.01), as well as frontal white matter volumes (p<0.05) compared with women. In the logistic regression, frontal total volume and frontal white matter volumes predicted gender assignment after controlling for age (p<0.01) in the depressed group, but not in controls.
Conclusions: Geriatric depression is associated with greater severity of medical comorbidity and brain structural changes. However, gender differences in brain structural changes appear to play a role in geriatric depression, thereby, indicating that gender differences in neuroanatomy may be important in the pathophysiology of geriatric depression.
Aripiprazole for Psychosis of Alzheimer's Disease
Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co, Ltd.

Peter P. De Deyn, M.D., Department of Neurology, Middelheim Hospital, Lindenlaan 1, Antwerp 2000, Belgium; Dilip V. Jeste, M.D., Philippe Auby, M.D., Harry Goyvaerts, M.S., Christopher Breder, M.D., Lon S. Schneider, M.D., Jacobo E. Mintzer, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should better understand the efficacy of aripiprazole in patients with psychosis associated with Alzheimer’s dementia.

Summary:
Objective: To evaluate the efficacy and safety of aripiprazole in patients with psychosis of Alzheimer’s disease (AD).
Methods: In a 10-week, multicenter trial, 208 outpatients with psychotic symptoms associated with (AD) (mean age 81.5y, baseline MMSE = 14.2) were randomized to placebo or flexible doses of aripiprazole, initiated at 2 mg/day for two weeks, with option to increase to 15 mg/day. Efficacy was assessed by Neuropsychiatric Inventory [NPI], Psychosis subscale, and Brief Psychiatric Rating Scale (BPRS).
Results: Mean dose of aripiprazole was 10 mg/day (range 1–17 mg). At week 10, NPI Psychosis score (mean baseline 12.3 aripiprazole and 12.1 placebo) was improved with both aripiprazole and placebo (–6.55 vs –5.52, P=0.17). Patients treated with aripiprazole experienced improvement in the BPRS Total score and a significant improvement in BPRS psychosis (hallucinations and delusions) subscore compared with placebo (–1.93 vs –1.27, P=0.03). Discontinuation rates due to adverse events were 8% with aripiprazole and 7% with placebo. Somnolence was mild and not associated with falls or accidental injury. There were no significant differences in ECG abnormalities, vital signs, labs, or weight.
Conclusions: Aripiprazole improved symptoms of hallucinations and delusions in community-living AD patients. Aripiprazole was well tolerated in this elderly population.

References:

Decreased Lymphocytes 3H-Paroxetine Binding in OCD
Donatella Marazziti, M.D., Department of Psychiatry, University of Pisa, Via Roma 67, Pisa 56100, Italy; Stefano Baroni, Ph.D., Irene Masala, Ph.D., Elena Di Masso, M.D., Gino Giannaccini, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should get deeper insights on the pathophysiology of OCD.

Summary:
Introduction: The pathophysiology of obsessive-compulsive disorder (OCD) is mainly focused on the serotonin (5-HT) system and transporter. Recent findings have indicated that this structure is expressed also on lymphocyte membranes and is similar to that present in the central nervous system and platelets. The aim of this present research, therefore, was to evaluate the 5-HT transporter by means of the specific binding of 3H-paroxetine (3H-PAR), the most appropriate ligand for labeling it, in lymphocytes of a group of OCD patients, as compared with healthy control subjects.
Methods: Ten patients (five women and five men, mean age±SD: 28±10 years), who met current DSM-IV-R criteria for OCD, were included in the study. The severity of the OC symptoms was evaluated by means of the Yale Brown Obsessive Compulsive Scale (Y-BOCS): the total score (mean±SD) was 30±6. Ten healthy, drug-free subjects, (five women and five men, mean age±SD: 24±7 years), with neither family nor personal history of any major psychiatric disorder, were included as control subjects. Lymphocyte membranes and 3H-PAR binding were carried out according to standard protocols.
Results: The results showed that the patients had a statistically significant lower density (Bmax, fmol/mg protein) of 3H-PAR binding sites than the control subjects (88±20 vs 220±26), with no change in the Kd (nM) (0.1±0.05 vs 1.17±0.02).
Discussion and Conclusions: On one side, this finding confirms previous data of abnormal platelet 5-HT transporter in OCD; on the other, it provides the possibility to explore the regulation of this structure in this and other disorders, since lymphocytes are nucleate cells. Future studies by means of hybridization techniques might help to determine whether or not the decreased 3H-PAR binding is due to an altered expression of the transporter protein.

References:
Educational Objectives:
At the conclusion of this session, the participant should learn that remission of symptoms for depression may occur by hospital discharge and recognize that improvement in depressive symptoms may vary by antidepressant treatment class in older adult female inpatients.

Summary:
Objective: To describe patient-reported remission of symptoms in older adult female inpatients treated with venlafaxine/venlafaxine XR (VEN/VENXR) versus SSRIs (citalopram, fluoxetine, paroxetine, sertraline) for depression.
Methods: Retrospective analysis was performed using Mental Health Outcomes data from the CCi+ Outcomes Measurement System. Analysis included females admitted to a geropsychiatric facility between 1/1/1994-12/31/01, >55 years of age, with a primary discharge diagnosis of depression (ICD-9 codes 296.2x, 296.3, 300.4, 311). Patients were prescribed VEN/VENXR (n=252) or SSRI (n=1,684) monotherapy. Remission of symptoms was defined as a score <11 on the Geriatric Depression Scale, Patient Version (GDS-P) at discharge.
Results: No significant differences in mean GDS-P were observed between patients prescribed VEN/VENXR (16.3) versus SSRIs (15.4) at admission. Mean improvement in GDS-P scores was 6.1 for VEN/VENXR versus 5.1 for SSRIs (P<0.03). Improvements occurred by 16-17 days from admission to discharge. Remission (GDS-P<11) rates were 32.9% for VEN/VENXR versus 29.9% for SSRIs (P=NS) at discharge.
Conclusions: While approximately one-third of patients achieved remission (GDS-P<11) by discharge after initial therapy with antidepressants, these patients reported significant GDS-P improvement with VEN/VENXR versus SSRIs at discharge. A longer length of follow-up may be desirable to confirm these findings on remission of symptoms.

References:

NR366 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Treatment Adequacy With Selected Antidepressants in Older Adults
Supported by Wyeth Research
George J. Wan, Ph.D., Health Outcomes, Wyeth Research, 555 East Lancaster Avenue, St. Davids, PA 19087; Kristina Yuansenberg, Ph.D., Christina L. Fontes, M.S., Erika C. Geissler, M.B.A.

Educational Objectives:
To learn how treatment adequacy can be used as a measure for effective antidepressant medication management; understand the relationship between continuous therapy and a specified dose; and recognize that adequacy rates vary by antidepressant treatment choice.

Summary:
Objective: To examine treatment adequacy with venlafaxine extended-release (VENXR) or fluoxetine.
Methods: Retrospective analysis was performed using Prescription Solutions data from Medicare health plans. Treatment adequacy was defined using the HEDIS Antidepressant Medication Management measures as continuous therapy for 84 or 180 days at a specified dose (75–150 mg/day for VENXR; 20 mg/day for fluoxetine). Pharmacy claims were obtained for 90 days prior and 270 days after the index prescription for either VENXR or fluoxetine during the index period (1/1/00-2/28/01). The cohort included patients ≥65 years old, newly starting with either VENXR or fluoxetine and remaining on the same medication for 84 or 180 continuous days.
Results: VENXR (n=295) had an adequate rate of 80% versus 56% for fluoxetine (n=507) for 84 continuous days (P<0.0001). VENXR (n=217) had an adequate rate of 82% versus 58% for fluoxetine (n=383) for 180 continuous days (P<0.0001). The adjusted odds ratios (OR) of achieving treatment adequacy with VENXR versus fluoxetine were 3.37 (95% CI=2.37-4.78) for 84 continuous days and 3.74 (95% CI=2.45-5.72) for 180 continuous days.
Conclusions: Older adult patients prescribed VENXR achieved higher treatment adequacy rates versus fluoxetine. High adequacy rates may lead to improved therapeutic outcomes in these patients treated with antidepressants.

References:

NR367 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Overview of Ziprasidone Tolerability in Patients 55 Years of Age and Older
Supported by Pfizer Inc.
Antony D. Loebel, M.D., Pfizer Inc, 235 East 42nd Street, New York, NY 10029; Cynthia O. Siu, Ph.D., Steven J. Romano, M.D.

Educational Objectives:
At the conclusion of this presentation, participants should be able to discuss the reported data from the ziprasidone clinical database on the general tolerability of ziprasidone in older patients with schizophrenia or schizoaffective disorder and on incidences of adverse events, laboratory abnormalities, and QTc prolongation.

Summary:
Objective: To evaluate the tolerability of ziprasidone in patients ≥55 years of age in the antipsychotic’s clinical development program.
Methods: The ziprasidone phase 2/3 clinical development program (through February 5, 2002) was reviewed for incidences of treatment-emergent (treatment-related) adverse events, clinically significant laboratory abnormalities, and categorical QTc prolongation among a subgroup of patients ≥55 years. These were compared with the incidences of these events for all patients in the database.
Results: Percentages of patients experiencing adverse events were comparable for the ≥55 and all patients populations (59.1%(55/93) vs 57.8%(773/1339)). Percentages of patients discontinuing treatment due to treatment-emergent (treatment-related) adverse events were likewise comparable (11.8%(11/93) vs 8.1%(108/1339)). Incidences of clinically significant laboratory abnormalities were also comparable between the two populations. The incidence of moderate to marked QTc prolongation (baseline correction factor), whether defined as absolute QTc values of ≥500
msec or ≥25% change from baseline, was comparable to previous
data presented on the all patients. (Romano APA 2001; no patient
≥55 exhibited a QTc ≥500 msec or ≥25% increase over base-
line value.

Conclusions: Among patients ≥55 years old, ziprasidone
demonstrated tolerability comparable to that observed in all patients.
Further studies are needed to evaluate ziprasidone in specific elderly populations.

References:
1. Gunasekara NS, Spencer CM, Keating GM: Ziprasidone: a
review of its use in schizophrenia and schizoaffective disorder
2. Romano SJ: Cardiovascular safety profile of ziprasidone: re-
view of clinical development data. Presented at the 154th An-
nual Meeting of the American Psychiatric Association, May 5–
10, 2001, New Orleans, LA.

NR368 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Anxiety and Depression as Predictors of Pain in
Older Women With Arthritis
National Institutes of Health
Bruce W. Smith, Mood and Anxiety Disorders Program,
National Institute of Mental Health, 15 K North Drive, Room
300C, MSC 267, Bethesda, MD 20892-2670; Alex J. Zautra,
Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be
able to demonstrate an understanding of the relationship between
anxiety and depression and the experience of pain and positive
and negative emotions in older women with arthritis.

Summary:
Objective: The purpose of this study was to examine the role
of anxiety and depression in predicting pain, negative affect, and
positive affect in older women with arthritis.

Method: Participants were 172 older women with osteoarthritis
(OA; n = 90) or rheumatoid arthritis (RA; n = 82). Trait and state
measures of anxiety and depression were administered initially
and scores for arthritis pain, negative affect, and positive affect
were aggregated across 12 weekly assessments.

Results: The hypotheses were that (1) anxiety and depression
would predict more arthritis pain and negative affect, (2) depres-
sion would be a stronger predictor of less positive affect than
anxiety, and (3) state measures alone would predict more pain
when entered in regression equations with trait measures. The
first hypothesis was supported except that trait depression was
unrelated to pain. The second and third hypotheses were fully
supported.

Conclusions: The findings indicate that anxiety and depression
may increase pain and negative affect, depression may be more
important in decreasing positive affect, and that short-term fluctua-
tions in anxiety and depression may be more important than dep-
ressive or anxious personality traits in increasing pain. This study
was supported by the National Institutes of Health and the Arthritis
Foundation.

References:
1. Schleman S: Age, physical impairment, and symptoms of anxi-
ety: A test of mediating and moderating effects. International
2. Vail CT, Walkup J: Combined medical and psychological symp-
toms: Impact on disability and health utilization of patients with
arthritis. Medical Care, 36 1998; 1073–1084.

NR369 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Results of a Memory Training Program for Older
Adults: U.M.A.M. Method
Maria D. Claver, M.D., Unidad Memorial, Ayuntamiento Madrid,
Rafael Calvo 6, Madrid, Spain; Pedro Montenegro, M.D.,
Mercedes Montenegro, P.S., Ana Isabel Reinoso, P.S., Maria E. De
Andres, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able
to obtain valuable information on the results of a training program
aiming at memory improvement in older people.

Summary:
Aging brings a decrease in cognitive performance, especially
in some types of memory. To improve those deficits numerous
experiments in cognitive training have been carried out. In the
CMS (Health Centers) of the City Council of Madrid, a memory
program has been going on with the aim of assessing memory
loss and to carry out a training program for people over 65. The
program results since 1994 are presented.

Objectives: To study memory levels. To assess the effects of
multifactorial training in memory and other variables.

Methods: Assessment: pre, post, and six months later. Screen-
ing: MMSE, and Geriatric Depression Scale. Specific: The River-
mead Behavioural Memory Test, Memory Failures Everyday,
and Nottingham Health Profile.

Training: 11 sessions in a group of 14 people with cognitive
processes stimulation, memory strategies, and technics and solu-
tion of daily forgetfulnesses.

Results: The results were analyzed using the SPSS program
for the statistical analysis. In this sample of 5,518 persons (M
Age = 69.52 years) (SD=5.22), 28.8% have a normal memory and
71.2% show memory disorders. The results pre-post (improve-
ment), pre-final (maintenance) was made with 2,635 trained partic-
ipants (p<0.0001):

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<th>Pre</th>
<th>Post</th>
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<tr>
<td>RBMT General Improvement</td>
<td>7.97</td>
<td>9.42</td>
<td>9.76</td>
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<tr>
<td>RBMT General Maintenance</td>
<td>8.03</td>
<td>7.87</td>
<td>7.88</td>
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<tr>
<td>GDS Improvement</td>
<td>9.94</td>
<td>7.87</td>
<td>9.40</td>
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<td>GDS Maintenance</td>
<td>10.03</td>
<td>16.9</td>
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<td>Health Profile</td>
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<th>T. par.</th>
<th>Change in memory levels</th>
<th>Pre</th>
<th>Post</th>
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<tr>
<td>35.16*</td>
<td>Normal Memory</td>
<td>24.8</td>
<td>56%</td>
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<tr>
<td>26.98</td>
<td>Weak Memory</td>
<td>52.2</td>
<td>34.6</td>
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<tr>
<td>-22.73*</td>
<td>Mild Impairment</td>
<td>21.7</td>
<td>8.8</td>
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<td>-15.46</td>
<td>Severe Impairment</td>
<td>1.3</td>
<td>6.8</td>
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Conclusions: The results show that the memory program yields
improvement in memory and in its keeping up in six months.
Besides it achieves benefits in mood, in memory complaints, and
in the perception of one’s health.

References:
performance in the aged through mnemonic training a meta-
2. Floyd M, Scogin F: Effects of memory training on the subjective
memory functioning and mental health of older adults: a meta-
NR370  Tuesday, May 20, 12:00 p.m.-02:00 p.m.
Mirtazapine Orally Disintegrating Tablets in Depressed Nursing Home Patients Greater Than or Equal to Age 85
Supported by Organon Pharmaceuticals Inc.

Steven P. Roose, M.D., Psychiatry, Columbia University, 1051 Riverside Drive, New York, NY 10032; Jerald C. Nelson, M.D., Carl Salzman, M.D., Steven B. Hollander, M.D., John H. Simmons, M.D., James V. Betzel

Educational Objectives:
At the conclusion of this presentation, the participant should be able to describe the design and methods of this clinical trial using mirtazapine orally disintegrating tablets in elderly nursing home subjects at least 85 years of age.

Summary:
Purpose: Study of mirtazapine orally disintegrating tablets in depressed nursing home patients with multiple comorbidities ≥ 85.

Methods: Analysis on patients ≥ 85 from a larger, 12-week, open-label trial. Inclusion criteria: physician diagnosed depression, MMSE scores ≥ 10; residence in a nursing home. Exclusion criteria: unstable medical illness, concomitant antidepressants. Dosage of mirtazapine 15 mg/d - 45 mg/d. At baseline and days 14, 28, 56, and 84 (or early termination), the investigator/nurse coordinator performed a Caregiver Interview with nurses/professionals in daily contact with the patient and recorded CGI; 16-item Ham-D (Ham-D 17 minus Item 14) and the Cornell Scale. CIRS-G was recorded at baseline. Weight measured at baseline, day 28, and day 84.

Results: Fifty patients at 23 sites. Mean daily dose was 18.5 mg/d. Mean CIRS-G was 11.9 at baseline. CGI and Ham-D 16 response was 55% and 57%, respectively. Mean Ham-D 16 score decreased from 16.9 at baseline to 7.3; mean Cornell Scale score decreased from 51.1 at baseline to 7.1. Adverse Events (> 10%) included urinary tract infection, fall, accidental injury, vomiting, somnolence, and upper respiratory infection. Rates for falls and accidental injuries resembled placebo in other nursing home studies. Mean weight change was +0.6kg at day 84. Dropouts due to an AE occurred in five subjects, and one subject discontinued due to lack of efficacy.

Conclusions: Mirtazapine orally disintegrating tablets were effective and well-tolerated in depressed nursing home patients with multiple comorbidities who were ≥ 85 years of age.

References:

NR371  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
New Antidepressants in the Treatment of Depressed Elders: A Meta-Analysis

Fernando Rico-Villademoros, M.D., Biometrica, Eloy Gonzalo 27 -7ª planta, 28010 Madrid, Spain; David Rossell, Margarida Garcia-Garcia, M.S.C., Jeronimo Saiz-Ruiz, M.D.

Educational Objectives:
At the end of this presentation, the participant should be able to recognize the efficacy and tolerability of the newer antidepressants in the treatment of elderly depressed patients.

Summary:
Purpose: Eight-week study of the efficacy and safety of mirtazapine vs. paroxetine in patients ≥ 65 with anxious and depression.

Methods: Subjects drawn from a larger sample of 255 outpatients > 65 participating in an eight-week, double-blind study comparing the efficacy and safety of mirtazapine (15–45 mg/day) with paroxetine (20–40 mg/day). Subjects met DSM-IV criteria for MDD and had a baseline Ham-D 17 score ≥ 18 and an MMSE score ≥ lowest 25th percentile. Only patients who also met criteria for anxious depression (HAM-D 17 anxiety/somatization Factor 1...
NR373 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Efficacy and Safety of Higher Olanzapine Doses in Acutely Agitated Elderly Patients
Supported by Eli Lilly and Company

Donald P. Hay, M.D., Lilly Corporate Ctr, Eli Lilly and Company, Drop Code 4133, Indianapolis, IN 46285; Catherine Zofkie, D.O., Eva Marquez, Ph.D., Hillary McGuire, M.Ed.

Conclusions: Both mirtazapine and paroxetine were shown to be effective and well tolerated in elderly MDD patients with anxious depression, although mirtazapine was associated with a more rapid onset of efficacy compared with paroxetine.

References:

NR374 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Bipolar Disorder in Older Adults

Martha Sajatovic, M.D., Department of Psychiatry, Case Western Reserve University, 345 Timberidge Terrace, Gates Mills, OH 44040; C. Raymond Bingham, Ph.D., Elaine A. Campbell, M.D., Diana F. Fletcher, M.D.

Educational Objectives:
1. To identify clinical practice guidelines and disorders that affect older adults.
2. To review treatment regimens and applicable evidence in older adults for the treatment of bipolar disorder.
3. To discuss the specific needs and treatment considerations associated with the care of older adults with bipolar disorder.

Conclusions: At the conclusion of this session, the participant will recognize that late onset bipolar illness is not uncommon among geropsychiatric patients, and that clinical presentation may differ between late onset and early onset illness.

Summary:
Objective: The prevalence of mania among elderly psychiatric patients may be as high as 19%, with an estimated prevalence in the order of 10% among nursing home patients. It has been proposed that patients with late-onset manic symptoms may have a disease process that is initiated by organic, particularly neurologic factors, whereas genetic factors may be more important in the genesis of early-onset mania. This retrospective record review study evaluated clinical characteristics and hospital-based resource use patterns among older adults with early and late onset bipolar disorder.

Methods: Consecutive hospital discharge records where assessed for 42 individuals with bipolar illness. Individuals were categorized as having either early onset illness (EOS) beginning before the age of 50, or late onset illness (LOS), beginning at age 50 or later.

Results: Mean age of the group was 66.4 years with no difference in age between EOS and LOS categories. Late onset illness was identified in 28.6% of the group (N=12). Compared with individuals with EOS, individuals with LOS were 2.4 times more likely to be female, and 4.6 times more likely to be prescribed antipsychotic medications. Both groups had extensive medical comorbidity (mean of 3.4 comorbid medical conditions) and substantial hospital usage (mean length of stay 15.3 days).

Conclusions: Late onset bipolar disorder is not uncommon in older adults. Clinical characteristics and medication usage may differ between individuals with early and late onset illness.

References:

NR375 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Endothelial Nitric Oxide Synthase Genotype and Korean Schizophrenic Patients

Sang Keun Chung, M.D., Dept of Psych Chonbuk, National University Medical School, 634-18 Keumam-Dong Dokjin-Ku, Jeonju 560-181, South Korea; Kwang Hyun Cho, M.D., Myung Soo Choi, M.D., Ik Keun Mwang

Conclusions: Agitation in elderly patients improved on higher olanzapine doses without significant adverse events. Results suggest that doses up to 15 mg/day p.o. or 10 mg/day IM may be used safely in elderly patients. Larger elderly studies are warranted.

References:
Objectives: There were several animal studies using mice lacking the endothelial nitric oxide synthase gene (eNOS-/-). One study suggested that NO produced by eNOS facilitates male aggression. Also, another study reported possible concomitant effects on physiological parameters or changes in vascular functions of brain, and effects on behavioral processes related to reinforcement, learning, and emotion. However, there is no human study on eNOS gene in the psychiatric field. We investigated the association to explore the role of eNOS gene in Korean schizophrenic patients. We also examined the relationship of clinical characteristics of them to eNOS genotypes.

Methods: eNOS genotypes were analyzed using polymerase chain reaction of eNOS polymorphism(eNOS 27-bp repeat polymorphism in intron 4) in 77 schizophrenic patients and 121 healthy controls.

Results: The distribution of the eNOS genotypes in schizophrenic patients with a/a, b/a, b/b were 2(2.6%), 16(20.8%), 59(76.6%) and in controls were 1(1.0%), 29(24.0%), 91(75.0%). There were no significant differences in the eNOS genotype($X^2=1.3$, df=2, $p=0.615$) and allele frequencies($X^2=0.003$, df=1, $p=1.000$) between schizophrenic patients and controls. The clinical variables of schizophrenia (family history, positive and negative subgroups by PANSS, etc.) also were not associated with each genotypes.

Conclusion: Our results suggest that eNOS gene may not be causally related to the development of schizophrenia in Korean population.

References:


NR376 Tuesday, May 20, 12:00 p.m.-2:00 p.m.

Mental Health Treatment and the Elderly: Going From Gotta to Wanna

Leila B. Laitman, M.D., Geriatric Mental Health Department, Visiting Nurses Service of New York, 1601 Bronxdale Avenue, Bronx, NY 10462; Rebecca Morales, C.S.W., Linda Sacco, C.S.W.

Educational Objectives:

At the conclusion of this session, the participant should understand issues involved in getting older patients to accept mental health treatment without the use of coercive techniques.

Summary:

Objective: The In Home Geriatric Mental Health Program of the Visiting Nurse Service of New York is a specialized outreach team. Staff assesses people over the age of 60 in their homes that have some kind of psychiatric symptom and links them with ongoing care by community resources within an eight-week period. In 1998, only 14% of the patients discharged from our service actually accepted a mental health treatment referral. A training program that focused on interviewing and engagement techniques to help staff overcome patient and family resistances to ongoing mental health follow up was instituted. Acceptance of mental health linkage increased to about 50% by 2002. We wanted to investigate the role which staff felt use of coercive techniques played in achieving our success and perhaps alter it. Our hypothesis was that training staff to understand defenses and accept resistances as opposed to challenging them would lead to patient cooperation. This would be reflected in a lower number of cases in which clinicians assessed coercive techniques were necessary to achieve linkage.

Method: All cases opened May-August 2002 were reviewed. Those cases in which patients accepted mental health linkage were included in the study (N=36). Each respective clinician provided an assessment as to whether the patients accepted the referral voluntarily or if they had to be pressured to do so. A new eight-session training program (September-December 2002) that concentrated on helping staff decrease the use of coercion through the above principles was instituted. Subsequently, cases that were opened and closed during the training program were reviewed and selected for study in the same way as in the previous four months (N=40). Ultimately, we will include additional data from the months since the training has been completed.

Results: Prior to the training program, staff assessed that 56% of the cases voluntarily accepted mental health treatment while they assessed that they “forced” 44% into linkage. Preliminary results show that three months into the training, staff used coercive techniques 25% less.

Conclusion: Training staff to pay attention to these issues can have a positive impact in increasing patient cooperation. Some literature reports that perhaps less than 5% of those in the geriatric age group who need mental health treatment actually receive it. This study shows that linkages to mental health treatment can be increased dramatically through specialized staff training.

References:


NR377 Tuesday, May 20, 12:00 p.m.-2:00 p.m.

The Impacts of Cognitive Dysfunction and Depressive Symptoms on the Quality of Life in an Elderly Korean Population: Iksan Study

Sang-Yeol Lee, M.D., Department of Psychiatry, Wonkwang University, 144-23 Dongsan-Dong, Iksan, Chonbuk, ON 570-080, Korea; Min-Cheol Park, M.D.

Educational Objectives:

At the conclusion of this session, the participants should be able to recognize the impacts of cognitive dysfunctions and depressive symptoms on the health-related quality of life in an elderly Korean population.

Summary:

Objectives: The number of elderly people is ever increasing in Republic of Korea. It is estimated that elderly population 65 years old and over will increase 13.1% by year 2021. It is important to recognize cognitive dysfunction and depressive symptoms, and these impacts on the health-related quality of life in elderly people. This study assesses the prevalence of cognitive dysfunction and depressive symptoms, and the impacts of cognitive dysfunction and depressive symptoms on quality of life.

Methods: In the survey of elderly Koreans aged 65 years and older, living in Iksan selected by random sampling from 20 Dongs (village), which are located in rural (10) and urban (10) area. The prevalence of depressive symptoms was determined using the Geriatric Depression Scale (GDS), and the prevalence of cognitive dysfunction was determined using Mini Mental Status Examination.

Summary:

Objectives: The number of elderly people is ever increasing in Republic of Korea. It is estimated that elderly population 65 years old and over will increase 13.1% by year 2021. It is important to recognize cognitive dysfunction and depressive symptoms, and these impacts on the health-related quality of life in elderly people. This study assesses the prevalence of cognitive dysfunction and depressive symptoms, and the impacts of cognitive dysfunction and depressive symptoms on quality of life.

Methods: In the survey of elderly Koreans aged 65 years and older, living in Iksan selected by random sampling from 20 Dongs (village), which are located in rural (10) and urban (10) area. The prevalence of depressive symptoms was determined using the Geriatric Depression Scale (GDS), and the prevalence of cognitive dysfunction was determined using Mini Mental Status Examination.

At the conclusion of this session, the participants should be able to recognize the impacts of cognitive dysfunctions and depressive symptoms on the health-related quality of life in an elderly Korean population.

Summary:

Objectives: The number of elderly people is ever increasing in Republic of Korea. It is estimated that elderly population 65 years old and over will increase 13.1% by year 2021. It is important to recognize cognitive dysfunction and depressive symptoms, and these impacts on the health-related quality of life in elderly people. This study assesses the prevalence of cognitive dysfunction and depressive symptoms, and the impacts of cognitive dysfunction and depressive symptoms on quality of life.

Methods: In the survey of elderly Koreans aged 65 years and older, living in Iksan selected by random sampling from 20 Dongs (village), which are located in rural (10) and urban (10) area. The prevalence of depressive symptoms was determined using the Geriatric Depression Scale (GDS), and the prevalence of cognitive dysfunction was determined using Mini Mental Status Examination.
The quality of life was assessed using the Short-Form 36-Health Survey (SF-36).

**Results:** From the total of 528 people (154 male and 374 female) the adjusted overall prevalence of cognitive dysfunction was 43.6%, and the prevalence of depressive symptoms was 42.2%. The prevalence of severe cognitive dysfunction (MMSE<17) was 16.3%. The elderly group with cognitive dysfunction showed significantly lower score in each dimension of SF-36 than group without cognitive dysfunction, and the elderly group with depressive symptoms also showed significantly lower score in each dimension of SF-36 than group without depressive symptoms. There were significant negative correlations between GDS and each dimension of SF-36.

**Conclusion:** The results of this study suggest that the prevalence of cognitive dysfunction and depressive symptoms in an Korean elderly population is 43.6% and 42.2%. Cognitive dysfunction and depressive symptoms have negative impact on health related quality of life in Korean elderly population. This study also suggest that we must realize that cognitive dysfunction and depressive symptoms are likely to be prevalent sources of excess poor general health among elderly people and that when cognitive dysfunction and depressive symptoms strike the elderly people, these often go unrecognized and untreated.

### References:

### NR378 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
**Public’s Ability to Recognize Dementia and Their Beliefs on How to Treat It**

FAPESP, Sao Paulo Brazil

Sergio L. Blay, D.R., UNIFESP, R Botucato 740, Sao Paulo, SP 04023-900, Brazil; Erica T.P. Peluso, M.A.

**Educational Objectives:**
At the end of this session, the participant should know that general public is able to recognise dementia but traditional treatments are considered harmful.

**Summary:**

**Aim:** The aim of this study was to assess the public’s recognition of dementia and their beliefs about the helpfulness of interventions.

**Method:** A representative city sample of 2,000 individuals aged 18 to 65 years were interviewed in São Paulo, Brazil. The ability to identify the disorder and 17 treatment proposals were presented to 500 respondents in respect to a vignette depicting dementia. Respondents were asked to indicate the presence of a health problem as well as its nature and to indicate the treatment proposals considered to be helpful or harmful.

**Results:** Most of the participants recognized the presence of a problem (92%) and nearly 90% properly identified it as mental or neurological in nature. When various treatment proposals were rated as helpful for a person described in the vignette the five leading actions were: counseling (96%); special diet (94%); “keep the mind busy” (88%); reading (85%); religious practice (83%). Many standard psychiatric treatments were considered to be harmful.

**Conclusion:** Dementia is clearly recognized as a mental problem by the population. However, there is a large discrepancy between recognition and appropriate intervention approach. There is room for a public education concerning dementia and its treatment.

### References:

### NR379 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
**Poor Compliance With Medication Use in Patients With Alzheimer’s Disease**

Supported by Janssen Pharmaceutica Products, L.P.

Tina Richmond, Janssen Pharmaceutica Products, L.P., 1125 Trenton-Harbourtown Road, Titusville, NJ 08560; Scott Deschene

**Educational Objectives:**
At the conclusion of this session, the participant should be able to discuss the habits of physicians caring for patients with Alzheimer’s disease in terms of diagnosis and treatment and patient compliance to the medication prescribed.

**Summary:**

**Objective:** To analyze diagnostic and prescribing habits of U.S.-based physicians caring for Alzheimer’s disease patients.

**Methods:** Diagnostic and prescribing habits were analyzed using the NDC Health Patient, IMS, and NDTI databases and Covance Health Economics and Outcomes Services. Patients diagnosed with AD and/or prescribed acetylcholinesterase inhibitor (AChEI) therapy were included.

**Results:** Approximately 900,000 patients received AChEI therapy from January 2002 to October 2002, with more than 41,000 new patients in October 2002. While 41% were new to AChEI therapy; 6% switched from other drug classes (eg, antidepressants) or other AChEIs. Antidepressants are the most common concomitant therapy in AD patients treated with AChEIs, followed by antipsychotics. AChEI therapy duration average is approximately six months; primary care physicians (60%), neurologists (20%), and psychiatrists (8%) are the main prescribers.

**Conclusions:** Significant advances have been made in the diagnosis of AD, demonstrated by the number of new patients prescribed AChEIs; however, considerable discontinuation and non-compliance still occurs in these patients. Although this problem is improving, continued efforts are needed to increase use of approved AD therapies beyond current levels. Long-term therapy is necessary to maintain or delay cognitive and functional decline in AD patients.

### References:

### NR380 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
**The Pharmacokinetics of Fluoxetine in the Elderly**

Supported by GlaxoSmithKline

James M. Ferguson, M.D., Pharmacology Research Clinic, 448 East Winchester Street, Suite 200, Salt Lake City, UT 84107-8525; Heather Hill, M.P.H.
Educational Objectives:
At the conclusion of this session, the participant should have knowledge about the metabolism of fluoxetine and or fluoxetine in volunteers, ages 65–85.

Summary:
Twenty-five elderly subjects (eight male and eight female, 65–74 years old; three male and six female, 75 and 85 years old) were enrolled in a 16-week clinical trial to study the pharmacokinetics of fluoxetine.

After a two-week baseline, subjects received 20 mg fluoxetine (Prozac-Dista) qd for one week, and 40 mg fluoxetine qd. for the subsequent five weeks, at which time the drug was discontinued (week 8). Blood was drawn for fluoxetine and nor-fluoxetine analysis weekly from screen to weeks post-drug discontinuation (week 16).

The average plasma concentrations at week 8 of fluoxetine was 303 ng/ml; nor-fluoxetine 231 ng/ml; and the combined value 533 ng/ml are higher than those previously reported. The two age groups had similar plasma levels of fluoxetine, and norfluoxetine. Women had significantly higher plasma levels of norfluoxetine (p=0.007) and combined fluoxetine and norfluoxetine plasma levels (p=0.007) than men. There was a greater plasma concentration of fluoxetine than norfluoxetine at all time points. No significant effects were observed for age or sex on the estimated elimination of half-life of fluoxetine (4.9 days). The estimated average elimination half life of norfluoxetine was 13.7 days; a significant difference was seen in estimated elimination half life between the two age groups: older (p=0.047) and sexes: women (p=0.009).

References:

NR381
Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Open-Label Duloxetine Treatment of Major Depression in Patients Older Than Age 65
Supported by Eli Lilly and Company
Madeleine M. Wohlreich, M.D., Neuroscience, Eli Lilly & Company, Lilly Corporate Center, Indianapolis, IN 46285; John S. Kennedy, M.D., Craig H. Mallinckrodt, Ph.D., Joel Raskin, M.D., John G. Watkin, Ph.D., Pierre V. Tran, M.D.

Educational Objectives:
At the conclusion of this session, participant should be able aware of the efficacy and safety of duloxetine in the treatment of elderly patients with MDD.

Summary:
Background: Long-term treatment of MDD in older patients presents many concerns and challenges. This report examines duloxetine in the treatment of MDD in patients ≥65 years.

Methods: Data were gathered from a 52-week, 52-center, open-label study in patients with MDD (n=101) and received duloxetine treatment (80 mg/d to 120 mg/d). Efficacy measures included HAMD, total score; BDI-II, CGI-S, and SDS.

Results: Mean changes in HAMD, total score at Weeks 6, 28, and 52 were -13.0, -17.4 and -17.5 (all p<0.001). Observed case response rates at 6, 28, and 52 weeks were 62.9, 84.9, and 89.4, respectively, while remission rates were 41.4%, 69.8% and 72.5%, respectively. Significant improvement (p<0.001) in both CGI-S and PGI-I measures of improvement were observed at Week 1 and sustained. Significant improvements (p<0.001) were also seen in all assessed HAMD subscales (core, anxiety, retardation, sleep, Maier), HAMD, items 1 and 3, BDI-II total score, and SDS subfactors (work, social, and family) at all scheduled assessment points (Weeks 6, 28 and 52). The most frequently reported treatment-emergent adverse events were dizziness, nausea, constipation and somnolence.

Conclusions: In this study duloxetine was reported to be safe and tolerable for the long-term treatment of elderly patients with MDD.

References:

NR382
Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Assessment of Cognitive Disorder Using the Cognitive-Evoked Potentials in Stroke Patients
Jin-Sook Cheon, M.D., Department of Neuropsychiatry, Konin University Hospital, 34 Amnam Dong Seo Gu, Pusan 602-702, South Korea; Heung-Chae Jung, M.D., Byoung-Hoon Oh, M.D., Han-Cheol Yoon, M.D., Woong Cho, M.D., Sung-Boo Kim, M.D., Young-Tae Choi, M.D.

Educational Objectives:
At the conclusion of this session, the participant should know the clinical values of cognitive evoked potentials to assess severity of cognitive deficit and prognosis in cerebrovascular diseases.

Summary:
Objective: The aim was to evaluate clinical applicability of cognitive evoked potentials (CEPs) to identify cognitive deficit in cerebrovascular diseases (CVD).

Methods: The P3 latencies, amplitudes and latency to amplitude ratios (LARs) of CEPs were measured in 25 healthy controls and 35 inpatients with CVD. Association of CEPs with age, sex, Mini-Mental State Examination (MMSE), CVD types, Brief Psychiatric Rating Scale (BPRS), Instrumental Activities of Daily Living (IADL) was also analyzed.

Results: 1) P3 latencies (447.87±113.06msec) & LARs (65.83±43.25) were prolonged in CVD (p<0.05), while amplitudes (8.18±2.51 μV) were not. 2) P3 latencies (537.31±101.14 μsec) & LARs (94.89±46.44 μsec) in CVD with MMSE<24 were prolonged, and amplitudes (6.45±1.96 μV) were reduced (p<0.05). 3) P3 latencies were correlated positively with age, BPRS & IADL, and negatively with MMSE. 4) LARs were correlated positively with age, BPRS & IADL, and negatively with MMSE. In CVD with MMSE<24, P3 latencies were correlated positively with BPRS and negatively with MMSE, while amplitudes were positively with age, and LARs were positively with IADL.

Conclusions: The P3 latencies and LARs of CEPs seemed to be a useful clinical measures to assess cognitive disorders in CVD as well as in vascular dementia.

References:

NR383  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Attempted Suicide in the Elderly: Epidemiology
Carlos A. Finkelsztein, M.D., Department of Psychiatry, Hospital Italiano, Gascon 450, Buenos Aires, Argentina; Daniel Matusевич, M.D., Eugenia Dabi, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the profile of elderly suicide attempters, in our culture and should diagnose the patients or situations more vulnerable or at high risk for commit suicide.

Summary:
Objective: The aim of this paper is to analyze some characteristics of 25 patients, over 60, who attempted suicide and were hospitalized in the department of psychiatry of a general hospital in Buenos Aires.

Methods: This is a retrospective study using data from the medical records of patients (1999 to 2002); based on a protocol comprising an analysis of attempted suicides, demographic and clinical variables.

Patients were diagnosed following the DSM-IV criteria by two trained GPs and were confirmed by MMPI and Rorschach.

Results: 72% were women. The average age was 72. 16% were divorced, 20% never married, 32% widowed and 32% married. The most frequent diagnosis was Major Depressive Disorder of late onset followed by Personality Disorder (96%; 48%). The most frequent method was intoxication, (68.75% BDZ). Almost half of the attempts were highly severe.

Discussion: We may infer that the elderly person who attempts suicide: is female, 68–78 years old, does not have a partner, lives with someone, has Major Depressive Disorder (at least half of them had Personality Disorder) and a clinical disease. This is her first attempt, is alone at home, and she does not advise others. Reduced hearing is a very frequent co-morbidity.

References:

NR384  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Development of WHODAS II in an Older Korean Population
Ministry of Health and Welfare of Korea
Jin-Sang Yoon, M.D., Psychiatry Department, CNU Medical School, 51 Hak-Dong, Dong-Gu, Kwangju 501-748, Korea; Jae-Min Kim, Ph.D., Kyung-Lyul Bae, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand that disability measured by WHODAS II may reflect physical illness, depression, and cognitive function in community living old people.

Summary:
Introduction: WHODAS (World Health Organization Disability Assessment Schedule) II interviewer version is a 36-item assessment scale for evaluating disability, developed by the WHO. This study aimed to develop its Korean version (WHODAS II-K) and to investigate factors associated with disability.

Methods: Formal permission to translate WHODAS II into Korean language was obtained, and the translation process followed the WHO translation guidelines. WHODAS II-K was administered to 1,204 community residents aged 65+. Characteristics on demographics (age, gender, education, living area, marital state, and religion), socio-economic factors (housing, number of rooms, past occupation, current employment, monthly income), social network, number of physical illness, depression (GMS), and cognitive function (MMSE-K) were gathered.

Results: Inter-rater and test-retest reliability, and internal consistency (Cronbach’s α) of WHODAS II-K were satisfactory. In the uni-variate analyses, score on WHODAS II-K was associated with most characteristics above in their worse state. However in the multi-variate analyses, it was associated with increased number of physical illness, having depression, and worse cognitive function, but not with demographic, socio-economic, and social network characteristics.

Conclusions: The WHODAS II-K was successfully developed. Clinicians and researchers should recognize that physical illness, depression, and cognitive function are associated with reported disability in old people.

References:

NR385  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Use of Higher-Dose Quetiapine in Elderly Inpatients: A Chart Review Study
Supported by AstraZeneca Pharmaceuticals
Franco Sicuro, M.D., 3938 S Broadway, St. Louis, MO 63118

Educational Objectives:
At the conclusion of this presentation, the participant should realize that quetiapine was effective and safe in treating elderly demented patients with psychosis and agitation in an inpatient setting.

Summary:
Objective: To identify elderly patients treated with >200 mg quetiapine and to evaluate both efficacy and safety parameters.

Methods: Charts of patients 65 years or older were reviewed at a geropsychiatric inpatient unit over 15 months to identify those taking quetiapine.

Results: Twenty-eight patients were analyzed and the mean age was 78.5 years. Mean quetiapine dosage on discharge was 450 mg/d, and average dosage increase during admission was 262 mg/d. Mean improvement in Clinical Global Impression (CGI) scores was 56.5% (from moderately-markedly ill to much improved). Nine patients (18 episodes) experienced falling during the course of hospitalization; 11 episodes occurred with as-needed medications (haloperidol, lorazepam, or fluphenazine), five episodes occurred while taking quetiapine and another neuroleptic, and two episodes occurred while the patient was not taking quetiapine. No patients reported falling while on quetiapine alone. Five patients experienced sedation unexplained by doses of as-needed medication. Two patients developed EPS while taking quetiapine; however, both patients were also receiving routine dosages of haloperidol.

Conclusions: This study was the first to identify that quetiapine was effective and safe at dosages >200 mg/d in treating elderly
demented patients with psychosis and agitation in an inpatient setting. Further prospective studies are needed.

References:

NR386 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Insight to Impact of Mild Cognitive Impairment and Early Alzheimer’s Disease
Supported by Eli Lilly and Company

Jennifer A. Flynn, M.S.P., DC 1834, Eli Lilly and CO, Lilly Corporate Center, Indianapolis, IN 46283; Lori Frank, Ph.D., Andrew Lloyd, D.P.H., Louis Matza, Ph.D., Lee Bowman, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize key features of mild cognitive impairment and early Alzheimer’s disease as determined by patients and their informants. The purpose of this study is to prospectively examine a carefully defined sample of patients with idiopathic Parkinson’s disease (PD) and determine the prevalence of depression and associated factors.

Methods: Patients with probable mild PD (NINCDS-ARDA criteria) or MCI (memory complaints with informant corroboration; no ADL impairment; normal cognitive function; no dementia) and their informants were recruited for focus groups. Data from six patient focus groups (3 MCI, 3 AD, total N=41) and four informant groups (2 MCI, 2 AD, total N=22) identified differences in symptom recognition and perceived impact between patients and informants.

Results: MCI patients reported a mix of self-recognition of symptoms and first recognition by others. Most AD patients reported others noticed memory problems before they did. Informants for both groups mentioned patient loss of emotional control in contrast to limited mentions of such emotionality from the patients themselves. Informants reported greater symptom severity than indicated by patients. Patients provided insight into symptom impact on daily functioning.

Conclusions: While informant information may enhance assessment of symptom onset and severity, patients provide unique information allowing for more comprehensive assessment of MCI and mild AD impact.

References:

NR387 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Parkinson’s Depression Associated With Functional Not Neurologic Impairment
American Parkinson’s Disease Association

Suzanne Holroyd, M.D., Department of Psychiatry, University of Virginia. Health Sciences/Box 800623, Charlottesville, VA 22908; G.F. Wooten, M.D., Lillian Currie, Ph.D.

Educational Objectives:
At the conclusion of this session, the participants will understand the correlates of depression in Parkinson’s disease, including associated disability.

Summary:
Objective: The purpose of this study is to prospectively examine a carefully defined sample of patients with idiopathic Parkinson’s disease (PD) and determine the prevalence of depression and associated factors.

Methods: One hundred consecutive patients attending a movement disorder specialty clinic in a university setting, with idiopathic PD as defined by international research criteria, were asked to participate. They were examined for depression using the Geriatric Depression Scale, cognition using the Telephone Interview for Cognitive Status (TICS) and neurological disease severity using the Unified Parkinson’s Disease Rating Scale (UPDRS) as well as demographic and clinical measures.

Results: Fifteen percent of patients were found to have major depression. There were no differences between those with or without major depression on age, gender, age of onset of PD, duration of disease, duration of L-dopa use, L-dopa dose, or medical comorbidity. Major depression was associated with a higher UPDRS score (50±19 vs. 39±17 p=.02) however closer inspection revealed this difference was due to differences in the ADL subscale (17±7 vs 12±6 p=.004) rather than differences in the motor subscale (30±13 vs 26±13 p=.27). In addition, depression was associated with worse cognitive function (TICS score 30±5 vs 33±4 p=.04).

Conclusion: Major depression in PD is not associated with disease severity but is strongly associated with functional impairment. PD patients should be carefully screened and treated for depression to maximize their function. In particular, patients with poor functioning should especially be assessed for presence of major depression.

References:

NR388 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Burden of Manic Versus Depressive Symptoms in Subjects With Bipolar Disorder
Supported by GlaxoSmithKline

Robert M.A. Hirschfeld, M.D., Psychiatry & Behavioral Science, University of Texas Medical Branch, 301 University Boulevard 1.302RSH, Galveston, TX 77555-0188; Joseph R. Calabrese, M.D., Mark A. Frye, M.D., Michael L. Reed, Ph.D., Karen D. Wagner, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to compare and contrast the impairment associated mania vs depression in subjects who screen positive for bipolar disorder.
Impact of Bipolar Depression Compared to Unipolar Depression and Healthy Controls
Supported by GlaxoSmithKline


NR389 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Predicting Response to Methylphenidate in Central Pontine Myelinolysis
Department of Veteran Affairs

Thomas P. Beresford, M.D., Department of Psychiatry, VMC/University of Colorado, 1055 Clement Street, Suite 116, Denver, CO 80220; Loraine K. Clapp, M.S., David B. Arciniegas, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the symptomology of Central Pontine Myelinolysis as well as predict possible responders to methylphenidate in its treatment.

Summary:
Objective: Central Pontine Myelinolysis (CPM) is a rare but devastating demyelinating disease of the brain stem that can affect extrapontine brain structures including fronto-subcortical pathways. We recently reported successful treatment the neuropsychiatric sequelae of CPM with methylphenidate. In the current study, we wished to elucidate the factors that predict a good response to methylphenidate in the treatment of CPM. We hypothesized that the presence of MRI-documented basal ganglia lesions would predict a useful response to methylphenidate.

Method: we tracked the frontal lobe functioning of 4 alcohol dependent, magnetic resonance image (MRI) confirmed, CPM cases by administering the UCLA Neuropsychiatric Inventory at baseline, two weeks, three weeks, and four weeks following drug administration. Target psychiatric symptoms were apathy, amotivation, lack of social propriety, inattention to activities of daily living, cognitive slowing and depressed mood.

Results: Of the four cases, the three subjects where MRI-documented basal ganglia lesions existed showed significant improvement in NPI scores while on methylphenidate. The forth case, without lesions in any of the basal ganglia structures, did not show significant improvement.

Conclusion: The existence of a basal ganglia lesion, as visualized on MRI scanning, may predict a good response to methylphenidate in the treatment of CPM.

References:
NR391  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
CNS Catecholaminergic Systems and Thyroid Hormone Metabolism
Rolf Yhede, M.D., Department of Anaesthesiology, Surgical Sciences, Åkerslundsövagen 12, Askim 43640, Sweden; Anders Forsman, M.D., Henrik Soderstrom, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to have an overview of possible interactions between the CNS monoaminergic systems and thyroid hormone metabolism in association with aggression

Summary:
To study possible relationships between the activity in the brain monoaminergic systems, peripheral thyroid hormone activity, and aggressive behaviour, we compared CSF metabolites of norepinephrine, dopamine, and serotonin to serum TSH, free (F) and total (T) T₃, T₄, binding proteins and the ratios between T₃ and T₄ fractions (reflecting the deiodination) and between F and T fractions (reflecting the degree of protein binding) in 56 violent offender undergoing pre-trial forensic psychiatric investigations. The serotonin metabolite 5-HIAA was unrelated to the thyroid hormone activity. The catecholaminergic metabolites HVA and MHPG were positively related to TSH and to diminished T₃ availability with increased T₄/T₃ ratios. The HVA/MHPG ratio correlated with the assessments of thyroid hormone activity in the same directions, indicating dopaminergic regulatory mechanisms for thyroid hormone activity, both in the TRH-TSH axis and in the peripheral hormone metabolism. Protein binding, hepatic pathology, age, sex, and any ongoing medication did not change this finding, which has bearing on the understanding of adaptation to change in the brain catecholaminergic activity due to chronic stress or to neurological or psychiatric diseases and their pharmacological treatments, and warrants further investigations. The HVA/5-HIAA and T₃/T₄ ratios correlated consistently with aggressive behaviour as measured by the Psychopathy Checklist Revised (PCL-R).

References:

NR392  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Risperidone Triggers Subventricular Zone Neurogenesis in Rats: Possible Implications for Improved Olfaction
Supported by Janssen Pharmaceutica Products, L.P.
Mohammed Khan, Ph.D., Department of Psychiatry and Health Behavior, Medical College of Georgia, 1 Freedom Way, Augusta, GA 30904; Vinay Parikh, Ph.D., Pinky Salat, M.S., Sahebarao Mahadik, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to compare the effects of a typical and atypical antipsychotic on neurogenesis in an animal model.

Summary:
Objective: Risperidone and haloperidol were compared for degree of neurogenesis in the subventricular zone (SVZ), a source of olfactory neural cells and site of their migration to the olfactory bulb (OB) and differentiation.

Methods: Adult male Wistar rats (250–300 gm) received oral haloperidol (2 mg/kg/day) or risperidone (2.5 mg/kg/day) for 45 days. For neurogenesis, all animals received two i.p. injections of 80 mg/kg of BrdU at nine-hr intervals on treatment days 14 and 45. Animals were then anesthetized, intracardially perfused with cold (4°C) PBS, and brains were sectioned coronally into two equal halves and cryopreserved in OCT. For immunohistochemical analysis, 20-uM sagittal sections were cut through the SVZ and OB and stained for BrdU (proliferating cells), OB protein (matured olfactory neurons), and glial fibrillar acidic protein (a glial marker).

Results: Risperidone significantly induced more neurogenesis (number of BrdU positive cells in SVZ and different OB layers than haloperidol (P=0.05). The maximum number of BrdU positive cells in the OB were found in the internal granule cell layer, followed by mitral cell layer and external glomerular layer.

Conclusion: These data provide a novel mechanism of neuroplasticity associated with risperidone.

References:

NR393  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Analysis of Using Binomial Forced-Choice Digit Memory Test in the Patients With Financially Compensable Head Trauma
Bellin Gao, M.D., Shenzhen Kangning Hospital, Cuizhu Road #1080, Shenzhen Gungdon 518020, China; Rengang Liu, M.D., Chiyi Hu, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to use Binomial Forced-Choice Digit Memory Test for patients with head injuries.

Summary:
Objective: To study the actual effect of the Binomial Forced-Choice Digit Memory Test (BFDMT) in detecting dissimulation of intellectual deficit.

Methods: 64 subjects with compensable head injury were assessed by BFDMT, experiential judgment, and Raven’s Standard Progressive Matrices (RSPM), and were finally diagnosed on intellectual deficit degrees.

Results: (1) The rate of malingering was 78.1% by assessing of the total score of BFDMT. The rate of malingering was 43.8% by experiential judgment. BFDMT had increased 34.3% of discerning rate. (2) There were no significant differences among the three groups of dissimulating, non-malingering, and uncertain by experiential judgment. All 16 cases in the uncertain group were assessed as malingering by BFDMT. (3) Only one case was considered as a misdiagnosis diagnosis by follow-up.

Conclusion: BFDMT is useful for detecting dissimulation of intellectual deficit. It is particularly effective in distinguishing the cases that are difficult to judge by clinical experience.

References:

NR394 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Detection and Incidence of Catatonic Syndrome in the National Institute of Neurology and Neurosurgery in Mexico City
Magdalena Ocampo, M.D., Department of Psychiatry, Neurology Institute, Insurgentes Sur 3877 La Fama, Mexico, DF 14269, Mexico; Ignacio Ruiz, M.D., Ricardo Colin-Plana, M.D., Ana Luisa Sosa, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the catatonic syndrome.

Summary:
Background: The catatonia is a syndrome with multiple and heterogenous etiologies. Around 10% of patients with severe acute psychiatric illness exhibit a cluster of motor signs that are identified as the catatonic syndrome.

Objective: The purpose of this study was to demonstrate that the catatonic syndrome can be present in patients with neurologic and psychiatric illnesses.

Methods: We evaluated all in-patients in the Neuropsychiatric unit of the national Institute of Neurology and Neurosurgery in a period from May 2000 to October 2001, through observation, clinical evaluation and the application of the Bush-Francis rating scale. The total patients evaluated was 341.

Results: We detected 21 patients which completed the criteria. 14 had a psychiatric illness and seven had neurological illness. The incidence was around the 8%. According to the Bush-Francis' catatonia scale the degree of intensity of the symptoms was 15.5 in all psychiatric patients, and 22 in all neurological patients. The clinical evaluation showed that all neurological patients had a higher degree of intensity.

Conclusions: With this study we were able to demonstrate that the catatonic syndrome exists in México. The absence of previous cases can be due to the lack of research and accurate diagnosis procedure.

References:

NR395 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Characterizing Psychiatric Comorbidity in Epilepsy Supported by GlaxoSmithKline
Jana E. Jones, Ph.D., Department of Neurology, University of Wisconsin, H4800CSC 600 Highland Avenue, Madison, WI 53792-6180; Bruce Hermann, Ph.D., John Barry, M.D., Frank Gilliam, M.D., Kimford Meador, M.D., Andres M. Kanner, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the importance of identifying psychiatric comorbidities in individuals with epilepsy. Axis I disorders are present in a large proportion of this population and frequently go unrecognized.

Summary:
Objective: This multicenter investigation: (1) examined the utility of the Mini International Neuropsychiatric Interview (MINI) to characterize psychiatric comorbidity in epilepsy (2) compared the validity of MINI diagnoses of current mood disorders to the Structured Clinical Interview for DSM-IV Disorders [SCID], and (3) developed a self-report instrument to detect depressive symptoms in epilepsy.

Method: Individuals with epilepsy (n=118) underwent standardized clinical interviews with the MINI and the Mood Disorders module of the SCID and completed several self-report mood questionnaires. Patients were > age 17, on stable AED treatment for 30 days, with intact reading ability, and no epilepsy surgery or vagal nerve stimulator.

Results: The MINI revealed that current Axis I disorders were common, with anxiety (57.6%) and mood (29.7%) disorders the most frequent. Among current mood disorders, most common were major depressive episodes (19.5%), past hypomanic episodes (7.6%), and dysthymia (6.8%). Correlation between the MINI and SCID for current major depressive episodes was .808.

Conclusion: These results indicate: (1) Axis I disorders are common among individuals with chronic epilepsy (50.8%), (2) the most common mood disorder is major depressive episode (19.5%), and (3) psychiatric comorbidity in epilepsy can be identified using standardized psychiatric interview procedures that have acceptable validity compared with the gold standard SCID.

References:

NR396 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
GABA Pentin Treatment Response in SSRI-Refractory Panic Disorder
Simon S. Chiu, M.D., Addiction Rehabilitation Unit, St Thomas Psychiatric Hospital, 467 Sunset Drive, St. Thomas, ON N5P 3V9, Canada

Educational Objectives:
At the conclusion of this session, the participant should be able to (1) To review current and emerging pharmacological approaches in panic disorder; and (2) understand the mechanisms of the putative anxiolytic activity of GABApentin

Summary:
Introduction: Despite the demonstrated efficacy of SSRI (selective serotonin reuptake inhibitors) in Panic disorder, the issue of SSRI-refractory panic disorder is emerging in clinical practice. Alternative treatment approach with anti-convulsants has been explored.

Objective: of the study: to evaluate the treatment response to GABApentin, a novel anticonvulsant, in patients unresponsive to previous SSRI therapy.

Method: The design was open-label and naturalistic. Patients with DSM IV diagnosis of panic disorder with history of treatment failures to two SSRIs at recommended optimal dosages (duration: 8 weeks for each SSRI) entered the study. Bipolar and major depressive disorders and seizure disorders were excluded. The dosage of GABApentin was titrated over the 12-week period. Efficacy measures: Hamilton Anxiety Rating scale (HAM-A), Panic and Agoraphobia Scale (PAS), Hamilton Depression Scale (HAM-D) and Clinical Global Impression Scale: Improvement score (CGI-I)., were conducted at baseline, 2 wk, 4 wk. 6 wk, and 12 wk. Tolerability was assessed with treatment emergent adverse events.

Results: 20 (male/female: 8/12, mean age: 35 years) entered the study. The mean dosage of GABApentin was 1400 mg per day (range: 600 mg to 2400 mg). As compared with the baseline
were mild headache and restlessness during the first 2 weeks.

Conclusion: The positive results in the open study warrant the design of placebo-controlled trials to validate the efficacy and safety of GABApentin in panic disorder refractory to SSRI treatment.

References:

NR397 Tuesday, May 20, 12:00 p.m.-2:00 p.m.

Immune Activity in Adults Suffering From Depression Supported by Universidade Estadual De Londrina

Sandra O.V. Nunes, M.D., Av Achemar de Barros #625, Londrina, Brazil; Edna Reiche, M.D., Helena Morimoto, M.D., Elko Itano, Ph.D., Mari Morimoto, M.D., Tiene Matsuo, Ph.D., Fernando Reiche, S.T.

Educational Objectives:

- The present study was undertaken to evaluate the levels of immune components in adults ambulatory patient with depression

Summary:

Objectives: This research has been undertaken to find if depression might suppress cellular immunity but boost humoral immunity.

Method: This study evaluated immune measurements in 40 non-medicated, ambulatory, adult patients with depression determined by C10-d criteria and compared with 34 healthy nondepressed subjects. The severity of the condition was determined with the Hamilton Depression Rating Scale. The immune measurements included C-reactive protein; total serum protein and fractions; serum immunoglobulins IgG, IgA, IgM, C3 and C4 complement; interleukin 1β; interleukin 6; tumor necrosis factor-α; soluble interleukin 2 receptor; and mitogen-induced lymphocyte stimulation.

Results: Of 40 depressed patients, 31 had very severe and nine severe or moderate depression. Twenty-nine (72.5%) were females and 11 (27.5%) were males (2.6:1 ratio). The results revealed a significant reduction of albumin, and elevation of alpha-1 globulins, alpha-2 globulins, beta-globulins and soluble interleukin 2 receptor in patients with depression compared with the values obtained for nondepressed subjects (p<0.05). The decrease lymphoproliferation in response to mitogen was significant lower in severely or moderately depressive patients when compared to control (p<0.05).

Conclusion: These results confirm the immunological disturbance in acute phase proteins and cellular immune response in patients with depression. The clinical relevance of these findings requires further investigation.

References:

NR398 Tuesday, May 20, 12:00 p.m.-2:00 p.m.

Immunological Measures in Women Outpatients With MDD

Andrea H. Marques, Ph.D., Department of Psychiatry, University of Sao Paulo, Rua Simao Alaves 785 AP71, Sao Paulo, SP 05417-030, Brazil; Francisco Lotufo-Neto, M.D., Wagner Dominguez, B.S.C., Euthymia B. Prado, Ph.D., Ana C. Solis, M.D.

Summary:

Introduction: Major depressive disorder (MDD) may be associated with several immunological alterations. This present study have investigated immunological measures and the activity of hypothalamic-pituitary-adrenal axis (HPA) in women outpatients with different subtypes of MDD (melancholic or atypical; acute or chronic; severe or moderate; unique or recurrent episode) before and after treatment and in a control group.

Hypothesis: Different immunological patterns should discriminate subtypes of MDD.

Methods: 46 women and 40 volunteers from the Department of Psychiatry, University of São Paulo were enrolled. Diagnosis was made with SCID (DSM-IV) and Hamilton Depression Scales (HDRS,21). The patients were medicated with sertraline or imipramine. The following laboratory evaluations were performed: IL-1β, IL-6, IFN-gamma, serum cortisol, leukocytes, monocytes, neutrophils, lymphocyte, CD3+, CD4+, CD8+ acute phase proteins, complement components and immunoglobulins.

Results: Significant differences were not found in the measures above between the group of patients before treatment and the control group. The group of patients after treatment had significant increase of cytokines levels, but not in others immunological parameters. The group of patients after treatment had no similar cytokines measures to the ones of the control group.

Conclusion: Women, outpatients, with MDD (in all subtypes) had no immunological and HPA axis activation. The antidepressant action can be related to the raise of cytokines after treatment.

References:

NR399 Tuesday, May 20, 12:00 p.m.-2:00 p.m.

Placebo Dose and Clinical Efficacy: Any Relation in Major Depression?

Supported by Eli Lilly Regional Operations Ges.m.b.H

Robert Lebeda, M.Sc., Department of Neuroscience, Eli Lilly Regional, Barichgasse 40-42, Vienna 1030, Austria; Istvan Bitter, M.D., Steven Metcalfe, M.Sc.

Educational Objectives:

- At the conclusion of this presentation, the participant should be able to recognize the importance of considering bias due to a possible dose response relationship of placebo when designing a clinical trial protocol as well as when presenting clinical trial data.

Summary:

Objective: The purpose of this review article was to investigate any dose response relationship for placebo in patients with major depression.

Method: A search in MEDLINE and EMBASE for randomized, placebo controlled clinical trials evaluating paroxetine, fluvoxamine, fluoxetine, citalopram, venlafaxine, duloxetine, mirtazapine or imipramine for depression treatment. Seventeen studies were identified after a review for topic relatedness and reliability according to predefined criteria. Dosage was extracted as the number of capsules or mg imipramine equivalent per day. Efficacy data were HAM-D, MADRS, CGI improvement, and the percentage of responders. Patients discontinuing treatment were analyzed for
safety. A statistically significant correlation should be identified using regression analyses.

Results: The percentage of patients discontinuing treatment due to adverse events increased significantly in relation to the number of placebo tablets per day. A similar increase was identified for this safety parameter for the active compounds and two subgroups.

Conclusion: This correlation may be related to patients’ expectations and/or severity of the disorder. Although no dose response relationship could be found for placebo in this analysis, it could arise under specific conditions. Bias of clinical data due to a possible dose response relationship of placebo should be carefully considered when designing clinical trial protocols.

References:

NR400 Tuesday, May 20, 12:00 p.m.-2:00 p.m. Pharmacokinetics and Safety of Divalproex Extended Release in the Pediatric Population Supported by Abbott Laboratories

Thomas Cummins, M.D., Abbott Laboratories, 200 Abbott Park, Abbott Park, IL 60064-6149; Sandeep Dutta, Ph.D., Kenneth Sommerville, M.D., James C. Cloyd, Pharm.D., Gregory H. Kearns, Ph.D.

Educational Objectives:
- At the conclusion of this session, the individual should be: (1) able to administer divalproex ER to the pediatric population in a safe and effective manner; (2) aware that similar to adults, once-daily divalproex ER could sustain valproate concentrations over 24 hours in the pediatric population.

Summary:
- Objective: Assess the pharmacokinetics and safety of once-daily divalproex extended-release (ER) tablets in children and adolescents and compare them with a healthy adult control group.
- Methods: This was a multiple-dose, non-fasting, open-label, multi-center, pharmacokinetic study in child (8–11 years) and adolescent (12–17 years) patients (bipolar disorder [N=11], migraine prophylaxis [N=9], seizure [N=7], ADHD [N=2]). Once-daily divalproex ER doses ranged from 250 to 1750 mg. Safety was evaluated based on adverse events (AE), physical examinations, vital signs, and laboratory assessments.
- Results: Two of 29 enrolled subjects discontinued for administrative reasons and one for flu syndrome. Once-daily divalproex ER produced sustained valproate concentrations in children and adolescents for 24 hours with mean clearances of 336 and 358 mL/h/m² respectively; not significantly different from the profile observed in adult control group (clearance = 321 mL/h/m²). AEs were generally mild to moderate in severity and similar to those reported in previous divalproex studies. The most common (≥10% prevalence) AEs reported were flu syndrome (17%, 5/29) and headache (10%, 3/29) with 33% (5/15) of children reporting AEs compared with 50% (7/14) of adolescents.
- Conclusions: Similar to adults, once-daily divalproex ER can sustain valproate concentrations among children and adolescents for 24 hours. Divalproex ER was well tolerated in this pediatric population.

NR401 Tuesday, May 20, 12:00 p.m.-2:00 p.m. Insulin Resistance in BPD With and Without MDD Medical University of Lubeck

Kai G. Kahl, M.D., Department of Psychiatry, Medical University, Rätteburger Allee 160, Luebeck 23538, Germany; Sebastian Rudolph, M.D., Beate Stockelhuber, Ph.D., Christoph Kroger, M.D., Fritz Hohagen, M.D., Leif Dibbelt, M.D., Ulrich Schweiger, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to recognize patients with borderline personality disorder and comorbid lifetime major depressive disorder as being at risk for developing diabetes mellitus type II.

Summary:
- Introduction: Increased visceral fat, a risk factor for the development of insulin resistance, has been observed in patients with major depressive disorder (MDD). A dysregulation of the hypothalamic-pituitary-adrenal axis (HPAA) has been discussed as a pathogenetic factor in insulin resistance. Since a dysregulation of the HPAA has been discussed in MDD and borderline personality disorder (BPD) our study aimed at examining whether insulin resistance and visceral fat are altered in BPD patients with and without comorbid MDD.
- Methods: Thirty-one BPD patients diagnosed according to DSM-IV and 13 age- and sex-matched healthy controls (CTRL) were included. Visceral fat was measured with abdominal MRT at lumbar vertebra 5 (L5). Fasting hormone levels and glucose were determined using standard laboratory methods. Insulin resistance and β-cell sensitivity were approximated with the homeostasis assessment model. Statistical analysis was performed with MANCOVA, Kruskal-Wallis test and Mann-Whitney-U test. A p-value <0.05 was considered significant.
- Results: MANCOVA revealed significantly increased visceral fat (F=2.74; df=5; p=0.047), serum insulin (F=3.19; df=5; p=0.027) and insulin resistance (F=3.65; df=5; p=0.016) in the subgroup of BPD patients with comorbid lifetime MDD (n=14) when compared with CTRL.
- Conclusions: A lifetime history of MDD in BPD patients may increase the risk for the development of diabetes mellitus type II.

References:

NR402 Tuesday, May 20, 12:00 p.m.-2:00 p.m. Alexithymia in Psychiatric Disorders

Feryal Cam-Celikel, M.D., Department of Psychiatry, Gaziosmanpasha Universities, Psikiyatri Ad Tokat, 60200, Turkey; Omer Saatcioglu, M.D.
Educational Objectives:

The educational objective of this research is to demonstrate that alexithymia does not have a diagnostic specificity in diverse psychiatric syndromes.

Summary:

Objective: Alexithymia has been an interesting area for psychiatric research. There is still limited data on the diagnostic specificity of alexithymia construct in patients with different psychiatric disorders. The purpose of this study is to evaluate alexithymia in depression and anxiety spectrum disorders.

Method: This is a preliminary report of an ongoing research. The Structured Clinical Interview for DSM-IV (SCID), the 20-item Toronto Alexithymia Scale (TAS), 17-item Hamilton Rating Scale for Depression (Ham-D), and Hamilton Anxiety Rating Scale (HARS) were administered to a sample of 52 subjects.

Results: The total sample was between 16 to 70 years (mean age 55, 61±11, 81). Thirty-seven patients (71, 2%) met DSM-IV criteria for depression, and 15 patients (28, 8%) for an anxiety disorder (due to small sample sizes, panic, obsessive-compulsive, and generalized anxiety disorder patients were combined in one group for statistical purposes). No statistically significant difference was found between TAS total scores and depression or anxiety severities of the entire sample. Depression or anxiety disorder diagnoses were not significantly related to elevated TAS scores.

Conclusion: Regarding these preliminary results of our ongoing research, alexithymia scores do not have a diagnostic specificity in diverse psychiatric syndromes.

References:


NR404 Tuesday, May 20, 12:00 p.m.-2:00 p.m.

Conversion Between Divalproex Sodium Extended Release and Divalproex Sodium Delayed-Release Tablets

Supported by Abbott Laboratories

Sandee Dutta, Ph.D., 4PK, Abbott Laboratories, 200 Abbott Park Road, Abbott Park, IL 60064-6149; Kenneth Sommerville, M.D., Yiming Zhang, Ph.D., James C. Cloyd, Pharm.D., Basim M. Uthman, M.D., Victor Bilon, M.D.

Educational Objectives:

At the conclusion of this session, the individual should be able to safely convert patients from their current divalproex DR dose to once-daily divalproex ER aware that the type of enzyme-inducing antiepileptic drug and the total daily divalproex DR dose does not affect the divalproex DR to ER dose-conversion ratio.

Summary:

Objective: Divalproex sodium extended-release tablets (ER) have 10% lower bioavailability than divalproex sodium delayed-release tablets (DR). This study evaluated the safety and bioavailability of 8% to 20% higher once-daily ER doses relative to DR Q8H regimens.

Methods: This was a multiple-dose, randomized, open-label, crossover pharmacokinetic study in adults (N=76). Total daily DR doses range was 875–4250 mg, and ER dose range was 1000–5000 mg (matched as 8% to 20% higher). Valproic acid (VPA) plasma concentration-time profiles were used to assess pharmacokinetics. Safety was evaluated based on adverse events (AE), physical examinations, vital signs, and laboratory assessments.

Results: ER QD and DR Q8H regimens were equivalent for exposure (area under the VPA concentration-time curve). ER VPA maximum concentration was significantly lower than and minimum concentration was not significantly different from, the corresponding values for the DR regimen. AEs were transient and generally mild. The most common AEs (≥3% incidence; ER vs. DR) were headache (1% vs. 4%), abdominal pain (0% vs. 3%), and viral infection (3% vs. 1%). AE incidence rate was not significantly different between ER and DR.

Conclusions: To switch patients from DR regimens to ER QD regimens, the total daily ER dose has to be increased by 8% to 20%.
References:


NR405 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Brain Music: A Novel Somatic Treatment for Insomnia and Anxiety
Leonid Kayumov, Ph.D., Department of Psychiatry, University of Toronto, 399 Bathurst Street, ECW 3D-P35, ON M5T258, Canada; Henry J. Moller, M.D.

Educational Objectives:

At the conclusion of this session, the participant should understand the rationale and evidence for use of the neurofeedback method of “Brain Music” therapy for insomnia and anxiety.

Summary:

Objective: “Brain-music” is a neurofeedback method that involves establishing optimal rhythmic and tonal parameters creating meditative conditions, based on an individual’s unique EEG-pattern, by influencing cortical bioelectrical activity. These EEG-patterns are converted into synthesizer-based music, tailored to the patient, and recorded on a compact disc (CD). Our purpose was to objectively assess the effectiveness of brain-music for treating insomnia in anxious individuals.

Methods: Eighteen volunteers with insomnia symptoms of at least two years duration and Zung Self-Rating Anxiety Scale scores>50 were randomized in double-blind format to two groups. Group I (7F/3M, aged 41.5±5.8) were provided with their own authentic brain-music. Group II (5F/3M, aged 42.8±7.8) received CDs with brain music of a different person. Subjects were instructed to listen to the music on a daily basis for four weeks. Athens Insomnia Scale (AIS) and 48-h actigraphy (pre- and post-study) assessed subjective and objective sleep quality.

Results: Both authentic and placebo brain-music reduced anxiety scores, with more pronounced effects observed in the experimental group (58.1±2.8 vs. 31±4.6 and 60±5.6 vs. 46.5±6.1 respectively, p<.01). There was dramatic improvement in AIS-rated sleep quality (p<.001). Actigraphic parameters characterizing insomnia were significantly improved only in the group using authentic brain-music.

Conclusion: A four week regimen of “brain music” therapy reduced clinical symptoms in anxious insomniacs treated with endogenously generated brain-music.

References:


NR406 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Phototherapy: Systematic Review of the Evidence
Bradley N. Gaynes, M.D., Department of Psychiatry, University of North Carolina at Chapel Hill, CB # 7160, School of Medicine, Chapel Hill, NC 27599-7160; David Ekstrom, M.A., Robert M. Hamer, Ph.D., Frederick M. Jacobsen, M.D., Charles B. Nemeroff, M.D., Patricia Suppes, M.D., Robert N. Golden, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to evaluate the existing evidence base for the efficacy of phototherapy in mood disorders, identify which specific interventions have been shown to improve outcomes, and appreciate where improvements in the existing evidencebase are needed.

Summary:

Objective: The APA Committee on Research on Psychiatric Treatments was commissioned to assess the evidence base for the efficacy of phototherapy in treating mood disorders.

Method: We systematically searched PUBMED (1975-August 2002) to identify randomized controlled trials of phototherapy for mood disorders meeting pre-defined inclusion criteria. These articles were abstracted, study quality assessed, and data synthesized by disease and intervention category.

Results: A fraction of the published studies met our inclusion criteria. Meta-analyses suggest significant reductions in depressive severity for bright lights in Seasonal Affective Disorder (SAD) (n=8 studies; Effect Size=0.84, 95%CI 0.60–1.08); for dawn simulation in SAD (n=4; ES=0.909, 95%CI 0.41–1.41); and for bright lights in non-SAD depression (n=4; ES=0.55, 95%CI 0.29–0.87). Adjunctive bright lights for non-SAD depression was not beneficial (n=5; ES=0.01, 95%CI –0.36–0.34).

Conclusions: Bright lights for SAD, dawn simulation for SAD, and bright lights for non-SAD depression appear efficacious, with effect sizes equivalent to those from antidepressant pharmacotherapy trials. Variability in study quality and possible publication bias makes cautious interpretation of these findings prudent. Additional high quality clinical trials and the establishment of accepted norms for treatment intensity, placebo conditions, and outcome measures are needed to clarify the benefit of this intervention.

References:


NR407 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Influence of rTMS on Motor Threshold in Depression Supported by NHS HTA Programme, Guy's and Thomas' Charitable Foundation
Declan M. McLouglin, Institute of Psychiatry, Post Office Box 070, De Crespigny Park, London SE5 8AF, United Kingdom; Savithasri V. Eranti, M.D., Andrew J. Mogg, M.R.C., Graham Pluck, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand that changes in MT are unlikely to be clinically relevant when treating depression with rTMS.

Summary:

Objective: To investigate changes in motor threshold (MT) in depressed patients during a course of rTMS.

Method: Study subjects are a subgroup of depressed patients participating in randomized, controlled trials of rTMS at the Maudsley Hospital, London. rTMS was administered to 13 patients and placebo rTMS to four. MT was assessed at baseline and after five daily rTMS sessions given at 110% of MT at 10Hz for five seconds, for 20 trains, with 55 second intervals.
Results: Linear regression analysis of baseline MT (n = 17; 11 females), using age and gender as independent variables revealed that MT was not influenced by age (p = 0.65) but was influenced by gender (p = 0.009), females having higher MT. Although there was only a very small decline in MT after five real treatments (1.4% of output) this change was just significant (p = 0.046). MT did not change with placebo rTMS. MT did not show any predictive value for change in Hamilton scores at the end of treatment course (R = 0.13, p = 0.70).

Conclusions: These preliminary results suggest that MT can change slightly during rTMS treatment. However, it is unlikely that such change is clinically relevant or likely to predict outcome.

References:

NR408 Tuesday, May 20, 2:00 p.m.-2:00 p.m.
20-Hz and 1-Hz Transcranial Magnetic Stimulation Combined as Add-On in Medication-Resistant Depression

Mauro Garcia-Toro, M.D., Department of Psychiatry, H. Son Llatzer, Ctra Manacor Km 4, Palma de Mallorca 07198, Spain; Javier Daumal, M.D., Joan Salva, M.D., Joana Andres, M.D., Maria Romera, M.D., Miguel Echevarria, M.D., Laura LaFuente, M.D.

Educational Objectives:
At the conclusion of this presentation, the participants should be able to recognize the advantages and disadvantages of using combined Transcranial Magnetic Stimulation in depressive patients.

Summary:
Objective: Both 20 and 1Hz Transcranial Magnetic Stimulation (TMS) have shown significant antidepressant properties. Although TMS tolerance and safety is considered to be excellent, the size of the therapeutic effect found is frequently modest. We decided to combine both types of TMS in this study.

Method: 22 DSM-IV Major Depression patients, who had failed to respond to at least two antidepressant trials in the present episode, have been recruited. They were randomized to receive 10 sessions of real or sham TMS. 30 trains of 60 s and 1 Hz were alternated with 30 trains of 2 s and 20 Hz in each session, with an eight shaped coil at 110% of motor threshold. Patients and raters were blind to the treatment condition.

Results: Real TMS decreased 7.3 +/- 6.5 Ham-D points vs 1.5 +/- 5.9 in the sham group (p=0.044). We found very good tolerance, but had technical problems due to overheating of the coils.

Conclusion: 20 Hz and 1 Hz TMS combined could be useful as antidepressant add-on, but we still do not know if the use of high and low frequency TMS combined has any clear advantages over using 20 and 1 Hz TMS separately.

References:

NR409 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Resource Utilization by Schizophrenia Patients in TMAP Supported by AstraZeneca Pharmaceuticals, L.P.

Alexander L. Miller, M.D., Department of Psychiatry, University of Texas Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 79229-3900; T. Michael Kashner, Ph.D., M. Lynn Crismon, Pharm.D., John A. Chiles, M.D., Madhukar H. Trivedi, M.D., Patricia Suppes, M.D., A. John Rush, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the impact of implementation of the set of interventions in the Texas Medication Algorithm Project on resource utilization by schizophrenia patients, as compared with resource utilization by schizophrenia patients receiving treatment as usual.

Summary:
In the Texas Medication Algorithm Project outpatients received algorithm-guided medication treatments, augmented by psychoeducational programs (ALGO), or treatment as usual (TAU) for one to two years. ALGO physicians were assisted by clinical coordinators. The goal was to assess the effects of ALGO on clinical outcomes and resource utilization. Outcomes were measured by independent assessors and by extracting data from multiple databases. Data on resource utilization covered the period from six months prior to study entry to at least one year after study entry. Resource utilization data were analyzed using hierarchical linear modeling, adjusted for need, enabling, predisposing, and demographic factors. ALGO patients spent significantly (25%) more time seeing physicians, but their time spent with nonphysician clinical providers was more than 50% lower than TAU patients. Since, in both groups, time with nonphysicians was substantially greater than time with physicians, the net effect was that ALGO patients spent only about half as much time seeing clinic providers as did TAU patients. Hospitalization rates did not differ significantly between groups, after adjusting for baseline rates.

These data, in conjunction with previously-reported clinical outcomes, show that the schizophrenia algorithm can be efficiently implemented and achieve as good or better outcomes than treatment-as-usual.

References:

NR410 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Modafinil Combined With SSRI Enhances the Degree and Rate of Benefit in MDD Supported by Cephalon, Inc.

Howard A. Hassman, D.O., CNS, Comp. Clinical Research, 130 White Horse Pike, Clementon, NJ 08021; Frank McManus, Ph.D., Steven J. Glass, M.D., Annette Sciamanna, C.C.R.C, Philip T. Ninan, M.D.
Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the significant benefits of using modafinil at initiation of SSRI therapy for rapidly treating depressive, sleepiness, and fatigue symptoms associated with MDD.

Summary:

**Objective:** In major depressive disorder (MDD) patients, SSRI treatment response typically takes several weeks. This open-label study is the first to evaluate modafinil combined with fluoxetine or paroxetine at treatment initiation in patients with MDD and fatigue.

**Methods:** Patients free from antidepressant therapy for ≥4 weeks were enrolled and started on a combination of modafinil and SSRI therapy. Modafinil was initiated at 100 mg/day for three days and then titrated to 200 mg/day. SSRI therapy was either fluoxetine or paroxetine 20 mg/d for six weeks. Assessments included the Hamilton Depression Scale (HAM-D-31), HAMD-21, Epworth Sleepiness Scale (ESS), and Fatigue Severity Scale (FSS). Adverse events were monitored.

**Results:** Fourteen of 18 evaluable patients (76%) completed the study. The average baseline HAMD-31 score was 31.72 ± 7.28. Modafinil combined with fluoxetine or paroxetine significantly improved total HAMD-31 scores within one week of initiation (mean: -9.47 ± 12.06; p < 0.01). Improvement was maintained throughout the study (mean: -23.06 ± 13.55; p < 0.01). 12%, 39%, and 60% of patients met HAMD-21 criterion for remission (≤7) by week 1, 2, and 6, respectively. Modafinil also significantly improved wakefulness (ESS) beginning at week 1 and reduced fatigue (FSS) beginning at week 2 (p < 0.05). The combination treatments were well tolerated. Three patients discontinued due to adverse events.

**Conclusion:** Modafinil combined with either fluoxetine or paroxetine may enhance the rate and degree of benefit in MDD patients.

References:


NR411

**Tuesday, May 20, 12:00 p.m.-2:00 p.m.**

**Interactive Voice Response as a Therapeutic Tool to Reduce Chronic Pain**

Magdalena R. Naylor, M.D., Department of Psychiatry, University of Vermont, 1 South Prospect Street, UHC Arnold 6, Burlington, VT 05401; John E. Helzer, M.D., Francis J. Keefe, Ph.D., James P. Rathmell, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize that Interactive Voice Response can be used as a therapeutic tool to improve adherence to pain coping skills learned in group cognitive behavioral therapy and prevent relapse into pain behavior. IVR is a cost-effective therapeutic tool, readily applicable in many clinical situations.

Summary:

**Objective/Aim:** To test whether Interactive Voice Response (IVR) can be used to prevent relapse into pain behavior.

**Method:** After completing 10 weeks of group CBT, ten subjects with chronic pain participated in four months of Therapeutic IVR (TIVR), a comparison group of eight subjects received standard care only. The TIVR is a computerized telephone system designed to reinforce pain coping skills learned in group CBT and provide messages for relaxation, sleep induction, and emotional support that can be accessed by patients on demand.

**Results:** Within subjects analysis (ANOVA) showed maximum positive change for nearly all outcome measures at the post TIVR point. Statistically significant improvements included SF-36 Mental Health Composite Score (p < 0.0004), MPQ pain (p < 0.01), CSQ Catastrophizing (p < 0.0006), TOPS Total Pain Experience (p < 0.03) and Perceived Family/Social Disability (p < 0.02). Between subjects analysis (ANCOVA) revealed significant inter-group differences in: TOPS Total Pain Experience (p < 0.01), TOPS Perceived Social Disability (p < 0.002), SF-36 Mental Composite (p < 0.05). Random Effects Linear Regression analyses demonstrated significant reductions in: highest pain level (p < 0.0001), highest stress level (p < 0.0001), and frequency of daily catastrophizing (p < 0.001).

**Conclusions:** Results suggest that TIVR can be used to improve coping skills adherence and decrease relapse rate into pain behavior.

References:


NR412

**Tuesday, May 20, 12:00 p.m.-2:00 p.m.**

**Randomized Clinical Trial of Selective PDE-5 Inhibitor (Sildenafil) Treatment of SSRI Treatment-Emergent Erectile Dysfunction**

Paula L. Hensley, M.D., Department of Psychiatry, University of New Mexico, 2600 Marble Avenue NE, Albuquerque, NM 87131; H. George Nurnberg, M.D., Maurizio Fava, M.D., Alan J. Gelenberg, M.D., John Lauriello, M.D., Susan Paine, M.P.H.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that sildenafil is an effective and well-tolerated treatment for male patients with erectile dysfunction associated with SSRI antidepressant therapy.

Summary:

**Objective:** The clinical question is whether sildenafil is efficacious in treating SSRI-associated ED.

**Method:** Male patients (n = 67) with clinically recovered major depression and a primary complaint of SSRI-associated ED were randomized to sildenafil (n = 35, 50 mg adjustable to 100 mg, based on efficacy and tolerability) or matching placebo (n = 32) for six weeks of double-blind treatment. Efficacy was assessed by the change in International Index of Erectile Function mean scores from baseline to end of treatment. Repeated measures analysis of variance was used to determine any treatment group differences in efficacy and depression severity (time x group interaction).

**Results:** The results were similar to previous analyses: after six weeks of treatment, sildenafil-treated patients showed statistically significant improvements in mean scores on IIEF Q3 and Q4 compared with those in the placebo-treated patients. At baseline, HAM-D scores were 5.4 (± 2.8) in the sildenafil group and 4.7 (± 2.9) in placebo group (p = 0.290). At the end of treatment, HAM-D scores were 3.3 (± 3.1) and 5.4 (± 4.0), respectively (p = 0.03), indicating that major depression in remission was maintained for the study duration. The most common AE was headache (21% sildenafil vs 10% placebo), followed by facial flushing (17% vs 3%), dyspepsia (7% vs 0%), nasal congestion (12% vs 3%), and transient visual disturbances (12% vs 5%).
Conclusion: Sildenafil was efficacious and well tolerated for the treatment of ED associated with SSRI therapy for major depression. Thus, sildenafil treatment of SSRI treatment-emergent ED may reduce the likelihood of antidepressant treatment discontinuation because of the sexual side effects, which in turn may reduce the likelihood of depression relapse or recurrence.

References:

NR413  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Do Clinical Practice Guidelines for Panic Work in Real World Settings?
John K. Lam-Po-Tang, M.D., 326 South Dowling Street, Darlinghurst, Sydney, NS 2010, Australia;

Educational Objectives:
At the conclusion of this session, the participant should be able to learn how to measure outcomes of treatment in panic disorder in a naturalistic clinical setting.

Summary:
Objective: Report data collected from standardized outcome measures in panic disorder at the commencement and conclusion of CPG-based treatment.
Method: A cohort of individuals diagnosed with DSM-IV panic disorder were prospectively studied. Participants were drawn from a private outpatient psychiatric practice in Sydney, Australia. Outcome measures used were the Agoraphobic Cognitions Questionnaire, Body Sensations Questionnaire, Mobility Inventory, and panic attack frequency. Outcome measures were administered at the beginning and conclusion of treatment. Individuals were treated with a cognitive-behavioral therapy program for Panic Disorder that adheres to a published CPG for panic disorder. Data on psychiatric and medical comorbidity, and psychotropic medication use was also collected.
Results: Forty-eight individuals entered the study. Psychiatric comorbidity was observed in 56% of the sample, and medical comorbidity in 46%. Effect sizes, calculated for each outcome measure, ranged between 0.51 and 1.20 standard deviations. There was no significant change in medication use over treatment.
Conclusions: CPG-based treatment of panic disorder was associated with acceptable changes in symptom severity, as measured by standardized instruments, and comparable to published data. Results suggest CPG-based treatment for Panic Disorder is feasible and generalizable to ‘real world’ settings.

NR414  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Substance Abuse in Adults With ADHD Supported by McNeil Consumer & Specialty Pharmaceuticals
Lily Hechtman, M.D., Department of Child Psychiatry, McGill University, 4018 St. Catherine Street West, Montreal, QC H2W 1X1, Canada;

Educational Objectives:
At the conclusion of this session, the participant should recognize that untreated ADHD children are at risk of developing a substance abuse disorder in later life. Treatment with stimulants does not increase this risk; on the contrary, it actually decreases the risk.

Summary:
Objective: Currently, the risk of development of substance abuse among adults with ADHD who were treated with stimulants as children is the subject of controversy. We aim to address this issue using data from a long-term, prospective study.
Methods: Substance abuse data (gathered at ages 19 and 26) from 10- and 15-year prospective, controlled, follow-up studies of 75 ADHD children who had received no stimulant treatment in childhood, 20 ADHD children who received ≥3 years of stimulant treatment in childhood, and 45 matched, normal controls were obtained via confidential interviews.
Results: There were no significant differences in illicit drug and/or alcohol use or abuse between untreated ADHD and control subjects. However, there was a trend for more untreated ADHD subjects to abuse alcohol. In addition, more untreated ADHD subjects had stopped using illicit drugs in the last 6 months. The ADHD subjects (at age 22) who received stimulant treatment during childhood were not significantly different from those ADHD subjects who did not receive treatment.
Conclusions: Stimulant treatment for ADHD in childhood does not increase the risk of substance abuse in adulthood. Previous studies have found that stimulant treatment in childhood is protective against substance abuse in adulthood. Other factors, e.g., antisocial comorbidity and persistence of ADHD symptoms, appear to be risk factors for later development of substance abuse in children with ADHD rather than stimulant treatment.

References:

NR415  Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Augmentation of SSRIs With Bupropion in Treatment-Resistant Depression in Adolescents
Maruke Yeghiyan, M.D., Child and Adolescent MH Center, 6 Yekmalian Street, Yerevan 375002, Armenia; Arman K. Danielyan, M.D., Khachatur Gasparyan, M.D., Armenak Mkhitaryan, M.D.

Educational Objectives:
At the end of this presentation the participants should be able to understand the effectiveness of augmentation of SSRIs with Bupropion in the treatment of refractory depression in adolescents.

Summary:
Objectives: To show the effectiveness of augmentation of SSRIs with Bupropion in the treatment of refractory depression in adolescents.
Methods: 23 adolescents, aged 15 to 19 years with treatment resistant depression were studied. All the subjects were chosen from a large group of referred patients, who at the time of referral were receiving following SSRIs—Fluoxetine (20–40 mg/day); Paroxetine (10–40 mg/day); Citalopram (20–60 mg/day) and Sertraline (50–150 mg/day). The review of medical charts showed, that previously the patients had been receiving either different SSRIs, including combination of SSRIs or TCAs and anxiolytics. All of the referred patients either had only a short remission with following relapse or had no clinical improvement at all according to results.
of Hamilton Rating Scale for Depression (HAM-D). After 10 weeks of unsuccessful treatment with SSRIs, the current treatment regimen was augmented with Bupropion SR in a dose range from 100 to 300 mg. The results were assessed in 4 weeks after the augmentation.

Results: Improvement in clinical picture, as reported by the patients and parents, was already observed within 2 weeks after the initiation of augmented treatment in 15 subjects (65.2%). However, 19 of 23 subjects (82.6%) showed HAM-D total score ≤8 within 6 weeks and CGI score of 1 or 2. No significant side effects were observed.

Conclusions: Augmentation of SSRIs, recommended for treatment of refractory depression, by Bupropion showed promising results. Studies with larger sample size are encouraged.

References:

NR416 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Mindfulness-Based Cognitive Therapy and Life-Role Substantiation in Comorbid Mood, Anxiety, and Substance-Related Disorders: A Pilot Study
Martin A. Katzman, M.D., Anxiety Clinic, Clarke Institute-CAMH, 250 College Street, Toronto, ON M5T 1R8, Canada; Andrew Welch, B.S.C., Kate Kitchen, M.S.W., Marci Rose, B.S.C., Irena Milosevic, B.S.C., Monica Verman, M.S.C., Lukasz Struzik, M.S.C.

Educational Objectives:
At the conclusion of this session, the participant should understand the role and changes that can be effected through participation in Mindfulness-Based Cognitive Therapy.

Summary:
Introduction: Mindfulness-based treatments involve the practice of moment-to-moment awareness of what is present and true. Previous reports have suggested their effectiveness in the management of a wide variety of stress-related and psychiatric conditions (Kabat-Zinn et al., 1988, 1992). Recently, mindfulness techniques in combination with Cognitive Therapy, entitled Mindfulness-Based Cognitive Therapy (MBCT), was shown to be effective in preventing depressive relapse (Siegal et al., 2002).

Objective: This study examined the impact of MBCT techniques on patients with a combination of co-morbid mood, anxiety and substance-related issues.

Method: Participants were randomly assigned to a 10-week MBCT group or a waitlist control group. Outcomes were assessed pre and post group enrollment, and within-group analysis was performed using the paired-samples t-test.

Results: Preliminary data from the first seven subjects in the MBCT treatment group revealed significant differences in Beck Depression Inventory scores (t = 3.63, P < 0.022) and on the Social Life / Leisure subscale of the Sheehan Disability Inventory (SDI): t = 3.14, P < 0.035. A trend towards improvement in Work Impairment scores (t = 2.33, P < 0.080) was also noted.

Conclusion: Significant reductions in depression and disability are suggestive of the short-term benefit of MBCT for symptom reduction and improved functioning.

NR417 Tuesday, May 20, 12:00 p.m.-2:00 p.m.
Low-Dose Naltrexone Administration Following Opiate Discontinuation
Paolo Mannelli, M.D., Department of Psychiatry, Thomas Jefferson University, 833 Chestnut East, Suite 210E, Philadelphia, PA 19107; Charles C. Thornton, Ph.D., Stephen P. Weinstein, Ph.D., Carlos Salazar, M.D., Edward Gotthelf, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize different techniques of antagonist drug administration and their use in the treatment of opiate dependence.

Summary:
Introduction: Adding up to 50 mg/day of the opiate antagonist naltrexone to the customary clonidine protocol shortens opiate withdrawal treatment, but increases discomfort and requires sedation. Following detoxification, naltrexone maintenance (50mg/day) induces residual withdrawal, is effective in preventing relapse only with selected populations and is related to overdose risks.

Objective: Recent findings on the utility of smaller quantities of antagonist drugs in managing opiate dependence require clinical confirmation.

Methods: We evaluated 65 consecutive inner-city opiate addicts who were administered low-dose naltrexone (1-10mg/day) and/or clonidine (0.2-0.6mg/day) after methadone tapered, inpatient detoxification. Patients were admitted to an outpatient interim treatment program shortly after being discharged on 5mg of methadone and received medications for physical discomfort, counseling and case management before moving to long term aftercare.

Results: Twenty-five patients (38.5%) failed to initiate naltrexone therapy. Naltrexone administration did not induce more intense withdrawal or require higher doses of palliative medications than clonidine alone, while being associated with less adverse events, a lower drop-out rate and increased treatment compliance.

Conclusion: Low dose naltrexone appears to be safe in the post-detoxification treatment of opiate addicts presenting with withdrawal symptoms. Studies controlling for the self selection bias will confirm if this administration modality is helpful in the early treatment of opiate discontinuation.

References:

NR418 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Low Dietary Omega-3s and Increased Depression Risk in 14,541 Pregnancies
Joseph R. Hibbeln, M.D., LMBB, NIAAA/NIH, 12420 Parklawn Drive, MSC 8115, Rockville, MD 20852; John M. Davis, M.D., Jon Heron, Ph.D., Johnathon Evans, M.D., Deiter F.H. Wolke, Ph.D., Jean Golding, Alspac Study Team

Educational Objectives:
At the conclusion of this session, the participant should understand the potential role of omega-3 fatty acids in reducing risk of depression in pregnancy.

Summary:
Objectives: The placenta selectively transports omega-3 essential fatty acids to the fetus from maternal stores as they are required for optimal neurological development. Because these fatty acids
cannot be made denovo, mothers can become depleted of omega-3 essential fatty acids during pregnancy and have increased risk of depressive symptoms.

Methods: The ALSPAC study enrolled 14,541 women who were expected to deliver between April 1, 1991, and December 31, 1992. We compared the dietary intakes of omega-3 essential fatty acids from seafood at 32 weeks gestation to Edinburgh Postnatal Depression Scores and Crown Crisp Experiential Index (CCEI) depression subscale scores at 18 and 32 weeks gestation and at eight and 32 weeks after birth.

Results: Deficient intake was associated with nearly a doubling of the risk of depression (EPDS > 12) at 32 weeks gestation (p < 1.4 x 10^-17) and at all other time points. Findings remained significant after assessment for confounding factors including young maternal age, prior history of depression, housing status, maternal education, smoking, alcohol use, and parity.

Conclusions: Omega-3 fatty acids have beneficial health effects with no adverse side effects; thus, clinical trials for reducing depressive symptoms related to pregnancy can be readily conducted.

References:
Pharmacologic Treatment of Hospitalized Patients With Bipolar Disorder
Supported by Eli Lilly and Company

Barbara L. Gaylord, M.B.A., Pharm Research, Premier Healthcare, 2230 Cascade Point Boulevard, Charlotte, NC 28266; Zhongyun Zhao, Ph.D., Peter F. Wang, M.D., Benjamin Gutierrez, Ph.D.

Educational Objectives:
At the conclusion of the presentation, participants should be able to describe recent prescribing practice and identify factors associated with for inpatients with bipolar disorder.

Summary:
Objective: To assess recent pharmacologic treatment patterns for hospitalized bipolar patients.
Methods: Using Premier's Perspective™ database, the largest U.S. hospital drug utilization database, hospitalized bipolar patients discharged between 01/1999 and 09/2001 were identified. Psychotropic treatment patterns and their relationship with diagnoses, illness severity, and patient and institution characteristics were analyzed.

Results: Of 36,339 patients (61% female, mean age 39.7 years), 28.9% were depressed, 21.6% manic, 21.0% mixed, and 28.5% other episodes. Valproate (45.9%) and olanzapine (30.2%) were most commonly prescribed (lithium, 24.9%). On average, patients received 3.87 psychotropics; 77.1% received ≥3 and 32.5% received ≥5. Only 7.2% received monotherapy. Antipsychotic + mood stabilizer combinations were used by 58.0%. Mood stabilizers or antipsychotics alone combined with other classes were used by 23.1% and 12.6% of patients, respectively. Among depressed patients, 79.1% used antidepressants versus 25.3% of manic patients. In depressed patients with psychosis, 74.5% received atypicals versus 42.8% of patients without psychosis. However, 61.5% of depressed patients received anxiolytics and 24.5% received hypnotics. Olanzapine use increased, and risperidone, valproate, and lithium use decreased from 1999–2001. Being female, greater severity, and depressed/mixed diagnosis increased pharmacotherapy complexity.

Conclusions: Pharmacotherapy for hospitalized bipolar patients is complex. Combinations of ≥3 psychotropics were dominant treatment regimens.

References:

Pharmacological Treatment of Bipolar Disorder: Medication Use in STEP-BD

S. Nassir Ghaemi, M.D., Department of Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139; Douglas J. Hsu, B.S., Michael E. Thase, M.D., Stephen R. Wisniewski, Ph.D., Gary S. Sachs, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the frequency of medication use and subgroup prescribing patterns for the treatment of bipolar disorder.

Summary:
Objective: To evaluate medication use in bipolar disorder, including the roles of bipolar subtype, history of rapid-cycling, and history of psychosis.
Methods: Cross-sectional medication use of the first 500 patients in the Systematic Treatment Enhancement Program for Bipolar Disorders (STEP-BD).

Results: 72% received mood stabilizers, most commonly lithium (38%) and valproate (37%). 41% received antidepressants, most commonly bupropion (15%). 30% received neuroleptics, mainly atypical agents (most commonly olanzapine, 14%). Only 11% received mood stabilizer monotherapy. Type I patients were more likely than type II patients to receive mood stabilizers (p = 0.005, RR = 1.19) and neuroleptics (p < 0.001, RR = 1.25), but less likely to receive antidepressants (p = 0.04, RR = 0.99). Patients with a history of psychosis were more likely to receive mood stabilizers (p = 0.01, RR = 1.17) and neuroleptics (p < 0.001, RR = 2.20) than patients with no history of psychosis. Notably, antidepressants were used similarly in rapid-cycling and non-rapid cycling patients.

Conclusions: Nearly three quarters of patients received mood stabilizers in treating bipolar disorder, with valproate and lithium equally used. Almost one half received antidepressants, and one third received atypical neuroleptics. Polypharmacy occurred in 89% of patients. Type II patients received less mood stabilizing and neuroleptic, but more antidepressant, treatment. Presence of psychosis predicted more mood stabilizing and neuroleptic treatment.

References:
ment in patients with HCV who develop IFN-α-induced major depressive disorder (MDD).

**Method:** Thirty-nine HCV patients on IFN-α combination therapy were monitored weekly using the Beck Depression Inventory (BDI). Thirteen of 39 patients (33%) developed IFN-α-induced MDD and were treated with citalopram, a selective SSRI antidepressant.

**Results:** All four symptom dimensions of the BDI increased significantly at week eight for those patients who developed MDD as compared with those who did not develop MDD. In patients who developed MDD, antidepressant treatment resulted in a significant reduction of BDI scores on the dimensions of psychomotor anhedonia, vegetative and somatic symptoms, but not the dimension of negative cognitions.

**Conclusions:** Although larger sample size studies are needed, these findings could have enormous implications for side effect management and may suggest strategies for improved adherence to IFN-α therapy.

**References:**


**NR424**

**Tuesday, May 20, 3:00 p.m.-5:00 p.m.**

### Risperidone Monotherapy in Acute Bipolar Mania

**Supported by Johnson & Johnson Pharmaceutical Research & Development**

Sumant Khanna, M.D., Department of Psychiatry, N. I. M. H. A. N. S., P O Box 2900 Hosur Road, Bangalore 560029, India; Robert M.A. Hirschfeld, M.D., Keith Katcher, M.S., Fred Grossman, D.O., Michelle L. Kramer, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to evaluate the efficacy and safety of risperidone monotherapy in the treatment of mania in patients with bipolar disorder.

**Summary:**

**Purpose:** To examine the safety and tolerability and continued efficacy of risperidone monotherapy in patients with Bipolar I disorder.

**Methods:** In a multicenter, open-label extension trial conducted in the U.S. and India, patients with manic or mixed episodes of acute bipolar mania received flexible doses of risperidone ranging from 1 mg/day to 6 mg/day for up to nine additional weeks. Subjects had to successfully complete a three-week, double-blind, placebo-controlled trial to qualify for inclusion. Efficacy was measured as change from baseline to endpoint in Young Mania Rating Scale (YMRS) scores. Safety measures included spontaneously reported adverse events.

**Results:** Of the 283 treated patients, 83 were at U.S. sites and 200 were at Indian sites. Overall, 71% of patients completed 9 weeks of treatment. The mean baseline YMRS score at entry was 14.6. The mean modal dose of risperidone was 4.6mg/day. At treatment endpoint, mean YMRS score was 7.9. No unexpected adverse events were reported, with extrapyramidal symptoms (mild) and somnolence being the most common.

**Conclusion:** Risperidone is efficacious in the treatment of acute bipolar mania over a 12-week period, and was well tolerated in this patient population.

**References:**


**NR425**

**Tuesday, May 20, 3:00 p.m.-5:00 p.m.**

### Primary and Secondary Distinction of Comorbid Substance Misuse in Bipolar Disorder

**Supported by the National Institute of Mental Health**

Mark D. Rossey, M.D., Schusterman Center, University of Oklahoma, 4502 East 41st Street, Tulsa, OK 74135; William R. Yates, M.D., Stephen R. Wilsniewski, Ph.D., Michael W. Otto, Ph.D., Jackie L. Neel, D.O., Roger D. Weiss, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should understand that the primary-secondary distinction in classifying comorbid substance misuse may be clinically useful in the assessment and treatment of bipolar patients with comorbid substance misuse.

**Summary:**

**Introduction:** Substance misuse (SM), i.e., the presence of substance abuse and/or dependence, is common in bipolar disorder (BD). Classifying comorbid SM on whether SM began before (primary SM) or after (secondary SM) the onset of BD may be more useful clinically than classifying BD patients solely on the presence or absence of SM.

**Methods:** Comorbid SM was examined using the primary-secondary distinction in 496 BD patients enrolled in the Systematic Treatment Enhancement Program for Bipolar Disorder (Gary Sachs, M.D., PI).

**Results:** 74% of this sample had BDI and 23% had BDI. 11.3% had primary SM, 30.7% had secondary SM, and 58.0% had no SM. Mean age of onset of BD was 21.5±6.1 in primary SM, 13.4±5.2 in secondary SM, 18.8±9.2 in BD alone. Mean age of onset of SM was 15.7±5.3 in primary SM and 20.1±8.0 in secondary SM. BD patients with secondary SM had more manic episodes (Fisher's p = .01) and depressive episodes (Fisher's, p = .01) than those with primary SM and those without SM. Patients with secondary SM had a lower mean SF36 Mental Score than patients without SM (28.6 ± 12.3 vs. 35.0 ± 13.8; Kruskal-Wallace, p = .0005).

**Conclusion:** In this sample, SM that follows the onset of BD is associated with increased severity of the mood disorder compared to BD without SM. In contrast, SM that precedes the onset of BD appears similar to BD without SM.

**References:**


**NR426**

**Tuesday, May 20, 3:00 p.m.-5:00 p.m.**

### Prophylactic Treatment of Recurrent Depression: A Randomized Controlled Trial of Sertraline in Remitted Patients

**Supported by Pfizer France**

Vincent F. Caillard, M.D., Psychiatre des Hopitaux, C.H.U. Cote de Nacre, Caen Cedex 14033, France; Patrice Boyer, M.D.,
Jean-Michel Hotton, M.D., Jean-Pierre Lepine, Ph.D., Sylvie Troy, M.D., Jean-Claude Bissserbe, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate that sertraline at doses of either 50 or 100 mg daily significantly prevent recurrences compared with placebo in patients who presented multiple depressives episodes.

Summary:

Objective: To determine if sertraline can prevent the occurrence of a new depressive episode in highly recurrent patients currently in remission.

Methods: It was a 20-month, randomized, placebo-controlled, double-blind, multicenter French study. Patients presenting at least three major depressive episodes (MDE) within the last four years and currently in full remission of the index episode were eligible. They initially entered a two-month, single-blind placebo period (n = 371) to confirm the stability of the remission, then were double-blind randomized (n = 288) to 50 mg or 100 mg of sertraline (Ser) or placebo (Pbo) for 18 months. The primary efficacy criterion was the occurrence of a depressive recurrence.

Results: During the placebo period, 61 of 371 patients discontinued, including 33 for relapse. Among 286 patients who entered the double-blind prophylactic phase, 72% had received an antidepressant (other that sertraline) during at least six months of their index MDE, and 26% have been hospitalised for depression. During the double-blind phase, 65 patients discontinued for recurrence. Recurrences were significantly (P = 0.002) lower in the sertraline group compared with placebo (Ser 50 + 100 mg 32/199 [16.1%]; Pbo 33/99 [33.3%]). These recurrences occurred at M1, M3, M6, and M12 after randomization for respectively 4%, 16.2%, 22.2%, and 29.3% in Pbo group compared with 3.7%, 6.9%, 9.5%, and 14.3% in Ser group. Globally, sertraline was well tolerated; however, the number of adverse events was slightly lower in the 50 mg group.

Conclusion: This study is the first one to prove a significant efficacy of an antidepressant i.e. sertraline in the prevention of recurrences of depressive episodes.

References:

NR427 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Defining Threshold and Dimensionality of Co-Existing Depression in Acute Mania Supported by Sanofi-Synthelabo, Inc.
Elle G. Hantouche, M.D., Department of Psychiatry, Pitie-Salpetriere Hospital, 47 BD DE L'Hopital, Paris 75013, France; Hagop S. Akiskal, M.D., Jean-Michel Azorin, M.D., Sylvie Lancrenon, Ph.D., Liliane Chatenet-Duchene, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize and diagnose "dysphoric mixed mania" with more precision on symptomatic threshold and dimensional components.

Summary:

Following EPIMAN study (Akiskal et al, 1996), a new multisite study was implemented with the objective of including 1000 patients with acute mania. In this report, data are focused on the mixed depressive acute mania.

Method: "EPIMAN-II Thousand" is a national multi-site collaborative study dedicated to the clinical sub-types of mania. It involved training 317 French psychiatrists working in different sites representative of France. The study actually succeeded in recruiting 1090 cases admitted for acute mania (DSM-IV criteria). A checklist of depressive symptoms (McElroy et al, modified by Akiskal) and the MADRS were used to assess co-existing depression.

Results: In the entire population, irritability (78.6%), mood lability (62.5%), and depressed mood (35.2%) were the most frequent symptoms. The rate of mixed mania, as defined by the presence of 2 depressive symptoms or more ("lability" and "irritability" items excluded), was 30.4%. MADRS global score was 15±7 in the entire population. A modified version of MADRS (four items excluded: appetite, sleep, concentration, inner tension) seemed to be the most sensitive to separate between pure (1,4±2) and depressive manias (9,7±5, p < 0.0001). The threshold of six had excellent specificity (94.2%) and the best sensitivity (79.8%). A principal factor analysis conducted on the list of depressive items, separated between two dimensions: "depressed mood factor", and "psychomotor factor".

Conclusions: In this largest study of acute mania ever conducted, depressive mixed mania concerned at least on third of acute cases. A refined version of MADRS (6 items) is suitable for dimensional assessment of co-existing depression, which turned out to be cognitive-emotional and psychomotor.

References:

NR428 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Changes in QEEG Cordance and Response in Treatment-Resistant Depression
Ian A. Cook, M.D., Department of Psychiatry, UCLA, 760 Westwood Plaza, Room 37-426, Los Angeles, CA 90024-1759; Andrew F. Leuchter, M.D., Melinda Morgan, Ph.D., Michelle Abrams, R.N.

Educational Objectives:

At the conclusion of this session, the participant should be able (1) to review the use of physiologic biomarkers in studying treatment response, and (2) to discuss the use of cordance in treatment resistant depression.

Summary:

Objective: Cordance is an EEG measure that is correlated with cerebral perfusion. In studies in major depression (MDD), decreases in prefrontal cordance early in treatment were predictive of response in subjects who were medication-free prior to the initial EEG. In clinical practice for treatment resistant depression (TRD), medications are often changed without washout. We hypothesized that cordance decreases would be associated with response in TRD subjects without wash-out between treatments.

Methods: Awake EEGs were recorded from 11 adults with unipolar MDD; treatment decisions were made naturalistically by their treating psychiatrists. Subjects had failed open-label SSRI monotherapy and were starting a new treatment; EEG data were recorded prior to the new regimen and after one week. Prefrontal cordance was computed by averaging Fp1, Fp2 and Fpz values.

Results: Six of 11 subjects responded (50% HAM-D decrease over 8-12 weeks). Cordance decreases were seen in 4/6 responders, and only 1/5 non-responders, yielding test sensitivity 80% and selectivity 66%.

Conclusions: In this pilot study in TRD, prefrontal cordance decreased in responders and did not decrease in nonresponders,
consistent with previous studies of non-resistant subjects with washout. These findings support the study of cordance biomarkers in treatment response in TRD.

Funding Source: NIMH

References:


NR429

Tuesday, May 20, 3:00 p.m.-5:00 p.m.

QEEG Cordance Predicts Treatment Response to Reboxetine in Major Depression

Ian A. Cook, M.D., Department of Psychiatry, UCLA, 760 Westwood Plaza, Room 37-426, Los Angeles, CA 90024-1759; Andrew F. Leuchter, M.D., Scott D. Greenwald, Ph.D., Melinda Morgan, Ph.D., Michelle Abrams, R.N., Barbara Siegman, B.A.

Educational Objectives:

At the conclusion of this session, the participant should be able (1) to review the use of physiologic biomarkers in studying treatment response, and (2) to discuss the use of cordance in studying response to antidepressants with different mechanisms of action.

Summary:

Objective: Cordance is an EEG measure that is correlated with cerebral perfusion. In studies in major depression (MDD), decreases in prefrontal cordance early in treatment were predictive of response to an SSRI (fluoxetine) or a mixed SSRI/SNRI (venlafaxine). We hypothesized here that early cordance decreases would be associated with response to reboxetine, an SNRI.

Methods: Awake EEGs were recorded from 25 adults with unipolar MDD (HAM-D ≥ 16), enrolled in an eight week treatment trial with reboxetine (4 - 8 mg/d). HAM-D and EEG were assessed at baseline and after 48 hrs, 1, 2, 4, and 8 weeks of treatment, with response defined as final HAM-D ≤10. Prefrontal cordance was computed by averaging Fp1, Fp2 and Fpz values.

Results: 11 of 25 subjects responded. Cordance initially decreased in the responder subjects, with mean changes between responders and non-responders showing significant differences at week 1 (p = 0.038). HAM-D for responders and nonresponders separated at week 4.

Conclusions: Prefrontal cordance initially decreased in responders during treatment with reboxetine, an SNRI antidepressant. This prospective evaluation supports prior work with cordance biomarkers as a clinical tool for response prediction in depression, and extends previous findings to include antidepressants with different mechanisms of action.

Funding Sources: Aspect Medical Systems, Inc., NIMH, Pharmacacia, Inc.

References:


NR430

Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Rehospitalization Rates of Patients With Bipolar Disorder

Supported by Eli Lilly and Company: Texas Department of Mental Health and Mental Retardation

Nick C. Patel, Pharm.D., Department of Pharmacology Practice, University of Texas, PHR 5.110, Austin, TX 78712; M. Lynn Crismon, Pharm.D., Michael Pondrom, Pharm.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize outcomes, specifically rehospitalization rates, associated with different psychopharmacological regimens in patients with bipolar disorder.

Summary:

Objective: This study examined one-year rehospitalization rates of patients with bipolar disorder discharged from a state psychiatric hospital while taking a mood stabilizer alone, a mood stabilizer plus a typical antipsychotic, or a mood stabilizer plus an atypical antipsychotic.

Methods: Time to rehospitalization was measured by the Kaplan-Meier formula. The Cox proportional hazards regression model was used to analyze covariates thought to affect time to rehospitalization.

Results: One-year rehospitalization rates for 479 patients were: mood stabilizer 23%, mood stabilizer + typical antipsychotic 27%, and mood stabilizer + atypical antipsychotic (olanzapine or risperdone) 25%. No significant differences existed between groups. More patients in the combination groups had psychotic symptoms. Previous hospitalizations were greater in the combination treatment groups and contributed to the risk of readmission. After adjusting for previous hospitalizations, there were no differences in rehospitalization rates.

Conclusions: No differences occurred in rehospitalization rates between patients discharged on any of the above drug regimens. The number of previous psychiatric hospitalizations was a predictor of rehospitalization. Mood stabilizer and antipsychotic combination treatment appeared to be used in a more severely ill patient population.

References:


NR431

Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Tolerability and Pharmacokinetics of Controlled- and Immediate-Release SSRIs

Supported by GlaxoSmithKline

Robert N. Golden, M.D., Department of Psychiatry, University of NC-Chapel Hill, CB#7160/Neurosciences Hospital, Chapel Hill, NC 27599-7160; Philip Perera, M.D., Simon Holdsworth, B.S.C., Barry Zussman, B.S.C.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize that tolerability is a major challenge in the treatment of depression. Well-tolerated antidepressants, such as controlled-release SSRIs may minimize tolerability-associated non-compliance.
Summary:

SSRIs are associated with a constellation of side effects, which usually arise early in treatment. These side effects are thought to be associated with an increase in monoamines within the CNS and periphery, and may lead to treatment non-adherence. Better tolerated formulations may increase the likelihood of treatment adherence. To estimate the tolerability profile of immediate- and controlled-release formulations of SSRIs, data from over 7000 patients treated in all available clinical trials in major depression using paroxetine immediate-release (IR) and controlled-release (CR) were pooled to calculate the rates of common side effects and treatment discontinuations due to adverse events. Each SSRI formulation was compared to placebo. Overall, the rate of discontinuation with paroxetine IR was 20% versus 9% with placebo. In trials that included both IR and CR, the rate of discontinuation for paroxetine IR was greater than that of placebo (p < .001). In contrast, the rate of discontinuation with paroxetine CR was 7% versus 6% with placebo. Data from three pharmacokinetic trials demonstrate that the slower absorption and reduced peak/trough plasma level fluctuations with CR may contribute to an enhanced clinical profile.

References:


NR432 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Quetiapine Monotherapy for Acute Mania Associated With Bipolar Disorder (STAMP 1 and STAMP 2) Supported by AstraZeneca Pharmaceuticals
Martin W. Jones, Ph.D., CNS, AstraZeneca, 1800 Concord Pike, PO Box 15437, Wilmington, DE 19850; Karin Huizar

Educational Objectives:

At the conclusion of this session, the participant should (1) recognize that quetiapine is effective, safe, and well tolerated as monotherapy for the treatment of acute mania associated with bipolar disorder, and (2) make more informed decisions regarding the use of quetiapine in patients with bipolar disorder.

Summary:

Objective: Evaluate the efficacy and safety of quetiapine monotherapy for the treatment of acute mania in a large cohort of patients.

Method: A pooled analysis of data from 604 patients (bipolar I disorder, manic episode) enrolled in two 12-week, randomized, double-blind, placebo-controlled quetiapine (QT, up to 800 mg/d) monotherapy trials. Assessments included YMRS, CGI, CGI-BP, MADRS, PANS, GAS, SAS, and BARS scores. Lithium and haloperidol controls were used to assess assay sensitivity.

Results: 60.8% (127/209) of QT vs 38.9% (77/198) PBO-treated patients completed the trial. A statistically significant improvement in YMRS total score was observed from Day 4 onward in the QT group vs PBO (P = 0.021). At Day 21, YMRS scores for QT vs PBO were -13.58 and -7.76, respectively (P < 0.0001), and increased by Day 84 (P < 0.0001). Significantly more QT patients achieved a response (250% decrease from baseline YMRS score) at Day 21 (QT 48.1%; PBO 31.3%; P = 0.0006). Lithium and haloperidol were similar to QT in all efficacy measures vs PBO by Day 84. Common adverse events for QT included insomnia, dry mouth, and somnolence. High rates of EPS and tremor were observed with haloperidol and lithium. Mean last-week quetiapine dose in responders at Day 21 was 575.5 mg/d.

Conclusions: Quetiapine monotherapy is effective, fast acting, and well tolerated in the treatment of acute mania.

NR433 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Phenomenology of Rapid-Cycling Bipolar Disorder From the STEP 500 Supported by the National Institute of Mental Health
Christopher D. Schneck, M.D., Univ North Pavilion, 4455 E 12th Ave, Box 011-07, Denver, CO 80220-2415; Joseph R. Calabrese, M.D., David J. Miklowitz, Ph.D., Stephen R. Wisniewski, Ph.D.

Educational Objectives:

After reading this poster, participants should be able to better understand many of the likely risk factors and characteristics of rapid cycling bipolar patients, including relationship to gender, bipolar subtype, age of onset of illness, association with psychosis and comorbidity.

Summary:

Objective: To compare demographic and phenomenological variables from rapid cycling bipolar patient to non-rapid cycling bipolar patients as a function of bipolar I versus bipolar II status.

Method: We examined several demographic, historical, and symptomatic features in a cross-sectional sample from the first 500 patients with bipolar I or bipolar II disorder enrolled in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), a multicenter NIMH-funded project designed to evaluate the longitudinal outcome of patients with bipolar disorder.

Results: Rapid cycling bipolar disorder occurred in 20% of the sample. Rapid cycling patients were more likely to be female, although the effect was significantly more pronounced in bipolar I patients than bipolar II patients. In addition, rapid cycling bipolar patients experienced a younger age of onset of their illness, were more often depressed at study entry, and had poorer psychosocial functioning in the year prior to study entry than non-rapid cycling patients. Rapid cycling patients also experienced a significantly greater number of depressive and hypomanic/manic episodes in the year prior to study entry. Lifetime history of psychosis was found to be equal between rapid and non-rapid cycling patients, but more often occurred in bipolar I than bipolar II patients.

Conclusions: Patients with rapid cycling bipolar disorder demonstrate a greater severity of illness on a number of clinical measures than non-rapid cycling patients. This study highlights the need to refine treatments specifically for rapid cycling in order to reduce the overall morbidity and mortality of this important subset of bipolar patients.

References:


NR434 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Duloxetine in the Long-Term Treatment of MDD Supported by Eli Lilly and Company
Joel Raskin, M.D., Eli Lilly and Company, Lilly Corporate Center, DC, Indianapolis, IN 46285; David J. Goldstein, M.D., Craig H. Mallinckrodt, Ph.D., Margaret Ferguson, M.D.
Educational Objectives:

At the conclusion of this session, the participant should recognize that duloxetine, an antidepressant that is a potent and balanced dual reuptake inhibitor of serotonin and norepinephrine, is safe and efficacious in the long-term treatment of depression.

Summary:

Background: Depression is a chronic, recurring disorder for which guidelines recommend long-term therapy. Evaluation of duloxetine in the long-term treatment of depression is crucial.

Methods: This was an open-label, 52-week, multi-national clinical trial in MDD outpatients (age ≥18) receiving duloxetine at 80 or 120 mg/d, administered (a 40 or 60 mg BID).

Results: A total of 1,279 patients had post-baseline data, of whom 520 were exposed to duloxetine for at least 360 days. Mean changes in CGI-Severity, HAMD7, total score, HAMD subfactors, BDI-II, Sheehan Disability Scale (SDS), and means for PGI-Improvement all showed highly significant (p < .001) improvements at all assessment times. Estimated probabilities of response and remission at Week 52 were 91.4% and 81.8%, respectively. Adverse events led to discontinuation in 17.0% of patients. Treatment-emergent adverse events reported by >10% of patients included nausea, insomnia, headache, and somnolence. Mean changes for pulse, blood pressure, corrected QT interval, and body weight were <2 bpm, <1.0 mm Hg, <1 msec, and 1.1 kg, respectively. Small mean increases were observed for some laboratory analytes; however, the incidence of laboratory values above or below normal limits was low.

Conclusion: Duloxetine is effective, safe, and well tolerated in the long-term treatment of major depression at doses of 80 and 120 mg/d.

References:


NR435 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Anxiety Comorbidity in Bipolar Disorder: The First 500 STEP-BD Participants

Naomi M. Simon, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 815, Boston, MA 02114; Kemal Sagduyu, M.D., Michael W. Otto, Ph.D., Stephen R. Wisniewski, Ph.D., Mark Fossey, M.D., Ellen Frank, Ph.D., Gary S. Sachs, M.D., Andrew A. Nierenberg, M.D., Michael E. Thase, M.D., Mark H. Pollack, M.D.

Educational Objectives:

At the conclusion of this session, participants should be able to recognize the prevalence and impact of anxiety disorder comorbidity on bipolar disorder, including its impact on course, period of time euthymic, role function and quality of life, and suicidality, and understand the critical need for greater clinical attention to anxiety comorbidity in this population.

Summary:

We provide a detailed perspective on the correlates of anxiety comorbidity in a large, well-characterized sample of bipolar patients. We examined anxiety comorbidity and its correlates in a cross-sectional sample from the first 500 participants with bipolar I or bipolar II disorder enrolled in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), a multicenter, NIMH-funded project designed to evaluate the longitudinal outcome of patients with bipolar disorder. Lifetime comorbid anxiety disorders were common, occurring in over half the sample, and were associated with younger age of onset, decreased likelihood of recovery, poorer role functioning and quality of life, less time euthymic, and greater likelihood of suicide attempts. Substance abuse disorders were particularly prevalent among patients with anxiety disorders, anxiety comorbidity appeared to exert an independent, deleterious effect on functioning, including history of suicide attempts. This study demonstrates an independent association of anxiety comorbidity with greater severity and impairment in bipolar disorder, and highlights the need for greater clinical attention to anxiety comorbidity, particularly for enhanced clinical monitoring of suicidality. It is important to determine whether effective treatment of anxiety symptoms can lessen bipolar disorder severity, improve response to treatment of manic or depressive symptoms, or reduce suicidality.

References:


NR436 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Predictive Validity of Primary/Secondary Bipolar Disorder and Comorbid Alcoholism

Ihsan M. Salloum, M.D., Department of Psychiatry, University of Pittsburgh, 3811 O’Hara Street, Pittsburgh, PA 15213; Jack R. Cornelius, M.D., Dennis Daley, Ph.D., Levent Kirisci, Ph.D., Antoine B. Douaihy, M.D.

Educational Objectives:

At the conclusion of session, participant should be able to recognize factors that predict changes in manic depressive symptoms & functioning status in bipolar disorder with comorbid alcoholism.

Summary:

Objectives: We examined whether the primary vs. secondary distinction (based on chronology of onset of the disorder, alcoholism vs. bipolar disorder) predicts depressive and manic symptoms and functioning changes over a 24 weeks follow-up period.

Method: Fifty-two patients with a DSM-IV/SCID comorbid diagnosis of bipolar disorder and alcohol dependence were assessed every two weeks using the Hamilton Scale for Depression-25, the Bech-Rafaelsen Mania Scale, and the Global Assessment of Functioning. The Mixed Model with restricted maximum likelihood procedure and unrestricted covariance matrix was used to analyze longitudinal data. Age, gender, ethnicity, bipolar subtypes, and alcohol and drug use were included in the model as co-variates.

Results: The primary vs. secondary distinction did not predict manic depressive symptoms over the follow-up period. Alcohol use was the strongest predictor for depressive (P < 0.01) and manic (P < 0.0002) symptoms, and functioning (P < 0.0001). Also reports of drug use significantly predicted changes in manic symptoms. Additionally, linear decrease in manic symptoms (p < 0.01) and linear increase in functioning (p < 0.01) were observed across assessment time.

Conclusion: Alcohol use, drug use, and time in treatment, and not the primary/secondary distinction, predicted mood and functioning changes. These findings stress the importance of maximiz-
ing treatment effort to address alcohol use and enhance treatment adherence among this group of high-risk patients.

Supported by USPHS Grants NIAAA (AA-10523) and NIAAA (AA-11929), Rockville, MD.

References:

NR437 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Duloxetine for the Long-Term Treatment of MDD in Hispanic Patients in Mexico
Supported by Eli Lilly and Company

Madelaine M. Wohlreich, M.D., Neuroscience, Eli Lilly & Company, Lilly Corporate Center, Indianapolis, IN 46285; Craig H. Mallinckrodt, Ph.D., Elizabeth Brunner, M.D., Hector J. Duenas, M.D., Pedro L. Delgado, M.D.

Educational Objectives:
At the conclusion of this session, participants should recognize that duloxetine was an effective, safe, and well-tolerated medication for the long-term treatment of depression in Hispanic patients.

Summary:
Background: The long-term safety and efficacy of duloxetine, a selective and balanced serotonin and norepinephrine reuptake inhibitor, was evaluated in the treatment of depressed Hispanic patients.

Methods: A subset of depressed Hispanic patients living in Mexico (N = 242) was obtained from an open-label, single-arm, multinational clinical trial of duloxetine (age ≥ 18, N = 1282). Patients received duloxetine 80 to 120 mg day (administered 40 to 60 mg BID) for up to 52 weeks.

Results: Mean changes in all efficacy outcomes at all measurement times showed highly significant (p < .001) improvements. The observed case remission rates (HAMD17 ≤ 7) at Weeks 6, 28, and 52 were 67.4%, 87.5%, and 91.4%, respectively. Adverse events most frequently leading to discontinuation were somnolence (2.9%) and vomiting (1.2%). The most common adverse events were somnolence and nausea. No clinically meaningful changes were observed for pulse, blood pressure, electrocardiograms, and laboratory analytes.

Conclusion: In this study, duloxetine was shown to be an effective, safe, and well-tolerated long-term treatment for depression in Hispanic patients.

Research was funded by Eli Lilly and Company.

NR439 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Methamphetamine Abuse and Emergency Psychiatry: A Chart Review
Louise M. Lettich, M.D., 359 Auwinala Rd, Kailua, HI 96734-3434; Mark P. Toles, C.N.S.

Summary:
Since the 1980s, abuse of crystal methamphetamine (MAP) has been a problem in emergency psychiatry. The scale of the MAP problem in Hawaii, at this time, is greater than many other parts of the country. Charts of all psychiatric emergency department visits to the Queen’s Medical Center in Honolulu, Hawaii, from March to May 2002 were reviewed (n > 1500). In the review, we find MAP abuse in one in five cases seen by psychiatry in the emergency department. We find no gender differences between MAP abusers and non-MAP abusers in the emergency department (the ratio for each is 1:2). We find that MAP abusers are younger than non-MAP abusers (36.1/44.3; F = 4.84, p = .03). We find that MAP abusers are primarily Asians and Pacific Islanders, minority groups in Hawaii. Finally, we find that MAP abusers discharged from the emergency department to the hospital or to the community were significantly more likely to be prescribed Risperdal than non-MAP abusers (30.4%/7.0%; x² = 9.51, p = .006). Zyprexa was prescribed less frequently with no significant difference between the MAP and non-MAP abusers. We conclude that MAP abuse is a major problem and that the effectiveness of Risperdal and Zyprexa in MAP abuse treatment needs more study.

References:

NR440 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Safety Profile of Duloxetine Versus Paroxetine Supported by Eli Lilly and Company
Pierre V. Tran, M.D., Lilly Research Labs, Eli Lilly & Company, Lilly Corporate Center, DC, Indianapolis, IN 46285; Yili Lu, Ph.D., Oleg Martynov, M.D., Michael J. Detke, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the evidence supporting the safety and tolerability of duloxetine, a potent and balanced dual reuptake inhibitor of serotonin and norepinephrine, in the treatment of major depressive disorder and how it compares with the SSRI paroxetine.

Summary:
Objective: To compare the safety and tolerability of antidepressant duloxetine, a dual reuptake inhibitor of serotonin and norepinephrine, over a wide dose range with the SSRI paroxetine in patients with major depressive disorder.

Method: Data from four eight-week, randomized, double-blind, placebo-controlled studies were pooled to compare the safety and tolerability of duloxetine at doses ranging from 40 mg—120 mg/d with paroxetine 20 mg/d.

Results: In the pooled database (placebo N = 371; duloxetine N = 736; paroxetine N = 359), 4% of placebo, 8% of duloxetine, and 6.1% of paroxetine patients discontinued due to adverse events with no statistically significant difference between duloxetine and paroxetine. The only significant difference between duloxetine and paroxetine in treatment-emergent adverse events was for decreased appetite (duloxetine: 4.2%; paroxetine: 1.4%). Nausea rates were 3.8% for placebo, 14.4% for duloxetine, and 12% for paroxetine. Changes in blood pressure measures and laboratory analytes were similar between duloxetine and paroxetine treatment groups. 1.6% of placebo, 1.5% of duloxetine, and 0.28% of paroxetine patients had three consecutive elevations of either systolic or diastolic blood pressure.

Conclusion: The safety and tolerability profile of duloxetine administered over a wide dose range compares very favorably with a low dose of paroxetine. Duloxetine is a safe and well-tolerated antidepressant.

References:

NR442 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Interactions Between Dopaminergic System and Thyroid Axis in Depression: Implication for Suicidal Behavior
Fabricie Duval, M.D., Department of Psychiatry, Centre Hospitalier, 27 Rue du 4eme RSM, Rouffach 68250, France; Marie-Claude Mokrani, Ph.D., Jose Monreal, M.D., Paul Bailey, M.D., Beatrice Hamel, Ph.D., Thomas Weiss, M.D., Jean-Paul Macher, M.D.

Educational Objectives:
At the end of this presentation, the participant should be able to understand that the absence of a functional link between thyroid and dopamine activity at the hypothalamic level may be implicated in the pathogenesis of suicidal behavior.

Summary:
Background: Recent studies have reported alterations in both hypothalamic-pituitary-thyroid (HPT) axis dopaminergic (DA) function in depression. The aim of this study was to investigate the functional relationships between these two systems in depressed patients, especially in those with suicidal behavior.

Method: Hormonal responses to 8 AM and 11 PM TRH tests and to apomorphine test (APO) were measured in 64 drug-free, DSM-IV major-depressed inpatients (35 with a history of suicide attempt, 29 without) and 34 hospitalized healthy controls.

Results: Compared with controls, patients demonstrated lower TRH-TSH responses (8 AM-ΔTSH, p<0.005; 11 PM-ΔTSH, p<0.0001; lower difference between 11 PM-ΔTSH and 8 AM-ΔTSH [ΔΔTSH], p<0.0001), and lower APO-induced prolactin (PRL) suppression (p<0.001). Patients without a history of suicide attempt when compared with patients with such a history showed reduced ΔΔTSH values (p<0.03), but comparable hormonal APO responses. In patients without a history of suicide attempt, a nega-
Conclusions: These results suggest that in major depression (1) co-occurrence of HPT axis and tubero-infundibular DA dysregulation is compatible with a decreased TRH and DA-D2 receptor function (possibly secondary to increased TRH tone) (2) the absence of a functional link between HPT and DA activity at the hypothalamic level may be implicated in the pathogenesis of suicidal behavior.

References:

NR443 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Long-Term Olanzapine/Fluoxetine Use in MDD: Final Data
Supported by Eli Lilly and Company
Sara A. Corya, M.D., Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Scott W. Andersen, M.S., Holland C. Detke, Ph.D., Luann E. Van Campen, Ph.D., Todd M. Sanger, Ph.D., Douglas J. Williamson, M.R.C., Sanjay Dube, M.D.

Educational Objectives:
At the conclusion of this presentation, participants should be able to describe the long-term effectiveness and safety profile of the olanzapine/fluoxetine combination treatment for major depressive disorder. Additionally, they should be able to identify possible treatment advantages and disadvantages for use with treatment-resistant patients.

Summary:
Background: This is the first study to examine long-term use of the olanzapine/fluoxetine combination. Efficacy and safety were investigated in a group of patients with major depressive disorder (MDD), with or without treatment-resistant depression (TRD).
Methods: 560 patients were enrolled in this 76-week, open-label study. The Montgomery-Asberg Depression Rating Scale (MADRS) was the primary efficacy measure. Efficacy analyses used a mixed-effects model repeated measures methodology.
Results: MADRS mean total scores decreased 6 points from baseline (31.6; n=552) at 1/2 week of treatment, 11 points at 1 week, 18 points at 8 weeks, and 22 points at 76 weeks. Response and remission rates for the total sample were high (62%, 56%), and the relapse rate was low (15%). Response, remission, and relapse rates for TRD patients (n=145) were 53%, 44%, and 25%, respectively. Adverse events included somnolence, weight gain, dry mouth, increased appetite, and headache. At endpoint, there were no clinically meaningful changes in vital signs, laboratory analytes, or electrocardiography, and no significant increases on measures of extrapyramidal symptoms.
Conclusions: The olanzapine/fluoxetine combination showed rapid, robust, and sustained improvement in depressive symptoms in patients with MDD, including patients with TRD. The combination's long-term safety profile was similar to that of its component monotherapies.

References:

NR444 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Bipolar Disorder With and Without Suicidal Ideation and Behavior
Michael H. Allen, M.D., Department of Psychiatry, University of Colorado, North Pavilion, 4455 E. 12th Avenue, #A011-95, Denver, CO 80220; Cheryl A. Chessick, M.D., Joseph F. Goldberg, M.D.

Educational Objectives:
After reading this poster, the reader should be able to describe factors associated with suicidal ideation/behavior in bipolar disorder.

Summary:
Objective: The evolution of suicidal ideation and behavior over time are poorly understood in Bipolar Disorder. The authors will attempt to identify biological and psychological factors that confer vulnerability and the disease states and life events that interact with them to increase or decrease suicidal ideation in this population.
Method: We examined intake measures for the first 482 patients with bipolar I or bipolar II disorder enrolled in the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD), a multicenter, NIH-funded project designed to evaluate the longitudinal outcome of patients with bipolar disorder.
Results: Those factors associated with current suicidal included difficulty with the law, being hot tempered, alcohol use, arriving late to work, clinical state of depression or mixed/rapid cycling, Montgomery-Asberg Depression Rating Scales score, Range of Impaired Functioning Tool score, levels of anxiety and fear, presence of neuroticism, and Yale-Brown Obsessive Compulsive Scale score. Conscientiousness, extraversion, and life satisfaction were negatively correlated. Among those with current suicidal ideation, factors associated with prior history of attempt included being hot tempered and alcohol use while extraversion was negatively correlated with attempting. Psychological factors combined with other risk factors may help to identify patients at greater risk for suicidal ideation and attempts.

References:

NR445 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Six-Month Placebo-Controlled Efficacy of Eszopiclone in Chronic Insomnia
Supported by Sepracor, Inc
Andrew D. Krystal, M.D., Department of Psychiatry, Duke University Medical Center, Box 3309/Room 54216/Trent Drive, Durham, NC 27710; James K. Walsh, Ph.D., Thomas Roth, Ph.D., David A. Amato, Ph.D., Thomas Wessel, M.D.
Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the unmet need for effective sleep maintenance treatment and discuss the first well-controlled six-month efficacy and safety study that addresses the long-term treatment of chronic insomnia.

Summary:

Objective: Long-term efficacy and safety data for anti-insomnia agents have been non-existent. This study determined the efficacy and safety of nightly eszopiclone (ESZ) - a novel, cyclopentylidine, non-benzodiazepine, over six months in patients with chronic insomnia.

Methods: In this randomized, double-blind, multicenter study, chronic insomniacs aged 21–69 years received nightly treatment of either placebo (PBO; n = 195) or ESZ 3 mg (n = 593) for six months. Subjective sleep maintenance, sleep latency, total sleep time (TST), and sleep quality were assessed weekly via an interactive voice response system. A last-observation-carried-forward (LOCF) approach was utilized. Safety was evaluated monthly.

Results: There were high completion rates in both groups (PBO, 56.8%; ESZ, 60.5%). At every month, ESZ improved sleep maintenance (wake time after sleep onset, number of awakenings, and number of nights awakened), sleep latency, TST, and sleep quality relative to PBO (p < .01) with no evidence of tolerance. There were no safety issues and the most common AE was unpleasant taste.

Conclusions: For the 471 adult patients with chronic insomnia who completed six months of nightly double-blind treatment, ESZ improved sleep maintenance, sleep latency, sleep time, and sleep quality, and was well tolerated.

References:


NR446 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Do Pregnancy Complications Increase Risk for Adult Anxiety and Depression?

Supported by H. Lundbeck A/S

Jan Berle, M.D., Department of Psychiatry, University of Bergen, Haukeland University Hospital, Box 7800, N-5021 Bergen, Norway; Arne Mykletun, M.A., Anne K. Dalvæit, Ph.D., Alv A. Dahl, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that in a general population birth weight and being small for gestational age increase the vulnerability for anxiety and depression in adult life.

Summary:

Objective: Pregnancy complications and poor neonatal outcome have been indicated as risk-factors for affective disorders, among them anxiety and depression, in adult life. A second trimester exposure to famine has been demonstrated to increase risk of affective psychosis in adulthood. An association between low birth weight and depressive disorder in late life has been reported in men but not in women. The aim of the present study based on a general population, is to test the hypothesis that low birth weight and small for gestational age increase the risk for anxiety disorders and depression in adulthood.

Methods: A health study based on all inhabitants aged 20 years and above in a region of Nord-Trøndelag County in Norway was performed during 1995–7. Birth weight and gestational length of participants aged 20–28 years (n=8269) were retrieved from the Medical Birth Registry of Norway. The outcome measures were self-assessed by Hospital Anxiety and Depression Scale by the participants.

Results: Birth weight and being small for gestational age correlate with anxiety and depression in adulthood.

Conclusions: In a general population we find that low birth weight and being small for gestational age were risk factors for anxiety and depression in adult life.

References:


NR447 Tuesday, May 20, 3:00 p.m.-5:00 p.m.

Does the Alleviation of Painful Physical Symptoms Associated With Depression Lead to Higher Remission Rates?

Supported by Eli Lilly and Company

Maurizio Fava, M.D., Psychiatry, Massachusetts General Hospital, 15 Parkman Street ACC812, Boston, MA 02114; Madelaine M. Wohlreich, M.D., Craig H. Mallinckrodt, Ph.D., John G. Watkin, Ph.D., Michael J. Delk, M.D.

Educational Objectives:

At the conclusion of this session, participant should be aware that depressed patients treated with duloxetine whose painful physical symptoms resolved demonstrated higher rates of remission.

Summary:

Background: Depression is a chronic disease consisting of emotional/psychological and physical symptoms. Treating both symptoms may lead to a higher percentage of patients achieving remission.

Methods: Efficacy data were pooled from two 9-week double-blind clinical trials of duloxetine 60 mg QD (N=244) and placebo (N=251). Efficacy measures included the HAMD17 total score, HAMD17-Maier subsfactor, CGI-S, PGI-I, and Visual Analog Scales (VAS) which assessed various types of pain and overall pain reported (VASOVER).

Results: Higher endpoint scores for overall pain were associated with lower estimated probabilities of remission both before and after accounting for core emotional depressive symptoms (Maier subscale) (p<.0001). The Week 9 means for VASOVER were 13.0 for remitters (last observed value for HAMD17 ≤7) compared with 22.7 for non-remitters (p < .001), respectively. The remission rate for pain responders (improvement in VASOVER from baseline to last observation ≥50%) was twice the rate of pain non-responders (36.2% vs. 17.8%, p < .0001). Lower endpoint pain scores were associated with favorable outcomes on the CGI-S and PGI-I. Furthermore, early favorable responses in VASOVER were associated with favorable endpoint outcomes.

Conclusion: These results suggest that depressed patients treated with duloxetine 60 mg QD whose painful physical symptoms resolved demonstrated higher rates of remission.

References:

NR448  Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Maintenance Treatments for Bipolar I Depression
Supported by GlaxoSmithKline
Frederick K. Goodwin, M.D., Department of Psychiatry, George Washington University Medical Center, 2150 Pennsylvania Avenue, N.W., 8th Floor, Washington, DC 20037; Charles L. Bowden, M.D., Joseph R. Calabrese, M.D., Robin White, M.S., Robert A. Leadbetter, M.D., Alan Metz, M.D.

Educational Objectives:
To compare and contrast the effectiveness of lithium and lamotrigine as maintenance treatments for bipolar I depression.

Summary:
Objective: Lithium, the only FDA approved agent for maintenance treatment of bipolar disorder, has shown to have some antidepressant activity. We compared lithium and lamotrigine as maintenance treatments for bipolar I depression.

Methods: Placebo, lithium (Li), and lamotrigine (LTG) were studied as maintenance treatments for 18 months in bipolar I patients who were currently or recently symptomatic. Results from two clinical trials comprising 463 patients (index depressed) and 175 patients (index manic) were examined for incidence of depressive events, HAMD-17 scores, and DSM-IV depression events by treatment group and index mood episode.

Results: In recently manic patients, fewer lamotrigine than lithium-treated patients required intervention for depression (LTG 14%, Li 22%), reported depressive adverse events (LTG 0, Li 4%), had DSM-IV depression (LTG 10%, Li 17%), or had HAMD scores > 20 (LTG 3%, Li 11%). In recently depressed patients, depressive symptoms were similar between treatment groups; intervention for depression (LTG 34%, Li 38%), reported depressive adverse events (LTG 4%, Li 3%), DSM-IV depression (LTG 31%, Li 36%) or HAMD scores > 20 (LTG 22%, Li 18%).

Conclusions: Lamotrigine provided more protection against depressive symptoms than lithium, regardless of index mood. Results suggest that lamotrigine therapy should be considered during or shortly after stabilization of mania, before depressive symptoms occur.

References:

NR449  Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Comparing the Economic Burden of Depression in 1990 and 2000
Supported by Eli Lilly and Company
Paul E. Greenberg, M.A., Analysis Group/Econ, 111 Huntington Avenue, 10th Floor, Boston, MA 02199; Ronald C. Kessler, Ph.D., Patricia Corey-Lisle, Ph.D., Howard G. Birnbaum, Ph.D., Stephanie A. Leong, M.P.P., Sarah W. Lowe, B.A.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the economic burden of depression in 2000 and how it has changed since 1990.

Summary:
Objective: The economic burden of depression was estimated at approximately $44 billion in 1990. A subsequent study reported a cost burden of $53 billion, using a refined morbidity costs estimation. The objective of this study is to provide a 10-year update of the economic burden of depression using the same refined methodology.

Methods: Using a human capital approach, we developed prevalence-based estimates of three major cost categories: (1) direct costs, (2) mortality costs arising from depression-related suicides, and (3) morbidity costs associated with workplace depression. Using current epidemiological data and publicly available cost data, estimates were updated to reflect 2000 values.

Results: We estimate that the total economic burden of depression increased from $76.1 billion in 1990 to $81.5 billion in 2000 (2000 dollars). Of this total, $26.1 billion—32%—are direct medical costs, $5.4 billion—7%—are mortality costs, and $49.9 billion—61%—are morbidity costs (work loss).

Conclusion: The estimated economic burden of depression increased by 7% in real-terms between 1990 and 2000. At the same time, health care utilization has increased substantially. Future research will incorporate additional costs associated with depression, such as medical comorbidities and the burden of family members, of depressed individuals.

Source of Funding: An unrestricted grant from Eli Lilly and Company.

References:

NR450  Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Inositol Augmentation of Mood Stabilizers for Bipolar Depression
Stanley Foundation
Andrew A. Nierenberg, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 815, Boston, MA 02114-3117; Eden A. Evins, M.D., Lori R. Eisener, B.A., Jacqueline O. Ogutha, B.A., Louisa D. Grandin, B.A., Christina M. Demopoulos, M.D., Gary S. Sachs, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the possible efficacy of inositol for bipolar depression.

Summary:
Background: Better treatments are needed for bipolar depression. One possible treatment inositol, is a natural substance involved in the phosphoinositide cycle, a key pathway for neuronal signal transduction. The purpose of this study is to assess the efficacy of adjunctive inositol for bipolar depression.

Methods: Subjects with Bipolar I or II DSM-IV depression with two or more weeks of therapeutic levels of lithium or valproate were enrolled in a six-week double-blind placebo-controlled study. Hamilton Depression Rating Scale (HAM-D) and Young Mania Rating Scale (YMRS) were performed weekly. Response was
defined as ≥50% reduction from baseline score in HAM-D at endpoint. The active and placebo group outcomes were analyzed with a two-sided Fischer’s exact test and t-tests.

Results: 16 subjects (6 females; aged 44.9 ± 12.0; baseline HAM-D score 24.6 ± 3.6) were randomized; 9 received active inositol (mean dose 13.67 ± 2.50 gm/day) and 7 received placebo. Response criteria were met by 33% of inositol subjects (95% CI: 23.3%–63.7%) and 0% placebo-treated subjects (Fischer’s exact test, p = 0.09). YMRS scores did not change significantly in either group. One placebo-treated subject was withdrawn from the study due to mania. No other serious adverse events occurred.

Conclusion: This small study provides preliminary data on the possible efficacy of inositol for bipolar depression. A larger sample size is needed for more definitive conclusions.

References:

NR451 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
The 6-, 17- and 21-Item Hamilton Depression Rating Scales (HDRS): Clinical Comparisons of the Spanish Version
Supported by GlaxoSmithKline
Julio B. Bobes, M.D., Department of Psychiatry, University Oviedo, Julian Claveria 6, Oviedo 33006, Spain; Antonio Bulbena, M.D., Antonio Luque, M.D., Rafael Dal-Re, M.D., Javier Ballesteros, M.D., Nora Ibarra, M.P.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the usefulness of the six-item HDRS.

Summary:
Objective: To compare the psychometric properties of the Spanish versions of the 6-, 17- and 21-item HDRS in depressive outpatients.
Method: We conducted an observational, prospective cohort and multicentre study in patients with DSM-IV diagnosis of affective disorders. We assessed the discriminant validity of the 6-, 17- and 21-item HDRS, reliability (internal consistency, test-retest and inter-rater reliability) and also their sensitivity to change.
Results: We entered 168 patients from 15 psychiatry centers. The 6-, 17- and 21-item version of the HDRS showed appropriate discriminant validity (HDRS scorings versus Clinical Global Impression Scale scorings: p < 0.0001 all comparisons); internal consistency (Cronbach α: six-item scale = 0.6; 17 / 21-item scale ≥0.7); one-week test-retest reliability [intraclass correlation coefficient (ICC): 6 / 17 / 21-item scale ≥ 0.9]; inter-rater reliability (ICC: 6 / 17 / 21-item scale ≥ 0.9) and six-week sensitivity to change as well (effect size ≥ 1.5 for the 6 / 17 / 21-item scale).
Conclusions: The clinical comparison of the Spanish versions of the 6-, 17- and 21-item HDRS showed no significant differences on psychometric properties between scales. Due to its conciseness, the 6-item scale is suitable for use in outpatient clinics and at primary care.
Study supported by GlaxoSmithKline (Spain).

References:


NR452 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Neuroendocrine Correlates of Temperament and Character Dimensions in Major Depression
Jose A. Monreal Ortiz, M.D., Psychiatry, Centre Hospitalier, 27 Rue Du 4 RSM, Rouffach 68250, France; Fabrice Duval, M.D., Marie-Claude Mokrani, Ph.D., Said Fattah, M.D., Luc Staner, M.D., Jean-Paul Macher, M.D.

Educational Objectives:
At the end of this presentation, the participant should be able to understand that 50 ml trends of temperament and character may be determinants of the neurobiological state of depression.

Summary:
Background: Cloninger, et al. have proposed a psychobiological model of personality that accounts for dimensions of both temperament and character (TCI). The aim of this study was to investigate the relationships between TCI scores and cortisol response to the dexamethasone suppression test (DST) and to the direct dopamine (DA) receptor agonist apomorphine (APO) test in depressed patients.

Methods: Cortisol levels following DST (1mg orally) and APO test (0.75mg s.c.) were measured in 16 drug-free, DSM-IV, non-psychotic depressed inpatients. All patients were rated for depression severity by means of the 17-item Hamilton Rating Scale for Depression (HAM-D) and completed the TCI.

Results: Persistence scores were negatively correlated with APO-stimulated cortisol values (rho=−0.79; p=0.002) and positively with basal cortisol values (rho=0.59; p=0.02). Cooperativeness scores were correlated positively with basal cortisol values (rho=0.74; p=0.004). HAM-D scores were correlated negatively with harm avoidance scores (rho=−0.57; p=0.03) but not with other dimension scores.

Conclusions: Our results support a link between the dimension persistence and central DA function connected with the regulation of the hypothalamo-pituitary-adrenal (HPA) axis. Moreover, the dimensions cooperativeness and persistence seem to be associated with basal HPA activity. Taken together these results suggest that some personality dimensions of the Cloninger model may be determinants of the neurobiological state of depression.

References:

NR453 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
The Relevance of Catatonia for the Mixed-Manic Episode
Stephanie Krueger, M.D., Department of Psychiatry, University of Dresden, Fetscherstr 74, Dresden, Germany; Peter Braeunig, M.D., Robert G. Cooke, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize catatonia in mixed mania, diagnose the catatonic syndrome, treat the catatonic syndrome.
Summary:

Background: Catatonic symptoms have been associated with mixed mania in the older psychiatric literature; however, to date no systematic studies have been performed to assess their frequency in these patients.

Method: Ninety-nine patients with bipolar disorder manic or mixed episode were assessed for the presence of catatonia using the Catatonia Rating Scale (CRS). Severity of the acute episode, associated psychopathology, comorbidity, overall functioning, and length of stay in hospital were also assessed and compared across catatonic and non-catatonic groups.

Results: Thirty-nine patients fulfilled criteria for mixed mania, of whom 24 were catatonic. Among the patients with pure mania, only three were catatonic. Eighteen catatonic patients with mixed mania required admission to the acute care unit (ACU). The catatonic group had more severe acute mood symptoms, more comorbidity (impulsivity spectrum disorders and anxiety disorders), had a lower level of interepisode functioning, and a longer stay in hospital.

Conclusions: Catatonia is frequently associated with the mixed episode and seems to be a marker of severity of the acute episode. Catatonia in mixed mania is likely to be found among the severely ill group of patients with mixed mania, who require emergency treatment. We suggest that in these patients, catatonia is routinely screened for.

References:

NR454 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Impairment in Memory Strategies Mediate Verbal Episodic Memory Impairments in Bipolar I Disorder
National Alliance for Research on Schizophrenia and Depression
Thilo Deckersbach, Ph.D., Department of Psychiatry, Massachusetts General Hospital, 50 Stanford Street, Suite 580, Boston, MA 02114; Stephanie L. McMurrich, B.A., Heather Schloss, B.A., Michael J. Ostacher, M.D., Gary S. Sachs, M.D., Andrew A. Nierenberg, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that episodic memory impairments in patients with bipolar I disorder are mediated by impaired use of memory enhancing strategies during learning.

Summary:

Objective: To investigate whether nonverbal episodic memory impairment in euthymic patients with bipolar I disorder is mediated by an impairment in the use of memory enhancing strategies during encoding.

Methods: Study subjects were 20 euthymic patients with DSM-IV bipolar I disorder and 20 healthy control participants matched for age, gender, education, and handedness. Subjects completed the Rey-Osterrieth Complex Figure Test (RCFT). In the RCFT, participants copy a complex geometric figure and redraw it from memory after a 20-minute delay. The RCFT makes it possible to assess the extent to which participants organize the geometric figure into meaningful units during copy (e.g., a large rectangle, diagonals, etc.). Organizing the RCFT figure into meaningful units during copy is known to enhance subsequent free recall performance.

Results: Individuals with bipolar I disorder copied the RCFT figure as well as control participants (t=3.32, df=38, p<.05), but organized the RCFT less than control participants (t=3.99, df=38, p<.001). The bipolar patients also recalled less of the RCFT figure after the 20-minute delay. Group differences in free recall between BP-I and normal control participants did not remain statistically significant when group differences in organization during copy were statistically partialled (p=.94).

Conclusion: Our results suggest that nonverbal episodic memory impairment in patients with bipolar I disorder is mediated by impaired use of memory enhancing strategies during encoding.

References:
1. van Gorp WG, Altshuler L, Theberge DC, Wilkins J, Dixon W: Cognitive impairment in euthymic bipolar patients with and
NR456 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Patterns of Weight Gain in Bipolar Patients Treated With Olanzapine or Divalproex
Supported by Eli Lilly and Company

Robert W. Baker, M.D., Eli Lilly and Company, Lilly Corporate Center, Drop Code 4133, Indianapolis, IN 46285; Eileen Brown, Ph.D.; Leslie Schuh, Ph.D., Jane Pinaire, Ph.D., Mauricio F. Tohen, M.D.

Educational Objectives:

At the conclusion of this session, participant should be able to discuss relative patterns of weight gain following olanzapine or divalproex treatment of bipolar mania and predictors and consequences of weight gain.

Summary:

Objective: To examine weight gain and related parameters for olanzapine and divalproex sodium.

Method: This post-hoc analysis of a 47-week, double-blind, randomized clinical trial compared olanzapine (5–20 mg/day) and divalproex (500–2500 mg/day) for bipolar mania (N=251). Weight was analyzed using mean change from baseline with ANOVA and categorically using Fisher’s exact test. Possible weight gain predictors were entered into ANOVAs (last observation carried forward) with all factors and their interaction with treatment.

Results: Patterns of weight gain differed between treatment groups. Olanzapine-treated patients had larger mean increases early in treatment which plateaued later. Divalproex-treated patients had more gradual weight increases with no significant differences from olanzapine from week 19 onward. At week 47, significant effects were found for remission status (mean change 4.42 kg for remitters and 2.69 kg for non-remitters, p<.014) and interaction of age by treatment (younger olanzapine-treated patients and middle-aged divalproex-treated patients gained more weight, p=.002). Correlations between change in weight and other variables (psychiatric ratings, glucose, cholesterol, and blood pressure) were small and did not differ between groups.

Discussion: Significant weight increase occurred with both treatments, albeit patterns differed. Weight increases over 47 weeks were weakly correlated with blood pressure, non-fasting glucose or total cholesterol.

References:


NR457 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Dysphoric Mania: A Controlled Study of the Benefits of Olanzapine Combined with Valproate or Lithium Supported by Eli Lilly and Company

Robert W. Baker, M.D., Eli Lilly and Company, Lilly Corporate Center, Drop Code 4133, Indianapolis, IN 46285; Eileen Brown, Ph.D., Mauricio F. Tohen, M.D., Leslie Schuh, Ph.D., Paula T. Trzepacz, M.D.

Educational Objectives:

At the conclusion of this session, participant should be able to discuss relative patterns of weight gain following olanzapine or valproate versus lithium treatment of bipolar mania and predictors and consequences of weight gain.

Summary:

Objective: To examine weight gain and related parameters for olanzapine and valproate versus lithium treatment of bipolar mania and predictors and consequences of weight gain.

Method: This post-hoc analysis of a six-week, double-blind, randomized clinical trial compared olanzapine 5–20 mg/day or placebo combined with ongoing open valproate or lithium treatment for patients in mixed or manic episodes (N=344). All patients had Young Mania Ratings (YMRS) ≥18 despite at least two weeks on lithium or valproate; this analysis focuses on a dysphoric subgroup (baseline Hamilton Depression Rating-HAM-D>20) contrasted with non-dysphoric patients.

Results: In dysphoric patients (n=85), HAM-D total score improvement was greater in patients receiving olanzapine co-therapy than those taking placebo plus ongoing lithium/valproate (p<.001); contributors to this superiority included HAM-D Core Mood cluster (p=.013) and the suicide item (p=.001). In the non-dysphoric group, HAM-D improvement was greater in olanzapine-treated patients (p=.002), although the effect was smaller than in dysphoric patients. Total YMRS improvement was superior on olanzapine co-therapy in both dysphoric and non-dysphoric groups; this effect had similar magnitude in both groups.

Conclusions: In patients with dysphoric mania, addition of olanzapine to ongoing lithium or valproate monotherapy simultaneously improved ratings of depression, mania, and suicidality.

References:


NR458 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Factors Related to a Good, Poor, or Fluctuating Course of Bipolar Disorder

Christine E. Ryan, Ph.D., Department of Psychiatry, Rhode Island Hospital, 593 Eddy Street, Potter 3, Providence, RI 02903; Gabor I. Keitner, M.D., David A. Solomon, M.D., Joan E. Kelley, Ivan W. Miller, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should understand the multi-dimensional factors that may affect the course of a bipolar illness.

Summary:

Objective: To determine a set of factors that will help distinguish the course of illness of patients hospitalized with bipolar disorder.

Method: 92 patients with bipolar disorder were randomly assigned to three treatment conditions (pharmacotherapy alone; pharmacotherapy + family therapy; pharmacotherapy multi-family psychoeducational group) and followed for 28 months post-hospitalization. Symptom severity was assessed monthly using the Bech-Rafaelsen Mania Scale, the Hamilton Depression Rating Scale, and the Brief Psychiatric Rating Scale. Scores for mania, depression, and psychosis were graphed from the acute phase through month 28 for each patient. Experienced clinicians, blind...
to treatment group, then categorized patient course of illness as good, poor, or fluctuating.

Results: There were no differences in course of illness by treatment group. There were significant differences in proportion of time well (symptom-free) between the three groups (F(2,61)=36.6, p<.001). The model for proportion of time in episode also reached a significant level (F(2,61)=40.5, p<.001). Those with a poor course were in episode 41% of the time and differed significantly from patients categorized as having a good course (3% of time in episode) as well as those having a fluctuating course (10% of time in episode). A series of bivariate and multivariate analyses indicated that age of onset of mania, gender, polarity at index episode, and family functioning are factors that may affect the course of a patient's illness.

Conclusion: A combination of clinical, psychosocial, and sociodemographic variables may be most useful for distinguishing a patient's illness course and suggesting treatment interventions.

References:

NR459 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Linking Instability to Mood-Incongruent Psychotic Features in Acute Mania Supported by Sanofi-Synthelabo, Inc.
Jean-Michel Azorin, M.D., Department of Adult Psychiatry, St. Marguerite Hospital, 270 Bd De Sainte Marguerite, Marseille 13274, France; Elie G. Hantouche, M.D., Hagop S. Akiskal, M.D., Sylvie Lancrenon, Ph.D., Liliane Chattenet-Duchene, M.D.

Educational Objectives:
To understand the phenomenology of mood-incongruent psychosis associated with acute mania

Summary:
Following the EPIMAN study (Akiskal et al, 1998), a new French study (EPIMAN-II Thousand) was initiated with the objective of including 1,000 patients with acute mania. In this report, data are focused on the role of mood instability in psychotic mania.

Method: "EPIMAN-II Thousand" is a national multi-site collaborative study dedicated to the clinical sub-types of mania. It involved training 317 French psychiatrists working in different sites representative of France. The study actually succeeded in recruiting 1,090 cases admitted for acute mania (DSM-IV criteria). Assessment of psychotic features was made using the full version of SANS (Andreasen). An agenda for mood stability was completed three times daily, and during the first week of hospitalization, by training 317 French psychiatrists working in different sites representative of France. The study actually succeeded in recruiting 1,090 cases admitted for acute mania (DSM-IV criteria). Assessment of psychotic features was made using the full version of SANS (Andreasen). An agenda for mood stability was completed three times daily, and during the first week of hospitalization, by nursing staff and patients.

Results: The rate of severe mania with psychotic features was 49.9%; 33.4% with mood-congruent (MCP) and 16.5% with mood-incongruent (MICP) features. The global group with psychotic mania was characterized by a younger age of disorder onset (26-27 years vs 30 years in Non Psychotic (NP) mania, p=0.05) and of seeking help (27-29 vs 32 years, p=0.05). In the MICP subgroup, prior diagnoses were more likely to be toward schizophrenic disorders (26.3% vs 17.6% (MCP) vs 6.5% in NP, p=0.001), schizoaffective disorder (24.0% vs 17.3% (MCP) vs 12.7% in NP, p=0.001). The mean of maximal daily variations on mood agenda, were significantly elevated (p<0.05). In the MICP during day 1-3: 2.3 vs others groups (1.7 in MCP and 1.8 in NP); and during day 1-7: 2.0 vs others groups (1.6 in MCP and 1.6 in NP).

Conclusion: Mania with mood-incongruent psychotic features begins earlier than other forms of mania, and is likely to be misrepresented as schizophrenia disorder. High mood instability could be one of the major factors related to mood-incongruence of psychotic features in mania.

References:

NR460 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Relapse Prevention With Gepirone Extended Release in Outpatients With Major Depression Supported by Organon Inc.
Frank J.L. Ruwe, Ph.D., Clinical-CNS, Organon, PO Box 20, Oss 5340BH, Netherlands; Michael Gibertini, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to (1) discuss and evaluate clinical evidence supporting the efficacy and tolerability of gepirone-ER in major depression; (2) discuss and evaluate clinical evidence supporting the efficacy of gepirone-ER for the short-term treatment of relapse prevention.

Summary:
Objective: To evaluate the long-term efficacy of gepirone-ER (a 5-HT1a agonist), a relapse prevention study was undertaken.

Methods: This was a multicenter, randomized, placebo-controlled trial of gepirone-ER for the prevention of relapse in patients with recurrent major depression. Eligible patients entered an 8-12 week, open-label phase. Patients initially received a dose of 20 mg/day and were titrated to a dose of 40-80 mg/day of gepirone-ER. Patients who achieved remission (HAM-D-17 score of <8) at weeks 8 or 12 were randomized to gepirone-ER 40-80 mg/day or placebo for 40-44 weeks. For the primary endpoint, relapse was defined as a HAM-D-17 score of >16 or discontinuation for lack of efficacy.

Results: In total, 303 completed the open-label phase and 250 fulfilled the criteria for remission. For the double-blind continuation phase, 126 patients were randomized to gepirone-ER and 124 to placebo. The relapse rate was 23.0% with gepirone-ER and 34.7% with placebo (p = 0.025 vs. placebo). During the open-label phase, adverse events that occurred in >5% of subjects were headache (12.9%), nausea (15.7%), dizziness (13.1%), insomnia (6.2%), and vertigo (6.0%). Gepirone-ER did not appear to cause significant weight gain over 40 weeks of treatment.

Conclusion: Gepirone-ER 40 to 80 mg/day is effective for relapse prevention in patients with recurrent major depression and is well tolerated during long-term treatment.

Funded by Organon Inc.

References:
NR462 Tuesday, May 20, 3:00 p.m.-5:00 p.m.  
Angr and Hostility Among Depressed Outpatients With Current or Past History of Anxiety Disorders  
David Mischoulon, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114; Pamela A. Roffi, B.S., Heidi D. Montoya, B.A., Rebecca Harley, Ph.D., Albert Young, M.D., Jonathan E. Alpert, M.D., Maurizio Fava, M.D.

Educational Objectives:  
At the conclusion of this session, the participant should understand the relationship between presence of comorbid anxiety disorders and degree of anger/hostility among outpatients with major depressive disorder.

Summary:  
Background and Rationale: Anger and hostility are common symptoms among psychiatric outpatients and have been associated with the presence of both major depressive disorder (MDD) and anxiety disorders. We wanted to compare levels of anger/hostility before and after antidepressant treatment between MDD outpatients with and without a history of past or current anxiety disorders.

Methods: 147 patients (58% female), ages 18-65 (mean age 41.0±10.8), diagnosed with major depressive disorder (MDD) by SCID-P and having a Hamilton D-17 score ≥ 16 were recruited into a study involving eight weeks of open-label treatment with fluoxetine 20 mg/day. Patients were administered the Kellner's Symptom Questionnaire (SQ) Anger/Hostility Scale before and after fluoxetine treatment. ANOVA was carried out to assess differences in pre- and post-treatment SQ scores between patients with and without a history of past or current anxiety disorders. Multiple linear regressions were used to assess these relationships adjusting for age and gender.

Results: Statistically significantly higher pre-treatment scores (p<0.05, both before and after adjusting for age and gender) on SQ anger/hostility scale were found among patients with comorbid lifetime anxiety disorders (n=69) compared with depressed patients without such disorders (n=78). A trend toward statistical significance (p=0.07) was observed comparing pre-treatment anger/hostility scores among patients with (n=55) and without (n=92) current comorbid anxiety disorders. Following eight weeks of treatment with fluoxetine 20mg/day, statistically significant higher post-treatment scores (p<0.05, both before and after adjusting for age and gender) on SQ anger/hostility scale were found among patients with comorbid lifetime anxiety disorders (n=69) compared with depressed patients without such disorders (n=78). No significant differences were observed comparing post-treatment anger/hostility scores among patients with (n=55) and without (n=92) current comorbid anxiety disorders.

Conclusion: Anger/hostility may be more prevalent both as a presenting and as a residual symptom among MDD outpatients with current or past history of anxiety disorders. Further studies need to evaluate the clinical implications of these findings.

References:

NR463 Tuesday, May 20, 3:00 p.m.-5:00 p.m.  
Effects of Mood Stabilizers on Body Weight in Bipolar I Disorder  
Supported by GlaxoSmithKline  
Lawrence D. Ginsberg, M.D., Red Oak Psychiatry, 17115 Red Oak Drive, Houston, TX 77090; Charles L. Bowden, M.D., Joseph R. Calabrese, M.D., Gary S. Sachs, M.D., Terence A. Ketter, M.D.

Educational Objectives:  
At the conclusion of this session, the participant will be able to compare and contrast the effects of mood stabilizers for bipolar I disorder on body weight.

Summary:  
Objective: To examine the effects of mood stabilizers for bipolar I disorder on body weight.

Methods: 638 patients randomized to 18 months of double-blind monotherapy with lamotrigine (n=280; 50-400mg/day fixed and flexible dose), lithium (n=167; 0.6-1.1mEq), or placebo (n=191) were grouped by pretreatment body mass index (BMI): not obese = BMI < 30, obese = BMI ≥ 30. Mean observed change in body weight was examined through 52 weeks of treatment. Random effects mixed model with subject as a random effect and treatment, BMI category, visit, BMI category by visit interaction, and treatment by visit interaction as fixed effects was performed.
After 52 weeks of treatment, mean change in body weight was significantly lower in the lamotrigine treatment group compared with placebo (p < 0.011) and compared with lithium (p<0.0001). These differences were evident in both BMI categories, but were most evident in the obese category of patients: placebo +1.46 kg, lithium +3.3 kg, and lamotrigine -2.96 kg.

Conclusions: Changes in body weight were correlated with choice of mood stabilizer and body mass index. Patients categorized as obese were at greatest risk for weight gain with lithium.

References:

Low Bone Mineral Density in Major Depression and BPD
Medizinische Universitätsklinik Lübeck
Kai G. Kahl, M.D., Department of Psychiatry, Medical University, Ratteburger Allee 160, Luebeck 23538, Germany; Sebastian Rudolf, M.D., Beate Stockelhuber, M.D., Christoph Kroger, M.D., Fritz Hohagen, M.D., Leif Dibbelt, M.D., Ulrich Schweiger, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that even young female patients with a lifetime history of major depressive disorder have low bone mineral density and are therefore at increased risk of developing osteoporosis.

Summary:
Introduction: Low bone mineral density (BMD) is a risk factor for the development of osteoporosis, and a dysregulation of the hypothalamus-pituitary-adrenal axis (HPAA) has been associated with the underlying pathogenetic process. A dysregulation of the HPAA has been discussed in major depressive disorder (MDD) and in borderline personality disorder (BPD). Therefore, our study aimed at examining whether patients with BPD and lifetime MDD, and BPD without MDD, display decreased BMD. Our study used the SCAN interview and diagnosed according to DSM-IV and ICD-10 using a computerized scoring program (CAPTUR). Polygenic correlations between 22 depression symptom items were calculated and a principal components factor analysis was performed on these symptom items based on the polychoric correlation matrix. Orthogonal rotation of the factor pattern was then performed by the VARIMAX method.

Results: Four interpretable symptom factors were identified with clear separation between melancholic and atypical features. For each symptom group a quantitative scale was constructed that took into account factor loadings and correlations between siblings were calculated. All four symptom factors showed positive familial correlation.

Conclusions: These preliminary findings indicate the potential usefulness of taking symptom patterns into account in genetic analysis.

References:

Metyrapone Reverses Impaired Endothelial Function in Depressed Patients
The British Heart Foundation
Anna Korszun, M.D., Adult Dental Health/Psychological Medicine, University of Wales- College of Medicine, Meath Park, Cardiff CF4 4XY, United Kingdom; Andrew J. Broadley, M.D., Valentina Moskina, Ph.D., Zainab Abood, M.D., Shyama Brewster, Ph.D., Nick Craddock, M.D., Caroline F. Drain, Ph.D., Heiner Fangerau, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the relationship between endothelial dysfunction and depression and the potential role of cortisol in this interaction.

Summary:
Objectives: Endothelial dysfunction (ED) is a common feature of major acquired risk factors for ischemic heart disease and can be demonstrated by decreased flow-mediated dilatation (FMD) of the brachial artery. Impaired FMD has also been shown in otherwise healthy subjects with both treated (Broadley et al. 2002) and...
uninhibited (Rajagopalan et al. 2001) depression. We examined the effect of acute inhibition of cortisol production, using oral metyrapone, on FMD in depressed subjects, to test the hypothesis that ED in depression is mediated by increased levels of cortisol.

**Method:** We measured baseline FMD in 24 depressed patients, without other cardiac risk factors. Subjects were then randomized in a double-blind fashion and received either 1500 mg metyrapone or placebo. FMD was re-measured five hours later.

**Results:** As in previous studies, the depressed subjects showed a reduced FMD at baseline (~0.55% ±0.92 SEM). In the placebo group there was no significant change in FMD (1.26% ±1.16 SEM p=0.46). However, subjects who received metyrapone showed significantly increased FMD (3.39% ±0.93 SEM p=0.008) approaching those of healthy controls.

**Conclusions:** Suppression of cortisol production with metyrapone partially reverses the impairment of endothelial function in depressed subjects.

**References:**
2. Rajagopalan S, Brook R, Rubenfire M, Pitt C, Young E, Pitt B: Suppression of cortisol production with metyrapone partially reverses the impairment of endothelial function in depressed subjects.

**NR467** Tuesday, May 20, 3:00 p.m.-5:00 p.m.
**Aripiprazole Versus Haloperidol for Maintained Treatment Effect in Acute Mania**
**Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co, Ltd.**

Michel Bourin, M.D., Department of Neurobiologie, Faculte de Medecine, 1 Rue Gaston Velin, Nantes Cedex 01 44035, France; Philippe Auby, M.D., Ronald N. Marcus, M.D., Rene Swank, M.S., Robert D. McQuade, Ph.D., Taro Iwamoto, Ph.D., Raymond Sanchez, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should have a better understanding of the efficacy and safety of aripiprazole for the treatment of acute manic episodes in patients with bipolar I disorder.

**Summary:**
**Objective:** To compare aripiprazole-treated patients with haloperidol-treated patients who continued on treatment and maintained response after 12 weeks of treatment of an acute manic episode in patients with bipolar disorder.

**Method:** This 12-week, multicenter, double-blind study randomized 347 inpatients and outpatients with acute mania or mixed bipolar episodes to either aripiprazole 15 mg/day or haloperidol 10 mg/day. Treatment doses could be titrated in weeks 1-3 to improve response and/or tolerability. The primary efficacy measure was response at Week 12, defined as ≥50% improvement from baseline in Young Mania Rating Scale (Y-MRS) score, and continuation of therapy.

**Results:** At Week 12, significantly more patients responded and remained on aripiprazole (50%) than on haloperidol (28%; p<0.001). There were marked differences in long-term continuation rates for the two treatments (29.1% of patients remained on haloperidol compared with 50.9% on aripiprazole). The major reason for discontinuation in the haloperidol group was adverse events. Extrapyramidal Syndrome was reported in 38% of haloperidol patients versus 9% with aripiprazole. Neither drug was associated with weight gain during the study period.

**Conclusion:** Aripiprazole treatment led to significantly higher response rates and improved tolerability over haloperidol for maintained treatment effect in acute mania at 12 weeks.

**References:**

**NR468** Tuesday, May 20, 3:00 p.m.-5:00 p.m.
**Panic Symptoms in MDD**

Paolo Cassano, M.D., Psychiatry Department, Harvard University, 15 Parkman Street, WAC 812, Boston, MA 02114; Dan V. Iosifescu, M.D., Naomi M. Simon, M.D., Jessica L. Murakami, B.A., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Maurizio Fava, M.D.

**Educational Objectives:**
At the conclusion of this session, our findings support the clinical relevance of panic symptoms in depressed patients as opposed to the traditional approach of panic disorder comorbidity.

**Summary:**
**Objective:** We assessed the impact of both DSM-IV panic disorder (PD) and panic symptoms (PA-sym) on antidepressant response to fluoxetine among outpatients with major depressive disorder (MDD).

**Methods:** We derived a measure of PA-sym at baseline (range: 0–17) from the self-rated Symptom Questionnaire (11 items) and Beck Anxiety Inventory (6 items), and defined high PA-sym scores as ≥8. 329 outpatients with MDD (SCID-DSM-IV criteria) who completed 8 weeks of treatment with fluoxetine (20 mg/day) were examined. Outcome variables were HAMD-17 change scores from baseline to week 8 examined as percentage change and as response, defined as a ≥50% reduction. In addition, remission was defined as a HAMD-17 score ≤7. Logistic and multiple regression analyses were performed.

**Results:** Mean score for PA-sym was 5.7±3.6. Fifteen (4.6%) and thirty-eight (11.6%) subjects had current and lifetime diagnosis of PD, respectively. Only 46.4% (vs. 67.5%) of patients with high PA-sym scores were responders (p=0.05) and 36.1% (vs. 54.7%) remitted (p=ns). PA-sym scores also predicted lower percent change of HAMD-17 score (p=.05). Severity of depression did not account for the predictive value of PA-sym. Diagnosis of PD did not significantly predict depression outcome.

**Conclusions:** Our data suggest that panic symptoms, but non panic disorder, significantly predict a poorer antidepressant treatment outcome among outpatients with MDD.

**References:**
NR469  Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Onset of Action of Olanzapine/Fluoxetine Combination in Bipolar Depression
Supported by Eli Lilly and Company
Sanjay Dube, M.D., Eli Lilly & Company, Lilly Corporate Center, Indianapolis, IN 46284; Gary D. Tollefson, M.D., Michael E. Thase, M.D., Susan D. Briggs, Ph.D., Luann E. Van Campen, Ph.D., Michael Case, M.S., Mauricio F. Tohen, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to compare onset of action with olanzapine/fluoxetine combination (OFC), olanzapine, or placebo for the rapid and sustained treatment of patients with bipolar depression.

Summary:

Purpose: We examined the onset of action of olanzapine/fluoxetine combination (OFC) in a study comparing OFC, olanzapine, and placebo for bipolar depression (n=833).

Methods: The primary efficacy measure of the study was the Montgomery-Asberg Depression Rating Scale (MADRS). Secondary analyses were conducted for traditional analysis, pattern analysis, mixed-effects curvilinear regression, and survival analysis of sustained response. Area under the curve assessed overall effectiveness.

Results: Traditional analysis revealed significantly greater improvement in MADRS scores at week 1 for OFC versus placebo (9.55 vs. -5.08, p<.001) and for olanzapine versus placebo (-8.31 vs. -5.06, p<.001). For pattern analysis, OFC had a significantly greater percentage of early persistent responders than the olanzapine or placebo groups (32.4% vs. 18.3%, p<.05; and 12.7%, p<.001, respectively). Survival analysis revealed a significantly shorter time to sustained response for OFC versus placebo (p<.001), for OFC versus olanzapine (p<.05), and for olanzapine versus placebo (p<.05). Mixed-effects curvilinear regression analysis revealed a significant therapy by time interaction (p<.001). Area under the curve analysis showed a significantly greater percentage of total possible improvement (48.2%) for OFC vs. olanzapine (38.5%, p<.01) or placebo (27.8%, p<.001).

Conclusion: Overall, OFC and olanzapine demonstrated rapid and sustained antidepressant action in a sample of bipolar depressed patients.

References:

NR471  Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Scope and Correlates of Caregiver Burden in Bipolar Disorder
National Institute of Mental Health
Deborah A. Perlick, Ph.D., Psychiatry Department, Yale University, 950 Campbell Avenue, 182, West Haven, CT 06516; David J. Miklowitz, Ph.D., Karen Menard, M.A., Nancy Wolf, Ph.D., Lauren B. Marangell, M.D., Joseph R. Calabrese, M.D., Michael J. Ostacher, M.D., Jayendra K. Patel, M.D., Terence A. Kelter, M.D., Robert A. Rosenheck, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize signs and risks of burden among caregivers of patients of bipolar disorder.

Summary:
Introduction and Methods: This study evaluates the scope and correlates of burden experienced by 106 primary caregivers of patients with bipolar disorder enrolled in the naturalistic treatment study, of Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD; Gary Sachs, M.D., P.I.). Caregivers were interviewed at study admission on measures of objective and subjective burden, illness appraisal, and coping.

Results: 91% of caregivers reported moderate or severe subjective burden regarding the patient's problem behaviors in 1+ areas; 44% were distressed in 10+ areas. The five most distressing behaviors were misery, irritability, mood swings, withdrawal, and underactivity. 33% of caregivers reported distress regarding role dysfunction, and 73% reported distress regarding household disruption. MR showed sociodemographic and clinical control variables did not account for a significant percent of variance in objective burden. However, addition of appraisal and coping variables to the model explained 40.5% unique variance (adjusted R² change = .405, p < .0001, total adjusted R² = .435). Caregiver perceptions of patient control over illness symptoms and criticism of the patient were both significantly associated with burden (p's < .0001). Results were comparable for subjective burden.

Conclusion: Caregivers of bipolar patients experience considerable burden related to illness coping, suggesting the need for intervention.

References:
2. Perlick DA, Clarkin JF, Sirey J, Raue P, Greenfield S, Struening E, Rosenheck R: Burden experienced by caregivers of persons...

**NR472**

**Tuesday, May 20, 3:00 p.m.-5:00 p.m.**

**Does Age Moderate Depression and Adaptation in Cancer Patients?**

**Department of Veteran Affairs**

Thomas P. Beresford, M.D., Department of Psychiatry, VAMC/University of Colorado, 1055 Clermont Street, Suite 116, Denver, CO 80220; Laura E. Mangun, M.S.W., Brandon K. Martin, B.A.

**Educational Objectives:**

At the conclusion of this session, the participant will be able to recognize the importance of assessing the effects of age in sorting types of depressive symptoms seen in cancer patients.

**Summary:**

**Objective:** Both cancer and depression are typically regarded as diseases of late life. Despite this, little is known about age effects on depressive symptoms among cancer patients. Because late stage cancer is a severe medical condition, we hypothesized that (1) age would correlate positively with depressive symptom frequency, and (2) age would be positively associated with defense style maturity.

**Method:** We administered the 21-item Beck Depression Inventory and the 40-item Defense Style Questionnaire to a sample of that (1) age would correlate positively with depressive symptom frequency, and (2) age would be positively associated with defense style maturity. We administered the 21-item Beck Depression Inventory and the 40-item Defense Style Questionnaire to a sample of adult subjects (N=99) receiving chemotherapy for varying types of Stage III or IV neoplastic illness. Subjects were free of delirium and of significant pain. The sample included 49 females and 50 males; ages ranged from 23 to 83 years (56.02, ± 12.80).

**Results:** Analysis found that (1) subject age was inversely associated with the frequency of depression symptoms (Pearsons r = −30, p<0.01), and especially symptoms of depressed mood (Pearsons r = −34, p<0.001), and 2) that the maturity of adaptive style bore no statistical relation with subject age.

**Conclusion:** These data suggest that age may moderate depression in cancer patients while psychological adaptation appears to be independent of subject age. Mechanisms explaining both effects deserve further study in cancer sufferers.

**References:**


**NR473**

**Tuesday, May 20, 3:00 p.m.-5:00 p.m.**

**Effect of Gepirone Extended Release on Sexual Function In Patients With Major Depression Supported by Organon Pharmaceuticals Inc.**

Jonathan R.T. Davidson, M.D., Department of Psychiatry, Duke University Medical Center South, Trent Drive, Room 4082B, Box 3812, Durham, NC 27710; Michael Gilbertini, Ph.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to (1) discuss and evaluate clinical evidence supporting the efficacy and tolerability of gepirone-ER in major depression, and (2) discuss and evaluate clinical evidence supporting the effect of gepirone-ER on sexual function.

**Summary:**

**Objective:** To evaluate the effects of gepirone-ER vs. placebo on sexual functioning in outpatients with major depressive disorder (MDD).

**Methods:** This was a double-blind, placebo-controlled, parallel-group study of gepirone-ER 20–80 mg/day. Patients were included in the analysis if they received baseline and endpoint assessment of sexual function with the DISF-SR (Derogatis Interview for Sexual Function-Self Report). Increases in the DISF-SR signify improvement in sexual functioning. Comparisons were performed with analysis of variance (ANOVA).

**Results:** Gepirone-ER (n=65) and placebo (n=73) groups were comparable at baseline. Mean baseline DISF-SR scores were 45.7 with gepirone-ER and 42.4 with placebo. A statistically significant difference was observed with gepirone-ER compared with placebo for the mean change from baseline to endpoint on the DISF-SR total score (P = 0.011). In females, the mean change from baseline in DISF-SR total score with gepirone-ER was 10.0 (n=46) and with placebo was −1.5 (n=42)[P=0.043]. In males, the mean increase in DISF-SR total scores with gepirone-ER was 11.1 (n=19) vs. 1.1 for placebo (n=31). This effect was not significant.

**Conclusions:** Gepirone-ER may have a positive effect on sexual function in patients with MDD. Funded by Organon Inc.

**References:**


**NR474**

**Tuesday, May 20, 3:00 p.m.-5:00 p.m.**

**Gepirone Extended Release in Patients With Anxious Depression Supported by Organon Inc.**

Jonathan E. Alpert, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114; Maurizio Fava, M.D., Charlotte Kremer, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to (1) discuss and evaluate clinical evidence supporting the efficacy of gepirone-ER for the short-term treatment of anxious depression.

**Summary:**

**Objective:** To evaluate the effects of gepirone-ER vs. placebo on sexual functioning in outpatients with major depressive disorder (MDD).

**Methods:** This was an eight-week, randomized, double-blind, placebo-controlled, parallel-group study of gepirone-ER 20–80 mg/day. Patients were included in the analysis if they received baseline and endpoint assessment of sexual function with the DISF-SR (Derogatis Interview for Sexual Function-Self Report). Increases in the DISF-SR signify improvement in sexual functioning. Comparisons were performed with analysis of variance (ANOVA).

**Results:** Gepirone-ER (n=65) and placebo (n=73) groups were comparable at baseline. Mean baseline DISF-SR scores were 45.7 with gepirone-ER and 42.4 with placebo. A statistically significant difference was observed with gepirone-ER compared with placebo for the mean change from baseline to endpoint on the DISF-SR total score (P = 0.011). In females, the mean change from baseline in DISF-SR total score with gepirone-ER was 10.0 (n=46) and with placebo was −1.5 (n=42)[P=0.043]. In males, the mean increase in DISF-SR total scores with gepirone-ER was 11.1 (n=19) vs. 1.1 for placebo (n=31). This effect was not significant.

**Conclusions:** Gepirone-ER may have a positive effect on sexual function in patients with MDD. Funded by Organon Inc.

**References:**

score was significantly different (P < 0.05) between groups at Days 14, 21, 28, 42, and 56 in favor of gepirone-ER. 

**Conclusion:** Gepirone-ER was effective and well tolerated in patients with anxious depression. Funded by Organon Inc.

**References:**

**NR475**  
**Tuesday, May 20, 3:00 p.m.-5:00 p.m.**

**Analysis of Treatment-Emergent Mania With Olanzapine/Fluoxetine Combination Supported by Eli Lilly and Company**

Paul E. Keck, Jr., M.D., Biological Psychiatry Department, University of Cincinnati, Medicine, 231 Albert Sabin Way, ML559, Cincinnati, OH 45267-0559; Sara A. Corya, M.D., Michael Case, M.S., Mauricio F. Tohen, M.D.

**Educational Objectives:**
- At the conclusion of this presentation, the participant should be able to compare the rates of treatment-emergent mania in bipolar depressed patients treated with olanzapine/fluoxetine combination, olanzapine, or placebo.

**Summary:**
**Objective:** Treatment-emergent mania is often associated with bipolar depression in patients treated with antidepressants without mood stabilizers. This study compares treatment-emergent mania rates in bipolar depressed patients treated with olanzapine/fluoxetine combination (OFC), olanzapine, or placebo.

**Methods:** In this eight-week, double-blind treatment, patients with bipolar depression (baseline MADRS total scores ≥20) were randomized to OFC (6/25, 6/50, or 12/50 mg/day, n=86), olanzapine (5–20 mg/day, n=370), or placebo (n=377), followed by an optional six-month, open-label extension phase (n=562).

**Results:** In the acute phase, treatment-emergent mania (baseline YMRS <15 and ≥15 at any subsequent visit) did not differ between groups (OFC 6.4%, olanzapine 5.7%, placebo 6.7%, p=0.861). Subjects on OFC (–1.38 ± 5.59 SD) and olanzapine (–0.55 ± 5.91 SD) had greater decreases in YMRS than those on placebo (0.57 ± 6.09 SD) (p<0.027 and p<0.001, respectively). In the extension phase (OFC n=404), OFC subjects’ treatment-emergent mania rate was 4.7% (n=19) at any time and only 4.0% (n=16) at endpoint. YMRS mean change from baseline (3.51 ± 3.69 SD) to endpoint (0.03 ± 5.42 SD) for OFC was not significant.

**Conclusions:** Neither OFC nor olanzapine had a greater risk of acute treatment-emergent mania than placebo. The rate of treatment-emergent mania for OFC was low during a six-month, open-label extension.

**References:**

**NR477**  
**Tuesday, May 20, 3:00 p.m.-5:00 p.m.**

**Comparison of Sexual Functioning in Patients Receiving Duloxetine or Paroxetine: Acute and Long-Term Data Supported by Eli Lilly and Company**

Stephen K. Brannan, M.D., Craig H. Mallinckrodt, Ph.D., Pierre V. Tran, M.D., Pedro L. Delgado, M.D.

**Educational Objectives:**
At the conclusion of this session, participant should recognize that the antidepressant duloxetine has low impact on overall sexual functioning in both acute and long-term treatment phases.

**Summary:**
**Objectives:** Evaluate sexual functioning following acute- and long-term treatment with duloxetine, paroxetine, or placebo.

**Method:** Acute-phase data obtained from four 8-week, double-blind studies, with patients randomized to duloxetine (20–60 mg BID; n=736), paroxetine 20 mg QD (n=359), or placebo (n=371). Long-term data obtained from extension phases, in which acute treatment responders received duloxetine (40 or 60 mg BID; n-
297), paroxetine 20 mg QD (n=140), or placebo (n=129) for 26 additional weeks. Sexual function evaluation was performed during the Arizona Sexual Experience (ASEX) questionnaire (McGahuey, 2000).

Results: In patients without initial sexual dysfunction, no significant difference existed in the rate of acute phase sexual dysfunction onset between duloxetine and paroxetine (p=0.492), although both rates were significantly higher than placebo (p<0.003 and p<0.002, respectively). Long-term data revealed that sexual function improved (ASEX total score reduced) in 70.9% of duloxetine-treated patients between baseline and endpoint, compared with 57.6% for paroxetine (p=0.06). For ASEX Questions 1 and 2, a significantly greater proportion of duloxetine-treated patients reported improvement compared with paroxetine (p<0.050 and p<0.037, respectively). No significant differences were found in Questions 3, 4, or 5.

Conclusion: In these studies, the incidence of sexual dysfunction development among patients receiving duloxetine across its dose range (40–120 mg/day) was comparable to paroxetine at the low end of its dose range (20 mg QD). On certain ASEX questions, a significantly higher percentage of duloxetine-treated patients reported improved in sexual function.

References:

NR478  Tuesday, May 20, 3:00 p.m.–5:00 p.m.
TEMPS-A: Reliability and Clinical Validity With a Japanese Sample
Tsuyoshi Akiyama, M.D., Department of Psychiatry, Kanto Medical Center, 5-9-22 Higashigotanda, Shinagawa-ku Tokyo 141-8625, Japan;

Educational Objectives:
At the conclusion of this session, the participant should recognize TEMPS-A as an effective auto-questionnaire on the temperaments in the Japanese.

Summary:
Introduction: This is the first report on the reliability and clinical validity of TEMPS-A developed by H.S. Akiskal, with a Japanese sample.
Hypothesis: TEMPS-A measures the temperaments with a high reliability and a clinical validity.
Methods: TEMPS-A was translated into the Japanese and implemented with 1,321 healthy subjects and 59 unipolar and bipolar disorders patients diagnosed with SCID.
Results: Test-retest reliability was examined with 426 healthy subjects. Spearman's coefficients for depressive, cyclothymic, hyperthyemic and irritable temperaments were 0.79, 0.84, 0.87 and 0.81 respectively. Internal consistency was examined with 1,391 healthy subjects and Cronbach's alpha coefficients were 0.69, 0.84, 0.79 and 0.83. Depressive and cyclothymic temperament scores were significantly higher (Mann-Whitney, p<0.01%) in the mood disorder patient than in the matched control subject. The scores of depressive, cyclothymic and irritable temperament showed significant inter-correlations (Spearman's coefficient, p<0.1–5%), while hyperthyemic temperament score did not. Between unipolar and bipolar disorders there was no significant difference in regard to the four temperaments, suggesting a temperamental commonality between the two groups.
Conclusion/Discussion: TEMPS-A is an auto-questionnaire that can be used to measure the temperaments in the Japanese with a high reliability. Depressive and Cyclothymic temperaments are characteristic with the mood disorder patient. The significance of hyperthyemic and irritable temperaments is to be investigated further. There may be a temperamental commonality between unipolar and bipolar disorders.

References:

NR479  Tuesday, May 20, 3:00 p.m.–5:00 p.m.
Tolerability of Mirtazapine Versus Other Antidepressants in Patients With Major Depression Supported by Organon Inc.
Silvia Van Der Flier, Ph.D., International Marketing, N.V. Organon, Molenstraat 110, 5342 CC OSS, OSS, Netherlands; Albert J. Schutte, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to (1) design the study and methods of this pooled analysis comparing mirtazapine with several SSRIs and a SNRI; (2) discuss the results of this pooled analysis and its implications for the clinical use of mirtazapine with respect to tolerability.

Summary:
Objective: To compare the tolerability between mirtazapine and various other antidepressants (SSRIs and SNRI) in a large group of patients with major depression by pooled analysis.
Methods: The data of six double-blind, randomized, parallel-group trials comparing mirtazapine with SSRIs (fluoxetine, paroxetine, citalopram, or sertraline) and SNRI (venlafaxine) were pooled and analyzed with regard to tolerability. In all trials tolerability was assessed during clinical interviews by registering treatment-emergent adverse events according to the WHO system organ class.
Results: A total of 1,428 patients (mirtazapine: n=720; SSRIs/SNRI: n=708) were included in this analysis. The number of drug-related adverse events were comparable for both treatment groups except for headache, nausea, and increased sweating, which had a lower incidence in the mirtazapine treatment group and dry mouth, weight increase, increased appetite, and somnolence, which had a lower incidence in the SSRIs/SNRI treatment group. The percentage of subjects that discontinued due to AEs during the treatment period was similar for both the mirtazapine and SSRIs/SNRI treatment group (11.1% vs. 10.9%). The adverse events most frequently reported as the primary cause for discontinuation were similar for both the mirtazapine and the SSRIs/SNRI treated patients (fatigue, dizziness, headache, dry mouth, nausea, insomnia, and somnolence).
Conclusion: The results of these analyses show that there are differences in side effects between mirtazapine and the SSRIs/SNRI, as expected, based on the difference in the mechanism of action. However, no difference in overall tolerability was shown, thus proving that mirtazapine has a good tolerability profile.

References:
NR480  Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Sexual Side Effects of Antipsychotic Medications in Schizophrenia
Supported by Bristol-Myers Squibb Company
Mark Olfsen, M.D., Department of Psychiatry, Columbia University, 1051 Riverside Drive, Box 24, New York, NY 10032; Eskinder Tafesse, Ph.D., William Carson, M.D., Steven Connolly, B.A., Christopher Guardino, B.A.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the frequency and pattern of sexual dysfunction associated with haloperidol, olanzapine, and risperidone.

Summary:
Background: Although sexual side-effects have been reported in relation to antipsychotic medications, little information exists concerning their frequency and extent.

Methods: A systematic sample of male outpatients with schizophrenia or schizoaffective disorder, aged 18 to 70, not on medications with known sexual side effects, treated with antipsychotic monotherapy (haloperidol, olanzapine, or risperidone) for at least six weeks are being assessed with the Changes in Sexual Function Questionnaire (CSFQ). A significant decrease in sexual activity was also frequently reported by patients treated with risperidone (56.3%), olanzapine (50.0%), and haloperidol (40.0%). Erectile problems (haloperidol [60.0%], risperidone [43.8%], olanzapine [40.0%]) as well as ejaculatory difficulties (haloperidol [64.3%], risperidone [42.5%], olanzapine [40.0%]) were also common. Several of the patients reporting sexual dysfunction thought that their antipsychotic medications caused one or more of their sexual problems (haloperidol [50.0%], olanzapine [22.2%], risperidone [21.4%]).

Conclusions: Sexual dysfunction is common in male patients with schizophrenia treated with haloperidol, olanzapine, or risperidone. Psychiatrists should routinely monitor male patients with schizophrenia who are receiving these medications for sexual side-effects.

References:

NR482  Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Quetiapine Adjunctive Therapy for Acute Mania Associated With Bipolar Disorder (SIAM)
Supported by AstraZeneca Pharmaceuticals
Jamie Mullen, M.D., U.S. Drug Dev, AstraZeneca, 1800 Concord Pike, Box 15437, Wilmington, DE 19850-5437; Nancy Devine, M.S., Dennis Sweitzer, M.D.

Educational Objectives:
At the conclusion of this session, the participant should (1) recognize that quetiapine is effective, safe, and well tolerated as add-on therapy for the treatment of acute mania associated with bipolar disorder, and (2) make more informed decisions regarding the use of quetiapine in patients with bipolar disorder.

Summary:
Objective: Evaluate the efficacy and safety of quetiapine as adjunct therapy to mood stabilizer (MS) (Lithium [Li] or divalproex [DVP]) in the treatment of acute mania.

Method: 191 patients (bipolar I disorder, manic episode) were randomized to 21 days double-blind treatment with quetiapine (QTP) (up to 800 mg/d) or placebo (PBO) and either Li or DVP (target trough serum concentrations 0.7–1.0 mEq/L and 50–100 μg/mL, respectively). Primary endpoint: change from baseline YMRS total score at Day 21 (QTP+MS vs PBO+MS; MITT, LOCF).

Results: Of the 191 patients (61.5%) randomized to QTP+MS and 49 of 100 (49.0%) randomized to PBO+MS completed the study. By final assessment, QTP+MS-treated patients had a significantly greater reduction in YMRS compared with PBO+MS (13.76 and –9.93; P<0.021). Significantly more quetiapine-treated patients achieved a response (≥50% decrease from baseline YMRS score)
NR483 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Previous Episode Burden and Response to Treatment in Bipolar I Disorder
Supported by GlaxoSmithKline

Mark A. Frye, M.D., Department of Psychiatry, University of California at Los Angeles, 300 UCLA Medical Plaza, Suite 1544, Los Angeles, CA 90095; Terence A. Ketter, M.D., Joseph F. Goldberg, M.D., Zoran Antonijevic, Ph.D., Joseph R. Calabrese, M.D.

Educational Objectives:
At the conclusion of this session, the participant will be able to discuss the impact of number and type of previous mood episodes on the effectiveness of maintenance treatments for bipolar I disorder.

Summary:
Objective: We examined the relationship between previous mood episode burden and response to lithium and lamotrigine in bipolar I patients enrolled in two large prophylaxis trials.

Methods: 638 patients were randomized to 18 months of double-blind monotherapy with lamotrigine (n=280; 50–400mg/day fixed and flexible dose), lithium (n=167; 0.8–1.1mEq), or placebo (n=191). The relationship between the number of mood episodes (manic + depressive, manic only, depressive only) in the three years prior to study entry and response to lithium or lamotrigine was examined using Kaplan-Meier estimates of time to intervention for a mood episode after six months of treatment. Hazard ratios were calculated using Cox proportional hazards model.

Results: Lithium (HR=0.597, 95% CI 0.445, 0.801) and lamotrigine (HR=0.645, 95% CI 0.495, 0.839) were effective regardless of episode burden. However, risk of intervention was generally highest for patients with more previous depressive episodes and lowest for fewer previous depressive episodes.

Conclusion: Burden of previous depressive, but not manic, episodes may be a predictor of outcome for bipolar I patients on mood stabilizer treatment.

References:
1. AC Swann, CL Bowden, JR Calabrese, SC Dilsaver, DD Morris: Differential effect of number of previous episodes of affective disorder on response to lithium or divalproex in acute mania. JAMA 2002; 288: 701-709.

NR484 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Sertraline Treatment for Depression Post ACS Reduces Total Treatment Costs
Supported by Pfizer Inc.

Christopher O’Connor, M.D., Department of Cardiology, Duke University Medical Center, Box 3356, Durham, NC 27710; Alexander H. Glassman, M.D., Louis T. van Zyl, M.D., David Harrison, M.A., Peter A. Shapiro, M.D., Robert Morlock

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the increased risk of morbidity and mortality associated with depression post ACS and the impact of appropriate antidepressant treatment on the rate of medical and psychiatric hospitalization, revascularization procedures, and reduction in total treatment costs.

Summary:
Background: Patients with major depression after hospitalization for acute coronary syndromes (ACS) are at a three–four fold increased risk of cardiovascular (CV) events. SADHART demonstrated the safety and efficacy of sertraline in patients with major depression following hospitalization for myocardial infarction or unstable angina. The purpose of this analysis was to compare the costs of major CV events, revascularization procedures, and psychiatric hospitalizations in the sertraline and placebo groups in the SADHART trial.

Methods: Hospitalization rates for cardiovascular events, revascularization procedures, and psychiatric hospitalizations were determined from serious adverse event reports and CEC records from the SADHART trial. Healthcare costs associated with these events were derived from the 2002 Medicare DRG schedule for inpatient hospitalizations.

Results: There were significantly fewer hospitalizations and revascularization procedures in the sertraline treated group compared with placebo (55 vs. 74; p=0.037), resulting in a lower average cost per patient. After including the cost of 6-months of treatment with sertraline, there was a net cost savings of over $350 per patient.

Conclusion: Treatment of depression with sertraline in patients recently hospitalized for ACS resulted in a significant reduction in cardiovascular and psychiatric hospitalizations and a net cost savings.

References:

NR485 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
The Internal Validity of Two Commonly Used Depression Rating Scales
Supported by Pfizer Inc.

Rasmus W. Licht, M.D., Mood Disorder Clinic, Psychiatric Hospital A, Skovagervej 2, Risskov 8240, Denmark; Susanne Qvitza, M.D., Peter Allerup, Ph.D., Per Bech, M.D.

Educational Objectives:
After the presentation, the participants should recognize that summing up individual item scores on a rating scale requires the fulfillment of specific criteria of unidimensionality. Also it should be recognized that such criteria are not fulfilled for the Hamilton Depression Scale, whereas they are fulfilled for The Bech-Rafaelsen Melancholia Scale.

Summary:
Introduction: Evaluation of antidepressants requires adequate rating scales for measuring the severity of depression. To reflect the illness severity by a total score, the scale must fulfill essential criteria of construct validity (or unidimensionality). This is the background for comparing the unidimensionality of the Bech-Rafaelsen Melancholia Scale (MES) and the 17-item Hamilton Depression Rating Scale (HAM-D17).
Methods: 1,629 patients with major depression were included and treated openly with a fixed oral dose of 50 mg sertraline daily for 4 weeks. The HAM-D17 and the MES were applied at baseline and at week 2 and 4. Unidimensionality was tested with Mokken and Rasch analysis.

Results: For the HAM-D17, the Loevinger coefficient of homogeneity (Mokken analysis) was below 0.30, even after four weeks. Furthermore, by the Rasch analysis, the HAM-D17 was neither accepted at baseline nor after two or four weeks of therapy (p<0.01). However, the six-item Hamilton Depression Subscale (HAM-D6), was accepted by the Rasch analysis both at baseline and after two and four weeks of therapy. In the Rasch analysis of the MES, two of the MES items caused problems. However, for the MES (as well as for the HAM-D6), a Loevinger coefficient of homogeneity above 0.40 (suggesting acceptance) was found at week 4.

Conclusion: The HAM-D6 and the MES did fulfill criteria for unidimensionality while the HAM-D17 did not. Therefore, the extended use of the HAM-D17 in drug trials may be questioned.

Funded by Pfizer Denmark

References:

NR486 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Escitalopram is Effective and Well-Tolerated in the Treatment of Severe Depression
Supported by Forest Laboratories, Inc., and Integrated Therapeutics, Inc.
Philip T. Ninan, M.D., Department of Psychiatry, Emory University, 1841 Clifton Road, 4th Floor, Atlanta, GA 30329; Daniel Ventura, Ph.D., Jin Wang, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the effect of escitalopram in the treatment of severe depression.

Summary:
Introduction: Escitalopram is the most selective SSRI antidepressant, and has been shown to be more effective than citalopram in the treatment of severe major depression.

Objectives: To determine prospectively the effect of escitalopram in the treatment of severe depression.

Methods: Patients with severe major depression (mean baseline 24-item HAMD = 30) were randomly assigned to eight weeks of double-blind treatment with 10-20 mg/day escitalopram (N = 147) or placebo (N = 153). Efficacy assessments included MADRS (primary efficacy measure), HAMD, and CGI. Response was prospectively defined in three ways: 50% decrease in MADRS, 50% decrease in HAMD, or CGI-I ≤ 2.

Results: Overall, 82% of patients completed the trial. For LOCF analyses, escitalopram treatment led to significant (p < 0.05) improvement versus placebo by week 2 in HAMD scores, and by week 4 in MADRS and CGI-I scores; statistically significant improvement compared with placebo was maintained at all subsequent visits. Approximately half of escitalopram treated patients (49-52%) at endpoint (LOCF) were responders, according to each definition, and these rates were significantly superior to placebo treatment (30-38%; p < 0.05). Incidence of adverse events was similar to those reported previously for escitalopram treatment. Discontinuation rates due to adverse events were low (6% escitalopram, 0 placebo).

Discussion: Escitalopram treatment is an effective and well tolerated treatment of severe major depression.

References:

NR487 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
R-Citalopram Attenuates Escitalopram in a Rat-Stress Model of Depression
Supported by H. Lundbeck A/S
Mariusz Papp, Ph.D., Department of Pharmacology, Institute of Polish Academy of Science, 12 Smetna Street, Krakow 31-343, Poland; Connie Sanchez, D.Sc.

Educational Objectives:
At the conclusion of this session, the participant should be able to appreciate that escitalopram more effective and with an earlier effect than citalopram due to an attenuating effect of R-citalopram.

Summary:
Introduction: Escitalopram is the most selective serotonin reuptake inhibitor in clinical use. We have previously reported that escitalopram has a more rapid effect than the citalopram racemate in a rat chronic mild stress (CMS) model of depression.

Objectives: To study the effect of escitalopram, citalopram, R-citalopram, and escitalopram plus R-citalopram in the CMS model.

Methods: The CMS model consists of sequential exposure of rats to a variety of mild stressors for a prolonged period. This results in behavioural hedonic deficits, measured as decreased consumption of a 1% sucrose solution. Prolonged antidepressant treatment (weeks) will gradually reverse the deficit. Doses (i.p. once a day) are expressed as mg/kg base.

Results: Escitalopram (3.9) significantly increased the CMS-induced reduction in sucrose intake compared to vehicle controls already from week 1. Citalopram (8.0) produced a significant increase in sucrose intake from week 2, although this increase was significantly lower than for escitalopram at the same time point. R-citalopram alone (7.8) and escitalopram (3.9) plus R-citalopram (7.8) did not differ significantly from vehicle-treated controls.

Conclusion: The present study shows that R-citalopram attenuates the effect of escitalopram in the rat CMS model of depression.

References:
Depression in Persons With Epilepsy and Associated Findings From the Epilepsy Impact Project
Supported by GlaxoSmithKline

Alan M. Ettinger, M.D., EEG Lab, Long Island Medical Center, 270-05 76th Avenue, New Hyde Park, NY 11040; Andres M. Kanner, M.D., Robert P. Kustra, Ph.D., Michael L. Reed, Ph.D.

Summary:
Objective: To assess disease related burden of depression among persons with epilepsy (PWE), asthma, and no chronic ailments (NoProb) in a general population sample.

Methods: 3,278 subjects from a general population epidemiologic study were mailed a follow-up survey containing: Mood Disorder Questionnaire (MDQ) and questions about depression symptoms and consulting; QOLIE/SF-36, Adverse Events Profile (AEP), Social Concerns Index (SCI) and questions about seizure severity and impact. Results were post-weighted to match U.S. demography and adjusted to control for demographic differences between groups.

Results: Survey response rate was 41% (775 PWE, 395 asthma and 341 NoProb). Ever consulting for depression was reported among 31% of PWE, 22% of asthma and 7% of NoProb groups (p<.001). CESD diagnostic threshold for major/moderate depression was reached in 37% of PWE, 28% of asthma and 8% of NoProb (p<.001). Among PWE who also reported depression, there was greater disease burden versus those with no depression, on AEP, SCI and overall quality of life, as well as seizure recency, severity, emotional effect, and physical effect (p<.01 for all).

Conclusions: Depression is more common among PWE versus asthma or NoProb and depression in PWE is associated with greater disease burden, seizure activity and impact.

The Use of Olanzapine in the Treatment of Delirium Among ICU Patients

Paul W. Ragan, M.D., Department of Psychiatry, Vanderbilt University, 1161 21st Avenue, Nashville, TN 37232; James C. Jackson, Psy.D., Sharon M. Gordon, Psy.D., E.W. Ely, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the complex issues involved in the pharmacological treatment of delirium among ICU patients. Additionally, he/she should recognize the potential role of atypical antipsychotics in the treatment of delirium and the need for future research.

Summary:
Introduction/Hypothesis: Delirium is extremely prevalent among mechanically ventilated ICU patients and has been associated with increased mortality, prolonged hospitalization, behavioral disturbances, and cognitive decline. The risks and benefits of atypical anti-psychotic medication should be explored to expand the treatment armamentarium of delirium in ventilated ICU patients.

Methods: A retrospective chart review of 8 patients treated for delirium at the Vanderbilt University MICU was conducted by a psychiatrist, intensivist, and psychologist. All patients were treated with olanzapine and had been assessed for delirium at least once daily.

Results: Four patients experienced resolution of delirium following treatment with olanzapine, while symptoms persisted in the remaining 4. In 3 patients, however, delirium resolution coincided temporally with the termination of benzodiazepines. The frequent use of large doses of benzodiazepines, opioids, and typical antipsychotics occurred in our sample.

Conclusions/Discussion: Olanzapine may be useful in the treatment of delirium among ICU patients but its' efficacy is difficult to discern due to the confounders that characterize critically ill populations—e.g. treatment with copious amounts of deliriogenic medication, complex medical presentations, and advanced age. Randomized controlled trials are necessary to determine the medication most appropriate in the treatment of delirious ICU patients.

References:

Improvement in Fatigue With Venlafaxine in Patients With Depression
Supported by Wyeth Research

Rajiv Mallick, Ph.D., Research, Wyeth, 500 Arcola Road, Collegeville, PA 19426; Huabin F. Zhang, M.D., George J. Wan, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that major depressive disorder is characterized by emotional and physical symptoms including fatigue; describe how effective antidepressant therapy that boosts noradrenergic or dopaminergic neurotransmission may enable improvement in physical symptoms like fatigue independent of improvement in emotional symptoms.

Summary:
Objectives: To evaluate improvement in fatigue with venlafaxine/venlafaxine extended-release (XR), selective serotonin reuptake inhibitors (SSRIs [fluoxetine, paroxetine, fluvoxamine]) or placebo.

Methods: Data from seven randomized, double-blind, SSRI-controlled, six to eight-week long trials of venlafaxine/venlafaxine XR in patients with depression (overall ITT = 1,712; 742 venlafaxine/venlafaxine XR, 639 SSRIs, 331 placebo) were retrospectively pooled and analyzed. The lassitude item on the Montgomery-Asberg Depression Rating Scale (MADRS) measured fatigue. Baseline severity and improvement on the lassitude item and total MADRS score were evaluated.

Results: At baseline, the median score on the 0–6 Likert-scaled lassitude item was 4, indicative of “difficulties in starting simple routine activities...” Approximately 13% of patients had a score of 5 or 6 indicating almost “complete lassitude.” Venlafaxine/venlafaxine XR was associated with significantly greater improvement on the lassitude item and total MADRS scores over placebo (both P<0.0001) and over SSRIs (both P<0.0002). A statistically similar, albeit numerically smaller, effect was observed for the pooled SSRIs versus placebo.

Conclusions: Given evidence that monoamine neurotransmitters are implicated in fatigue, it is not unexpected that venlafaxine/venlafaxine XR, given its dual effects on serotonin-norepinephrine neurotransmission, and, to a lesser extent, SSRIs were associated with significant improvement on the lassitude item of the MADRS.

References:
Extended Release Carbamazepine in Bipolar Disorder: A Six-Month Open Trial

Supported by Shire Pharmaceutical Development Inc.

Mark B. Hamner, M.D., Department of Psychiatry, Medical University of South Carolina VAMC, 109 Bee Street, # 116A, Charleston, SC 29401; Terence A. Ketter, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to discuss the efficacy and safety of extended-release carbamazepine (CBZ-ERC; Carbaltrol) in the prevention of relapse and recurrence over six months in patients with bipolar disorders after manic or mixed episodes.

Summary:

Objective: Carbamazepine is a commonly prescribed therapy for bipolar disorder (BD), but few large trials have assessed its use as a maintenance therapy. We studied the efficacy and tolerability of long-term, open, extended-release carbamazepine (CBZ-ERC, Carbaltrol) in BD patients.

Methods: A total of 92 BD patients (most recent episode: 67% mixed, 33% manic) who had participated in a three-week, double-blind, placebo-controlled study received open CBZ-ERC (mean blood CBZ concentration at endpoint 6.6 ± 4.25 μg/mL) for six months. The primary efficacy variable was time to relapse. Secondary efficacy variables included the Young Mania Rating Scale (YMRS), and Clinical Global Impression Scale (CGI).

Results: Of 77 patients in the intent-to-treat sample, 11 (14.3%) relapsed during the study. The estimated mean time to relapse (Kaplan-Meier model) was 141.8 ± 5.6 days. Patients previously treated with placebo showed significant improvements in YMRS and CGI scores and patients previously treated with CBZ-ERC maintained improvements. There were no serious AEs or change in mean weight (−0.4% at endpoint, +0.7% in completers). The most common AEs were headache, dizziness and rash.

Conclusion: CBZ-ERC appeared effective in bipolar disorder patients for up to 6 months of continuation treatment. AEs were generally mild to moderate and typical of those associated with carbamazepine.

References:


Hippocampal FGF2 and FGFR1 in Depression, Schizophrenia, and Bipolar Disorder

Stanley Foundation

Fiona P. Gaughan, M.D., Instituto de Psychiatry - London, Ladywell Unit, Lewisham Hospital, London SE13 6LW, United Kingdom; Joachim Payne, Ph.D., Philip Sedgwick, Ph.D., David Cotter, Ph.D., Martin Berry

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the differences between depressed patients and controls in the expression of FGF2 and its receptor.

Summary:

Objectives: Basic fibroblast growth factor (FGF2) mediates trophic activity in dopaminergic neurons. It also regulates neuroglial serotonin transporter gene expression.

Subjects: Post-mortem brains of patients with schizophrenia, major depression, bipolar disorder and controls.

Methods: FGF2 and FGF receptor (FGFR1) mRNA was measured within hippocampal CA1, CA4 and the dentate gyrus (DG), using in-situ hybridisation. We also performed double labeling immunohistochemistry for FGFR1 protein and the 5-HT transporter, and for FGFR1 and the DA transporter.

Statistics: Within hippocampal regions, cellular staining was compared between diagnostic groups, using repeated measures analysis of variance.

Results: The density of FGF2 mRNA+ cells in CA4 differed between groups (depression 185cells/mm²; controls 185cells/mm², P = 0.01). The percentage of FGFR1 mRNA+ cells was higher in depression (CA1 29.4%, CA4 31.5%) and schizophrenia (23.45%; 27.2%) than in controls (17.5%; 19.8%)(P=0.03). FGFR1 mRNA expression was lower in depression than in other groups (p=0.04). FGF2 mRNA expression was lower in DG than in CA1 & CA4 (adjusted means = 113.2, 134, 130.3 respectively) (P=0.01). The percentage of DA or 5HT neurons positive for FGFR1 did not differ between diagnostic groups.

Conclusions: There are alterations in expression of FGF2 and FGFR1 mRNA in major depression and less so, in schizophrenia.

References:


Noise Intolerance and Major Depression

Marie-Josee Filteau, M.D., Clinique Marie Fitzbaech, 1085 de la Tour, Quebec, QC G1R 2W8, Canada; Patricia Gravel, B.A., Jacinthe LeBlanc, D.P.H., Marie-France Demers, M.S.C.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize noise intolerance as a possible risk factor for depression.

Summary:

A frequent but overlooked symptom in major depression is patients' subjective increased noise sensitivity.

Methods: This prospective study included 49 patients with unipolar major depression, 23 with and 26 without noise intolerance, as defined by two or more of the following symptoms: greater irritability to noise, need to decrease noise, active avoidance of noise. Assessments performed at baseline and at six months included disease severity (Clinical Global Impression (CGI); Hamilton Depression Scale-17 (HAM-D-17)) and noise intolerance evaluations.

Results: Both groups were comparable on age (mean age 46.27 ± 10.19 years) and depression severity (mean CGI-S score 4.2 ± 0.68; mean HAMD-17 score 22.53 ± 2.96). At six months, 16/23 patients with phonophobia experienced remission (HAM-D-17 score ≤ 7) compared with 18/26 patients without noise intolerance (p=NS). Out of the 16 remitted patients with noise intolerance, six had still this symptom at six months. Five of them had been treated with selective serotonin reuptake inhibitors, while the remitted
patients who no longer had noise intolerance, interestingly, had all been treated with dual uptake antidepressants.

Conclusion: Noise intolerance is a distinct symptom of unipolar major depression, which might predict a more complete response to dual uptake antidepressants.

References:

NR494 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Mirtazapine Orally Disintegrating Tablet Versus Sertraline: Factor Analysis of Onset of Therapeutic Effect
Supported by Organon Inc.
Estelle D. Vester-Blokland, M.D., Global Marketing, Organon International Inc., 56 Livingston Avenue, Roseland, NJ 07068; Silvia Van Der Flier, Ph.D., Albert J. Schutte, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to (1) describe the design and methods of this meta-analysis comparing mirtazapine with several SSRIs and a SNRI, (2) discuss the results of this pooled analysis and its implications for the clinical use of mirtazapine with respect to onset of therapeutic effect.

Summary:
Objective: The efficiency of antidepressants is seriously impaired by the delay in onset of their therapeutic action. This is the first prospective trial comparing mirtazapine's efficacy and onset of action with that of sertraline.
Method: Subjects with a major depressive episode were treated with either mirtazapine orally disintegrating tablet or sertraline for eight weeks. Inter-treatment differences in the onset of antidepressant action in the first week of treatment were assessed as of day 4. Change from baseline (HAM-D-17), responder rates (≥ 50% reduction on HAM-D-17), and remitter rates (HAM-D ≤ 7) were analyzed. Furthermore, the antidepressant response on the Bech depression factor, HAMD Factor 1, Factor 5, and Factor 6 was evaluated for the first two weeks of treatment.
Results: A statistically significant advantage in the mean change in total HAM-D score from baseline (p<0.05) in favor of mirtazapine was shown at days 4, 7, 10, and 14. The difference in responder rates was in favor of mirtazapine at all assessments except day 42. At all assessments, higher percentages of patients were classified as HAMD remitters in the mirtazapine group. The change from baseline on the HAMD Bech depression factor showed no significant difference between both treatments. An advantage for mirtazapine over sertraline was shown for Factor 1 at day 4 and day 10 of treatment (p<0.05). No significant difference between mirtazapine and sertraline was found for Factor 5. Factor 6 was found to be significantly lower for mirtazapine at all assessments.
Conclusion: These results endorse the faster onset of action of treatment with mirtazapine orally disintegrating tablets as compared with SSRIs treatment. In this study the fast onset of action of mirtazapine is mainly reflected in its anxiolytic and sleep improving properties.

References:

NR495 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Sexual Function of Patients With Major Depression Treated With Mirtazapine Orally Disintegrating Tablet or Sertraline
Supported by Organon Inc.
Estelle D. Vester-Blokland, M.D., Global Marketing, Organon International Inc., 56 Livingston Avenue, Roseland, NJ 07068; Silvia Van Der Flier, Ph.D., Rapid Study Group

Educational Objectives:
At the conclusion of this session, the participant should be able to (1) describe the design and methods of this double-blind study comparing mirtazapine orally disintegrating tablet and sertraline in subjects with a major depression.
Methods: Subjects with a major depressive episode (according to DSM-IV criteria) were treated with either mirtazapine 30–45 mg/day or sertraline 50–150 mg/day. Subjects between 18–70 years with a minimum score of at least 18 on the 17-item HAMD scale were included. Sexual functioning was assessed, according to gender, at baseline, and week 2, 4, 6, and 8 using the Changes in Sexual Functioning Questionnaire (CSFQ). ITT, and LOCF. Previously defined risk factors for sexual dysfunction were explored.
Results: The ITT group consisted of 339 patients (mirtazapine: n=171; sertraline: n=169). Mean daily doses were 38.3 mg for mirtazapine and 92.7 mg for sertraline. For female and male patients, the total CSFQ score at baseline was 38.2 and 46.9 in the mirtazapine treated group and 37.9 and 45.9 in the sertraline treated group. After eight weeks of treatment, the total scores for mirtazapine-treated females (41.4) and males (48.8) were in the normal range (≥41 for females, ≥47 for males), whereas the total scores of sertraline-treated females (39.5) and males (46.2) were below the normal range.
Conclusion: These results provide evidence that treatment with mirtazapine improves sexual function in patients with major depression in contrast to sertraline.

References:

NR496 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Early-Onset and Course Profiles of Major Depression After Cognitive-Behavior Therapy
Jackie K. Gollan, Ph.D., Department of Psychiatry, University of Chicago, 5841 S Maryland Avenue NC3077, Chicago, IL 60637; Brian Raffety, Ph.D., Keith Dobson

Educational Objectives:
At the conclusion of this session, the participant should be able to elucidate risk factors of poor course of depression after successful CBT.

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Summary:

Objective: New research is needed to examine how clinical characteristics (e.g., early onset of depression, severity of index episode) influence the risk, timing, and duration of relapse among recovered patients. Such analyses will increase our understanding about patterns of relapse among recovered adult depressed outpatients.

Method: The experimental approach was evaluating 78 recovered patients from a RCT examining the efficacy of CBT for depression (Jacobson et al., 1996). A standardized definition of recovery was used (Frank et al., 1991). Subjects completed five follow-up assessments of psychiatric status during the 2 year follow-up.

Results: Profile analyses revealed the following: (1) higher severity of index depression predicted higher risk of relapse, (2) age of onset for first depression was associated with timing of relapse, and (3) age of onset for first depression was associated with different levels of residual depression during the 24-month follow-up period. Depression before age 20 was linked with a stable course profile of residual symptoms after response to treatment.

Conclusions: Findings suggest that early onset depression and later onset depression are associated with distinguishably different course trajectories. Such work is directly relevant to prevention strategies.

References:

NR497 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Symptomatological Differences and Overlaps Between Depression and Bereavement

Kitty Kiss, Department of Psychiatry, Number 13, National Institute of Psychiatry, Budapest 27 PF 1 1281, Hungary, Zoltan Rihmer, M.D., Erika Szadoczky, M.D., Sandor Rozsa, Janos Furedi, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that some symptoms and prior history of panic disorder as well as suicide attempt can help in the separation of bereavement and depression.

Summary:

Objective: The aim of our study was to compare the frequency of depressive symptoms in major depressive episode and grief-reaction with a structured and internationally accepted questionnaire in the Hungarian adult population.

Methods: Randomly selected subjects (2793 females and 1951 males) were interviewed by the Hungarian version of the Diagnostic Interview Schedule (DIS) which generated DSM-III-R diagnoses.

Results: Thoughts of death were significantly more frequent in grief-reaction, while hypersomnia, feeling of guilt and worthlessness, low self-esteem, suicidal ideas and attempted suicide, as well as history of comorbid panic disorder were significantly more common in depression.

Conclusions: Our findings suggest that in spite of great overlap in the symptomatology between grief-reaction and major depression, some symptoms (e.g., hypersomnia, guilt, worthlessness) and prior history of panic disorder as well as suicide attempt can help in the separation of the two conditions.

References:

NR498 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Economic Burden of Not Recognizing Bipolar Disorder Patients
Supported by Eli Lilly and Company

Howard G. Birnbaum, Ph.D., Analysis Group/Econ, 111 Huntington Avenue, 10th Floor, Boston, MA 02199; Ellison Dial, B.S., Emily F. Oster, B.A., Paul E. Greenberg, M.A., Liheng Shi, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the attendee should be able to recognize that it is important to know the prevalence, treatment patterns, and costs of unrecognized, recognized, and induced BP in the AD-treated MDD population.

Summary:

Objective: We compared treatment patterns and costs for bipolar disorder (BP) patients (recognized and unrecognized) with major depression (MDD) patients without a BP claim (non-BP) during the observational period.

Methods: An employer claims database (1998–2001) was used to identify 9,099 patients (aged 18–65) diagnosed with MDD and initially treated with antidepressants (AD). Of these, unrecognized BP (UBP) patients received initial BP diagnosis and/or mood stabilizer (MS) prescription after AD initiation, whereas recognized BP (RBP) patients had these records on/before AD initiation. Induced BP patients were defined as those manifesting mania within six months after starting AD.

Results: BP patients accounted for 7.0% of the research sample (3.7% UBP and 3.3% RBP). Induced BP represented 7.5% of all BP patients. RBP patients had a slightly lower rate of mania induction (3.4%) than UBP patients (4.2%). UBP patients incurred significantly more total monthly medical costs in the 12 months following AD initiation than RBP patients ($1179 versus $801, respectively); total monthly medical costs ($585) for non-BP patients were significantly lower than for both RBP and UBP patients.

Conclusions: Bipolar patients were associated with worse outcomes than MDD patients. Recognition of BP disorder lowers medical costs.

References:

NR499 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Depression, Panic Disorder, and Smoking

Zoltan Rihmer, M.D., Department of Psychiatry, XIII, National Institute of Psychiatry, Huvosvolgyi Ut 116, Budapest 1021, Hungary; Peter Mandi, M.D., Peter Pestalilly, M.D., Peter
Dome, M.D., Istvan Kecskes, M.D., H. Gergely Kiss, M.D., Nora Belso, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the current and lifetime prevalence of smoking is more prevalent in patients with major mood disorders than in the general population.

Summary:
Objective: The aim of this study was to analyze the smoking habits among remitted outpatients with bipolar disorder, unipolar major depression, and panic disorder.

Method: The smoking habits of 41 bipolar patients (12 bipolar I and 29 bipolar II), 30 unipolar major depressives and 61 panic disorder patients were assessed by a structured interview.

Results: The rate of current smoking among the bipolar, unipolar, and panic disorder patients were 56%, 43% and 31% respectively, while the same figure in the general population of Hungary was 35% (bipolars vs control: chi-square=5.35, p=0.05). The lifetime history of smoking in the three patient groups were 66 percent, 66% and 50% respectively and the same rate in the general population of Hungary was 44% (bipolars vs control: chi-square=5.55, p=0.05, unipolars vs controls: chi-square=4.74, p=0.05).

Conclusion: The findings support previous results on the strong relationship between major mood disorders (particularly bipolar illness) and smoking, but this connection needs further investigations.

References:

NR500 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Effectiveness of Mirtazapine in the Treatment of Major Depression With Somatic Symptoms: An Open Trial
Supported by Organon Pharmaceuticals Inc./Akzo Nobel
Javier Garcia-Campayo, M.D., Department of Psychiatry, Miguel Servet Hospital, Isabel La Catolica 1, Zaragoza 50009, Spain; Pilar Martinez, M.D., Jose M. De Pedro, M.D., Marta Aloa, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the usefulness of mirtazapine in the treatment of major depression with somatic symptoms.

Summary:
Aim: To assess the effectiveness of mirtazapine in the treatment of major depression with somatic symptoms.

Method: A multicenter, observational, prospective, open, and non-controlled study. The participants were 711 patients from 100 outpatient psychiatric clinics in Spain. The patients were followed up over three months with visits at baseline, 15, 30, and 90 days.

Measures: Hamilton Rating Scale for Depression (HRSD) and Standardized Polyvalent Psychiatric Interview, an interview widely used on somatization that allows DSM-IV diagnosis.

Results: The total HRSD score decreased from 23.2 at baseline to 6.7 at 90 days. At three months, 84.5% of the patients had decreased in 50% or more the baseline HRSD. The number of somatic symptoms decreased from 7.6 at baseline to 2.2 at 90 days. Seventy and disability of somatic symptoms improved at 90 days. All the different groups of somatic symptoms (gastrointestinal, pain, conversion, sexual, and cardiological) decreased from baseline to the three months consultation.

Discussion: This is the first study that assess the effectiveness of mirtazapine on the treatment of functional somatic symptoms of depression. Mirtazapine demonstrated high effectiveness and tolerability/security in the treatment of depressive patients with functional somatic symptoms.

References:

NR501 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Tiagabine for MDD With Anxiety
Supported by Cephalon, Inc.
Linda L. Carpenter, M.D., Department of Psychiatry, Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI 02906; Audrey R. Tyra, M.D., Jordan M. Schecter, B.S., Ryan Haggarty, B.A., Lawrence H. Price, M.D.

Educational Objectives:
At the conclusion of this session, the participant should appreciate the therapeutic potential of tiagabine for treatment of major depressive disorder comorbid with significant anxiety.

Summary:
Introduction: Gamma-aminobutyric acid (GABA) plays a key role in the pathophysiology and treatment of depression and anxiety. Tiagabine, a selective GABA reuptake inhibitor (SGRI), which enhances normal GABA tone, was assessed for depression comorbid with significant anxiety.

Methods: In this eight-week, single-center, open-label study, adults with major depressive disorder and significant anxiety received tiagabine 4 mg/day (dosed bid, am/pm) during week 1. Tiagabine was individually titrated for optimum response as tolerated to maximum dose 20 mg/day. Assessments included the Hamilton Rating Scale for Depression (HAM-D28), the Inventory for Depressive Symptoms, Self-Report (IDS-SR), and the Hamilton Rating Scale for Anxiety (HAM-A).

Results: Twelve patients (7 male, 5 female) began a trial of study medication and eight completed eight weeks of treatment; enrollment is ongoing. Tiagabine significantly reduced depression, as shown by a reduction in mean HAM-D±SEM scores from baseline (31.2±1.9) to endpoint (15.8±4.7; P<0.01). Self-report depression scores similarly dropped (IDS-SR baseline 67.2±20.5 vs. endpoint, 49.8±4.6, p<0.0001). Categorical response rate was 50% (n=6 of 12). Tiagabine also significantly improved anxiety (HAM-A: baseline, 21.8±1.4 vs endpoint, 11.6±2.6; P<0.01). Mean daily dose was 10 mg (12 mg/d for completers). Most commonly reported AEs were headache (n=4), dizziness (n=4), and sedation (n=3).

Conclusion: These results suggest the potential of the SGRI tiagabine in the treatment of depression with anxiety.

References:
NR502 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Utilization and Cost of Atypical Antipsychotics in Medicaid Patients With Depression
Supported by Janssen Pharmaceutical Products, L.P.
Jeffrey Markowitz, Ph.D., Health Data Analytics, 35 Arnold Drive, Princeton Junction, NJ 08550; Dennis M. Meletiche, Pharm.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the differences in cost of mental health services in Medicaid patients with depression treated with risperidone or olanzapine as augmentation to antidepressants.

Summary:
Objective: To quantify differences in resource utilization and health care cost between olanzapine and risperidone when used as augmentation agents in patients with depression.
Methods: We conducted a retrospective analysis using the California Medicaid database (Medi-Cal 1996-2000). Adult patients aged 18 to 65 with one year of continuous enrollment and one or more medical claims for depression were included in the analysis. Patients with schizophrenia or psychotic depression were excluded. Treatment groups consisted of patients who received augmentation with risperidone or olanzapine after completing at least four weeks of antidepressant treatment. Cost comparisons were made using the amount paid by Medi-Cal to providers over the six-month period following the initiation of antidepressant treatment.

Results: No statistically significant differences were observed with respect to length of treatment, use of antidepressants, or occurrence and number of outpatient and inpatient visits. Mean antipsychotic costs per month were significantly lower for risperidone (N=130) and olanzapine (N=130) groups compared to placebo (N=350) group. The mean antipsychotic cost for risperidone was $154.31 and for olanzapine was $258.13, with p<0.0001. A significantly higher proportion of risperidone subjects (62.9%) vs. 39.2% for olanzapine) achieved remission (YMRS <8) with risperidone than with olanzapine (chisq=39.5; p<0.0001). The remission rate was higher for risperidone/MS than placebo/MS by all three criteria: YMRS <12; 57.1% risperidone/MS and 32.6% placebo/MS; YMRS <8: 46.9% risperidone/MS and 23.9% placebo/MS; and YMRS and HAM-D both <8: 28.6% risperidone/MS and 10.9% placebo/MS. Ten-week open-label data showed high rates of remission with risperidone/MS by all criteria: YMRS <12: 73.5%; YMRS <8: 59.0%; and YMRS and HAM-D both <8: 33.7%.

Conclusion: Higher 3-week remission rates were seen with risperidone/MS than placebo/MS by standard and more stringent criteria. Continued treatment with risperidone/MS further increased these remission rates.

References:

NR504 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
In Vitro and In Vivo Effects of Citalopram Enantiomers on 5HT Transporter
Supported by H. Lundbeck A/S
Arne Mork, M.D., Department of Neurochemistry, Lundbeck A/S, Ottiliavej 9, Copenhagen-Valby, DK 2500, Denmark; Mads Kreilgaard, Ph.D., Connie Sanchez, D.Sc.

Educational Objectives:
At the conclusion of this session, the participant should appreciate that R-citalopram attenuates the 5-HT enhancing effect of escitalopram at 5-HT concentration, functional and behavioural levels in pre-clinical studies.

Summary:
Introduction: Escitalopram mediates the inhibition of the 5-HT transporter (SERT) by citalopram and presumably its antidepressant activity.

Objectives: To investigate in vitro and in vivo effects of citalopram, escitalopram, and R-citalopram on brain SERT.

Methods: Radioligand binding and uptake assays were used to assess in vitro interaction with SERT. Extracellular 5-HT and escitalopram levels were studied in frontal cortex of conscious rats by microdialysis. 5-HT and escitalopram concentrations in dialysates were measured by HPLC-EC and LC-MS-MS. Functional consequences of increased 5-HT levels were measured as serum corticosterone levels and behavioural correlates were assessed as potentiation of 5-hydroxytryptophan (5-HTP)-induced behavioural changes. Results: R-citalopram attenuated the effect of escitalopram. The 5-HT concentration increased more with escitalopram than citalopram, while R-citalopram was inactive. Moreover, R-citalopram reduced the response to escitalopram. The escitalopram concentration in frontal cortex was unaffected by concomitant administration of R-citalopram, ruling out a pharmacokinetic interaction between escitalopram and R-citalopram. R-citalopram also...
attenuated escitalopram-induced increases of serum corticosterone and potentiation of 5-HTP-induced behavioral changes.

**Conclusions:** R-escitalopram attenuates the 5-HT enhancing effects of escitalopram and indicates an improved efficacy of escitalopram compared with citalopram.

**References:**


**NR505 Tuesday, May 20, 3:00 p.m.-5:00 p.m.**

**Prevalence of the Metabolic Syndrome in Hispanic Patients With Mood Disorder: A Pilot Study**

Martha M. Kato, M.D., Department of Psychiatry, University of Miami, 1400 N.W. 10th Avenue, Suite 304A, Miami, FL 33136; Jorge L. Sotelo, M.D., Giselle Ferreira, M.D., Christina M. de Guia, M.D., Ana C. Perez, M.D., Ronny Valenzuela, M.D., M. Beatriz Currier, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to diagnose the metabolic syndrome in patients with mood disorders.

**Summary:**

**Aim:** The Third Report of the National Cholesterol Education Program Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (ATP III) highlights the importance of treating patients with metabolic syndrome to prevent cardiovascular disease. In this pilot study we determine the prevalence of metabolic syndrome in Hispanic patients with mood disorders.

**Method:** Cross-sectional study of 11 female and five male patients recruited from an outpatient psychiatric clinic. Psychiatric diagnoses were based on DSM-IV criteria. Metabolic syndrome was defined by the ATP III criteria.

**Results:** The prevalence of the metabolic syndrome was 75% in Hispanic patients with mood disorder. The mean age was 55.00 ± 10.10 years for patients with metabolic syndrome and it did not differ significantly from patients without metabolic syndrome (46.25 ± 11.70). Seventy-five percent of the patients with metabolic syndrome were female and 100% were white. In patients with metabolic syndrome, 94% had abnormal waist circumference, 69% had abnormal high density lipoprotein, 67% had increased triglycerides, 63% had hypertension, and 25% had abnormal glucose.

**Conclusion:** In this pilot study, the prevalence of metabolic syndrome in Hispanic patients with mood disorder is 75%. This is far greater than the 22% prevalence reported in the general population and the 32% prevalence reported in Mexican Americans. Data suggest that Hispanic patients with mood disorders may be at an increased risk to develop metabolic syndrome which is a predictor of cardiovascular disease and type 2 diabetes. Given that patients with chronic mental disorders often fail to receive adequate medical care, early identification of metabolic syndrome may provide primary prevention of cardiovascular disease and type 2 diabetes. Further prospective studies are needed to corroborate our findings.

**References:**


**NR506 Tuesday, May 20, 3:00 p.m.-5:00 p.m.**

**Citalopram Treatment of Dysthymic Disorder Supported by Forest Laboratories, Inc.**

David J. Hellerstein, M.D., Department of Psychiatry, New York State Psychiatric Institute, 1051 Riverside Drive, Unit 101, New York, NY 10032; Sarai Batchelder, Ph.D., Ruben A. Miozzo, M.D., David Kredit, M.D., Steven E. Hyler, M.D., Dinu Ganguire, M.D., Joy A. Clark, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to describe the efficacy and tolerability of citalopram in the treatment of dysthymic disorder, based on the results of this study.

**Summary:**

**Background:** Our aim was to provide preliminary data on the tolerability and effectiveness of citalopram for patients with dysthyemic disorder (DD).

**Method:** Twenty-one adult subjects meeting DSM-IV criteria for DD were enrolled in this 12-week, open-label study. Citalopram was initiated at 20 mg/day, and increased to a maximum of 60 mg/day. Response was defined as 50% or greater drop in score on the Hamilton Depression Rating Scale (HDRS) and a CGI-I score of 1 (very much improved) or 2 (much improved).

**Results:** Of these 21 subjects, 14 (66.7%) were treatment responders. All paired sample t-tests were highly significant, demonstrating significant average improvement on all measures of symptomatology and functioning. Scores on the 24-item HDRS decreased from 23.4±4.7 at baseline to 8.8±6.8 at Week 12 (t(19)= 8.1, p<.001). The average final dose was 39 mg/day. One subject dropped out during the trial. Side effects were reported by 15 of 21 subjects (71.4%), most frequently GI symptoms (n=8), dry mouth (n=5), and sexual side effects (n=4).

**Conclusion:** These findings, similar to those of Dunner et al., suggest the effectiveness and high tolerability of citalopram in treating dysthymic disorder. Double-blind, prospective studies are needed comparing citalopram both to placebo and to other medications, assessing both initial and sustained response to treatment.

**References:**


**NR507 Tuesday, May 20, 3:00 p.m.-5:00 p.m.**

**Combination of Topiramate in Acute Mania**

Bo-Hyun Yoon, M.D., NAJU National Hospital, Sanje Sampo, Naju Jeonnam S20-830, Korea; Seung-Oh Bae, M.D., Jin-Sang Yoon, M.D., Myung-Kyu Kim, M.D., Young-Wha Sea, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to treat the acute manic patients with appropriately designed combination regimen.
Summary:

Objectives: The rapid therapeutic action of mood stabilizers is critical to the initial management of acute mania, because it enables to minimize the psychological sequelae of the patients commonly occurring in post manic episodes and to increase the compliance to the medications. The aim of this study was to evaluate the efficacy and safety of topiramate as the combination regimen in the treatment of acute mania.

Methods: Twenty manic patients were selected through various screening tests. Ten patients were randomly assigned to valproate alone and the other ten patients to the combination of topiramate and valproate. Antipsychotics were not allowed and benzodiazepines were available as needed. Young Mania Rating Scale (YMRS) and Clinical Global Impression severity of illness scores (CGI-S) were used to evaluated the improvement of manic symptoms at pre-drug baseline and at 1st, 2nd, 4th and 8th week of post-drug. UKU side-effect rating scales were done for assessment of drug-induced side effects. Additionally, body weights were checked at weekly basis to monitor the weight change. Repeated measures ANOVA was done to compare the effects between two groups.

Results: YMRS of topiramate combination group were significantly decreased than those of valproate alone group. These effects were especially significant at 1st, 2nd week after treatment in post hoc analysis. There were no marked differences in side effects. There were significant decreases of weight in topiramate combination group whereas the increases of weight in valproate alone group.

Conclusion: The results suggest that the combination of topiramate may be the effective and safe treatment in acute mania and can be the good choice in manic patients with weight problem.

References:

NR508 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Topiramate as Adjunctive Therapy to Mood Stabilizers in Patients With Bipolar I or II Disorder Supported by Janssen-Ortho, Inc.
Vivek Kusumakar, M.D., Department of Research, Johnson & Johnson, 1125 Trenton-Harbourton Road, Titusville, NJ 08550-0000; Roger S. McIntyre, M.D., Carin Binder, M.B.A., Rosanna Riccardelli, B.S.C.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the efficacy and safety of adjunctive topiramate in the treatment of persons with bipolar I/II disorder not adequately managed with current mood stabilizing therapy.

Summary:
Objective: Evaluate safety/efficacy of adjunctive topiramate (TPM) to mood stabilizers (MS) in Bipolar I/II patients experiencing chronic mood instability.
Method: 109 outpatients (manic=39, hypomaniac=18, mixed=42, depressed=56) with DSM-IV bipolar I/II, insufficiently managed with current MS, (CGI-S >= 4 & a YMRS >= 13 or MADRS >= 12), received open-label TPM for up to 16 wks, (25-400 mg/day) as add-on to MS (lithium, valproate or combination). MS and any concomitant psychotropics had to remain stable for ≥4 wks pre-entry.
Results: Mean modal dose of TPM = 145.0 mg (SD=91.8). TPM + MS achieved statistically significant improvements in YMRS & MADRS scores from wk 2 of treatment with hypomanic/depressed sub-groups = p<0.05 from wk 4 on YMRS, mixed group = p<0.001 from wk 2. Mixed & depressed sub-groups = p<0.001 on MADRS at wk 2. Significant improvement also noted in CGI-S (p<0.001). Commonly reported AEs were headache (28%), nausea (22%), diarrhea (15%), fatigue (13%), somnolence (13%). Mean change in body weight for all patients at endpoint was = 1.8 kg. No clinically significant changes were observed in vital signs or laboratory parameters at endpoint.
Conclusion: Adjunctive TPM to MS is safe and effective in treating persons with bipolar disorder.

References:


NR510 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Long-Term Use of Olanzapine or Olanzapine/Fluoxetine for Bipolar Depression Supported by Eli Lilly and Company

Mauricio F. Tohen, M.D., Department of Research, Eli Lilly and Company, One Lilly Corporate Center, Indianapolis, IN 46285; Terence A. Ketter, M.D., L. Joseph R. Calabrese, M.D., Scott W. Andersen, M.S., Holland C. Detke, Ph.D., Richard C. Rissler, M.S., Sara A. Corya, M.D.

Educational Objectives:

At the conclusion of this presentation, the attendee should be able to discuss the efficacy of olanzapine and olanzapine/fluoxetine combination in maintenance treatment of bipolar depression and will have information regarding the use of MADRS and YMRS scores in treatment decisions.

Summary:

Background: Olanzapine/fluoxetine combination (OFC) has shown efficacy in treating bipolar depression. Present analyses examined six-month maintenance data for subjects who achieved remission of depressive symptoms following acute treatment.

Methods: A total of 377 subjects with bipolar depression completed eight weeks of randomized, double-blind treatment using olanzapine (OLZ, n=179), placebo (n=145), or OFC (n=55). Of these, 192 were in remission (MADRS ≤12) upon entering open-label treatment, at which time they were switched from their acute-phase treatment to 5–20 mg/day open-label OLZ. After one week on OLZ, subjects could be switched to OFC as needed. Primary efficacy measure was the Montgomery-Åsberg Depression Rating Scale (MADRS). Manic symptoms were monitored using the Young Mania Rating Scale (YMRS). Time to relapse (MADRS > 15) was estimated using Kaplan-Meier survival analysis.

Results: Of the 192 remitters, 120 (62.5%) remained free from relapse over the six-month open-label period. For the 72 subjects (37.5%) who relapsed, median time to relapse was 194 days. Mean MADRS total score at open-label endpoint was 7.93 (SD 9.24, n=192) using a last-observation carried-forward (LOCF) methodology.

Conclusion: This open-label study suggests that OLZ and OFC may represent treatment options in the long-term management of bipolar depression. Further studies are necessary to replicate these findings using appropriate controls and double-blind methodology.

References:


NR511 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Mood Changes Related to Antidepressants in Patients With Bipolar Disorder

Michael Bauer, M.D., Department of Psychiatry, Charité University Hospital, Humboldt University Schumannstr 20121, Berlin 10117, Germany; Natalie L. Rasgon, M.D., Paul Grof, M.D., Laszlo Gyulai, M.D., Tasha Glenn, Peter C. Whybrow, M.D.

Educational Objectives:

At the conclusion of this presentation, the attendee should know more about the influence of antidepressants on mood changes in bipolar disorder.

Summary:

Objective: With the risk for antidepressants to induce mania or cycling unclear, mood patterns in patients with bipolar disorder taking or not taking antidepressants were compared.

Method: A total of 80 patients entered data daily for three months into self-reporting software. Data from 47 patients taking antidepressants (5,119 days) and 33 not taking antidepressants (3,543 days) were analyzed by group and individual. There were no statistically significant demographic differences between groups.

Results: For all days, patients taking antidepressants were depressed 29% of days, normal for 65.1% and manic for 6.0%. Patients not taking antidepressants were depressed 13.8% of days, normal for 76.0%, and manic for 10.2% (p<0.01). In both groups, two thirds of all mood changes for a lag of one to three days were small, between –5 to 5 on a 100-point scale. Switches between depression and mania were rare with no statistical difference in frequency (0.7% not taking antidepressants vs. 0.9% taking antidepressants). There was no statistical difference in frequency of large mood changes (>10 on a 100-point scale).

Conclusions: The primary difference was the time spent depressed or normal. Patients taking antidepressants were depressed twice as often and appear to have a downshift in baseline mood. From their respective baselines, the frequency and size of mood changes was similar in both groups.

References:


NR512 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Relation Between Number of Medications and Self-Reported Mood in Bipolar Disorder

Michael Bauer, M.D., Department of Psychiatry, Charité University Hospital, Humboldt University Schumannstr 20121, Berlin 10117, Germany; Paul Grof, M.D., Natalie L. Rasgon, M.D., Laszlo Gyulai, M.D., Tasha Glenn, Peter C. Whybrow, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should know more about the relation between the number of daily medications and self-reported mood in bipolar disorder.

Summary:

Objective: Since polypharmacy is a common approach for treating patients with bipolar disorder (BP), the relation between the daily number of medications and self-reported mood was investigated.

Method: Eighty patients (35 men and 45 women) with a diagnosis of BP I or II entered their mood, sleep, and medications daily for three months into software (ChronoRecord) on a home computer. A total of 8,662 days of data was received (mean 114.7 days).

Results: A total of 79 patients took a mean of 3.8 ± 1.7 medications daily (range 1–9); one patient took none. Patients reporting
normal mood more frequently took fewer medications. Those normal >90% of days (n=16) took a mean 2.06 medications, those normal 75% and <= 90% (n=16) took a mean 3.83 medications, those normal >50% and <=75% (n=19) took a mean 3.84 medications, those normal >25% and <=50% (n=11) took a mean 4.56 medications, and those normal <=25% (n=16) took a mean 5.0 medications. The correlation coefficient between the number of medications taken and the percent of days normal was −0.481 (p<.001). Grouping by number of medications, ANOVA analysis also showed those taking fewer medications were normal more frequently (p<.001).

Conclusions: Controlled long-term outcome studies of combination treatment regimens are suggested.

References:

NR513  Tuesday, May 20, 3:00 p.m.-5:00 p.m.
An Illustration of How a Self-Report Diagnostic Screening Scale Could Improve the Internal Validity of Antidepressant Efficacy Trials
Mark Zimmerman, M.D., Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905; Iwona Chelminski, Ph.D., Michael A. Posternak, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to describe possible problems with the internal validity of antidepressant efficacy trials and how a self-report scale could help in detecting problems.

Summary:
Background: Variable competence and quality of diagnostic raters in antidepressant efficacy trials (AETs) introduces error variance in the data collected, and this error variance may contribute to the difficulty in detecting differences in outcome between active medication and placebo. During the past 20 years semi-structured diagnostic interviews have become the standard for diagnostic evaluations in psychiatric research; however, only a minority of AETs employ these interviews. This might be important insofar as several studies have found that clinicians conducting unstructured clinical interviews underrate differences in diagnostic comorbidity. Because of the financial incentives to recruit patients into AETs quickly, there is little incentive to vigorously determine the presence of comorbid conditions that should result in exclusion from the trial. We demonstrate how a self-report diagnostic screening scale could be used to identify systematic differences in diagnostic practice across research settings, and how such a scale could be used to compare samples of patients who pass screening evaluations and are accepted into an AET.

Methods: Depressed patients drawn from the same clinical practice completed the Psychiatric Diagnostic Screening Questionnaire (PDSQ), and were evaluated with either an unstructured clinical interview or with the Structured Clinical Interview for DSM-IV (SCID).

Results: The two samples were clinically comparable based on their scores on the self-administered PDSQ. However, consistent with the greater thoroughness of the SCID interview, compared with unstructured diagnostic evaluations more patients administered the SCID were diagnosed with comorbid conditions. After excluding patients with disorders that might be the basis for exclusion from an AET, the two samples then differed in their scores on the PDSQ. That is, more patients in the sample evaluated by an unstructured interview had "occult" pathology than patients evaluated with the SCID.

Conclusion: These findings demonstrate how systematic differences in diagnostic practice might be detected across sites when conducting AETs.

References:

NR514  Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Analysis of Gepirone Extended Release on the Bech-6 and Individual Ham-D Item Scores
Supported by Organon Pharmaceuticals Inc.
Michael Gibertini, Ph.D., Organon Inc., 375 Mt. Pleasant Avenue, West Orange, NJ 07052; John H. Simmons, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to (1) Assess and treat the core symptoms of depression utilizing the Bech-6 and individual items of the Ham-D-17; (2) discuss the clinical evidence supporting the efficacy of gepirone-ER for major depression.

Summary:
Objective: To evaluate the effect of the 5HT1A agonist gepirone-ER on core depressive symptoms of depression as measured by the Bech-6 and individual Ham-D-17 items.

Methods: This eight-week, double-blind, placebo-controlled study of gepirone-ER was conducted in patients aged 18–70 who met DSM-IV criteria for major depressive disorder. Patients were randomized to placebo or gepirone-ER, which was initiated at 20 mg/d for 3 days, increased to 40mg/d with titration to 80mg/d per investigators’ discretion. Participants were evaluated at baseline and weeks 1, 2, 3, 4, 6, and endpoint, week 8.

Results: In 204 patients, gepirone-ER produced a statistically significant difference compared to placebo for the mean change in Ham-D-17 total score at weeks 3 and 8. Further analysis revealed that gepirone-ER caused a statistically significant decrease from baseline on the Bech-6 at all study visits compared with placebo. Statistically significant improvements were also found between baseline and endpoint visits in the following Ham-D-17 items: depressed mood, work and activity, genital symptoms, psychic anxiety, and psychic retardation. The most commonly reported adverse events were dizziness, headache, and nausea.

Conclusion: The Bech-6 and individual Ham-D-17 item scores showed statistically significant improvement compared to placebo, which, when taken together, lend support to gepirone-ER’s efficacy in the treatment of major depressive disorder. Further, the Bech-6 was shown to be more sensitive to the effect of gepirone-ER than was the Ham-D-17.

Funded by Organon Inc.

References:
NR515 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Mania Remission Rates in a Randomized-Controlled Trial of Risperidone
Supported by Johnson & Johnson Pharmaceutical Research & Development

Srihari Gopal, M.D., Johnson & Johnson Pharmaceutical Research & D, 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Michelle L. Kramer, M.D., Maren K. Olsen, Ph.D., David C. Steffens, M.D.

Educational Objectives:

At the end of this presentation, the participant should be able to differentiate between risperidone and placebo remission rates in bipolar mania.

Summary:

Objective: The purpose of this analysis was to compare remission rates of mania between risperidone and placebo in a randomized controlled trial.

Method: Two hundred ninety (290) adult patients who met DSM-IV criteria for bipolar I disorder, manic or mixed episode were randomized to flexible doses of risperidone (1 mg-6 mg daily) or placebo for up to three weeks. An entry YMRS score of ≥20 was required at trial screening and baseline. Time to first onset of remission (as defined as a YMRS score of ≤8) was assessed using Cox proportional hazards. Presence or absence of sustained remission was analyzed using logistic regression. Sustained remission was defined as maintaining a YMRS ≤8 for the remainder of the trial or until censor.

Results: Forty-one percent (41.7%) of patients on risperidone and 6.2% of patients on placebo achieved remission by the third week. The unadjusted odds of sustained remission for subjects on risperidone was 5.0 (95% Cl: 2.8, 9.1; χ² = 31.4, P < 0.0001). The unadjusted hazard of remission for subjects on risperidone was 5.0 (95% Cl: 2.8, 9.1; χ² = 31.4, P < 0.0001).

Conclusions: Risperidone was superior to placebo in achieving remission of bipolar mania.

References:

NR517 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Investigation of Fluoxetine and Testosterone, Apathy Ratings and Testosterone

Dwight S. Bell, M.D., 150 North Santa Anita Avenue, Suite 300, Arcadia, CA 91006-3113; Mark Shipman, M.D., Alexander Bystritsky, M.D.

Summary:

Objective: Two published case studies reported SRI/SNRI-associated low testosterone levels. Apathy and low testosterone, observed during venlafaxine treatment in one report, both resolved upon venlafaxine discontinuation. No studies have investigated the effect of chronic SRI treatment on human testosterone levels.

As decreased testosterone has several negative health effects, we conducted a pilot study investigating the effect of fluoxetine treatment on testosterone levels.

Methods: 15 depressive disorder patients in good health (BDI ≥15) were studied. In addition, four non-depressed patients were studied. Testosterone levels were drawn, and an apathy questionnaire (under development, not yet validated) was administered at intake. Fluoxetine was provided (10 mg/day for 7 days then 20 mg/day). To measure outcome, a follow-up testosterone level was drawn after one month's treatment.

Results: 11 depressed, and three non-depressed, patients completed the study; some patient's testosterone levels increased up to 105%, others decreased up to 39%. There was no relationship (depressed patients, p=0.4; non-depressed patients, p=0.3) between fluoxetine treatment and testosterone levels.

Conclusions: Further, larger, studies correlating changes in testosterone levels during SRI treatment with changes in apathy levels and possibly sexual dysfunction seem indicated.

NR516 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
5-HT1A Receptor Binding in Bipolar Patients Using PET With 11CWAY-100635
Supported by AstraZeneca Pharmaceuticals

Peter A. Sargent, M.D., Department of Psychiatry, Warneford Hospital, Warneford Lane, Oxford OX3 7JX, United Kingdom; Eugenie A. Rabiner, M.D., Guy M. Goodwin, D.Phil., Paul M. Grasby, M.D.

Summary:

Objective: The 5-HT1A receptor has a pivotal action in control of mood. This study was undertaken to examine whether 5-HT1A receptor binding was reduced in euthymic bipolar patients, as has previously been found in both unipolar and bipolar depressed patients.

Method: Eight medicated euthymic bipolar patients and 8 healthy volunteer subjects underwent positron emission tomography scanning using the selective 5-HT1A receptor radiotracer [11C]WAY-100635. Regional and global postsynaptic values for Binding Potential (BP) and were obtained from parametric BP images using a template of regions of interest.

Results: No difference in global BP was found between medicated euthymic patients (mean ± SEM, 4.26 ± 0.23) and healthy volunteers (mean ± SEM, 4.34 ± 0.21) on unpaired t-test (P = 0.85). Similarly, there were no significant differences in mean BP for any region of interest.

Conclusions: In contrast to previous findings of markedly reduced 5-HT1A receptor binding in untreated unipolar and bipolar depressed patients, this study found no difference in 5-HT1A receptor binding in medicated euthymic bipolar patients. Normal 5-HT1A receptor binding in these patients could occur either as a result of drug treatment or could indicate that reduced 5-HT1A receptor binding occurs only in the depressed state in bipolar patients.

Summary:

NR518 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Family Therapy and Family Functioning in Patients With Mood Disorders

Gabor I. Keitner, M.D., Department of Psychiatry, Rhode Island Hospital, 593 Eddy Street, Providence, RI 02903; Christine E. Ryan, Ph.D., David A. Solomon, M.D., Joan E. Kelley, Ivan W. Miller, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize the value of adjunctive family interventions in the treatment of mood disorders.
Summary:

Objective: We examined the impact of adjunctive family therapy on the functioning of families of patients with major depression and with bipolar disorders.

Method: Data are presented from two treatment studies: (1) 92 patients with bipolar disorder were randomly assigned to three treatment conditions: pharmacotherapy alone (PT), PT + family therapy; PT + multifamily psychoeducational group therapy, and (2) 121 depressed inpatients were randomly assigned to follow-up care in four treatment conditions: medication + clinical management (MCM); cognitive therapy (CT) + MCM; family therapy (FT) + MCM; and CT + FT + MCM. Family therapy and subjective and objective measures of family functioning were based on the McMaster Model of Family Functioning.

Results: Bipolar patients with poor family functioning at index episode significantly improved their family functioning in all but one dimension by month 28. Even patients with good family functioning at index episode significantly improved their family functioning in three dimensions. Improvement in family functioning was not related to symptom reduction ($\chi^2(1)=.191,NS$) whether measured by a priori (Bech-Rafaelsen and Hamilton Depression Rating) or post hoc (median split) definitions. Improvement was related to receiving family treatment. Depressed patients with poor family functioning significantly improved their family functioning by six months and were able to sustain the improvement through 18 months. Patients with good family functioning also improved by six months but then lost some of the gains. Improvement in family functioning was not related to improvement in symptoms ($t(86.0)=1.10,NS$) based on a 50% reduction in Hamilton Depression Rating Scores. Improvement in family functioning (by number of family dimensions that improved significantly and by level of significance) was related to receiving family treatment. Depressed patients with poor family functioning significantly improved their family functioning by six months and were able to sustain the improvement through 18 months. Patients with good family functioning also improved by six months but then lost some of the gains. Improvement in family functioning was not related to improvement in symptoms ($t(86.0)=1.10,NS$) based on a 50% reduction in Hamilton Depression Rating Scores. Improvement in family functioning (by number of family dimensions that improved significantly and by level of significance) was related to receiving family therapy.

Conclusions: Despite improvement in mood symptoms, pharmacotherapy alone does not lead to improvement in family functioning in patients with mood disorders. Adjunctive psychosocial (especially family) interventions were related to significant improvement in family functioning, particularly in families experiencing the greatest distress.

References:

NR519 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Retrospective Chart Review on the Use of Oxcarbazepine in Patients With Bipolar Disorder Supported by Novartis Pharmaceuticals Corporation

Dennis E. Platt, M.D., Psychiatric Department, Tallahassee Memorial Hospital, 1457 M.D. Lane, Suite A, Tallahassee, FL 32306; Faisal A. Munasifi, M.D., L.M. McKay, R.N.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize a new powerful agent for the treatment of bipolar affective disorder.

Summary:
Rationale: Oxcarbazepine is related to carbamazepine, a recognized therapeutic agent in the treatment of bipolar illness. Oxcarbazepine possesses similar efficacy with an improved safety profile. Oxcarbazepine may have mood-stabilizing effects in patients with bipolar disorder.

Methods: A retrospective chart review of patients with bipolar disorder who receive oxcarbazepine was conducted. Oxcarbazepine total daily dose ranged from 75mg to 2400mg/day as monotherapy and adjunctive therapy. The mood-stabilizing effects of oxcarbazepine were evaluated using Hamilton and Ziegler scores.

Results: Data from 146 charts were collected. The mean age was 33 years. (range: 5–74) and mean final dose was 739mg/day (range: 75–2400mg/day). Forty-three patients received oxcarbazepine as monotherapy and 103 patients as adjunctive therapy. Hamilton scores were available for 88 patients and mean scores decreased from 16.6 (range: 5–36) pre-oxcarbazepine to 7.5 (range: 0–23) post-oxcarbazepine. Ziegler scores were available for 46 patients and mean scores decreased from 27.1 (range: 9–40) pre-oxcarbazepine to 3.8 (range: 0–17) post-oxcarbazepine. A total of 42 (29%) patients discontinued oxcarbazepine; 22 (14%) due to adverse events, 22 (14%) due to inadequate response, and two (1%) for other reasons.

Conclusion: The data from this study suggest that oxcarbazepine may be useful in the treatment of bipolar disorder.

References:

NR520 Tuesday, May 20, 3:00 p.m.-5:00 p.m.
Influence of Gender on Clinical Course in Bipolar Disorder

Natalie L. Rasgon, M.D., Department of Psychiatry, Stanford University, 401 Quarry Rd, Room 2360, Palo Alto, CA 94305-5722; Michael Bauer, M.D., Paul Grof, M.D., Laszlo Gyulai, M.D., Tasha Glenn, Peter C. Whybrow, M.D.

Educational Objectives:
At the conclusion of this session, the participant should know more about differences in the clinical course of bipolar disorder in men and women.

Summary:
Objective: The clinical course of men and women with bipolar disorder (BD) was compared.

Methods: 80 patients with BD (I or II) recorded mood, sleep, and medications daily for three months into self-reporting software (ChronoRecord) on a home computer. Women also recorded menstrual data. 3,483 days of data from 35 men and 5,179 days of data from 45 women were analyzed by group and by individual.

Results: For all days, men were depressed 15.9% of the time, normal 79.6%, and manic 4.5%; women were depressed 24.8%, normal 67% and manic 8.2%. Women reported severe symptoms of depression about twice as often as males (17.1% vs 10.9%) and severe symptoms of mania about five times as often (18.7% vs 3.2%). Large mood fluctuations were rare for both men and women; however more women than men (33.0% vs 17.2%) experienced large mood fluctuations (greater than 20 on a 100-point scale). 65% of women had significant mood changes across the menstrual cycle.

Conclusions: Women were depressed more frequently, reported more severe symptoms, and had large mood changes about twice as often as men. Women also experienced mood changes across the menstrual cycle.

References:
Objective: To compare direct long-term effects of aripiprazole and haloperidol on the control of negative symptoms associated with schizophrenia.

Method: Changes in PANSS negative subscale scores were examined over the course of a 52-week, multicenter, double-blind clinical trial, which randomized patients with acute relapse of chronic schizophrenia to aripiprazole 30 mg/d (n=861) or haloperidol 10 mg/d (n=433). The direct effect on negative symptoms was estimated using a path analysis approach, by controlling for the effect on positive symptoms, depressive symptoms, and EPS.

Results: The overall mean reduction in PANSS negative score was significantly greater among patients treated with aripiprazole than among those treated with haloperidol (−5.7 vs −3.59, P=0.011). The direct effect on negative symptoms was also greater in the aripiprazole group than in the haloperidol group (P=0.033). Among patients with more pronounced negative symptoms (PANSS negative >24), the mean changes in PANSS negative score from baseline were −6.97 in the aripiprazole group and −5.25 in the haloperidol group (P=0.005). The reduction in negative symptoms following stabilization of acute symptoms was also greater with aripiprazole than with haloperidol (P=0.02).

NR523 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Long-Term Effects of Aripiprazole on the Negative Symptoms of Schizophrenia
Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co, Ltd.
George Manos, Ph.D., Bristol-Myers Squibb, 5 Research Parkway, Wallingford, CT 06492; Elyse G. Stock, M.D., Darlene Jody, M.D., Donald G. Archibald, M.Phil., Stavros Tourkodimitris, Ph.D., Ronald N. Marcus, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to compare the long-term effects of aripiprazole and haloperidol on the control of negative symptoms associated with schizophrenia.

Summary:
Introduction: Previous studies have found that depressive symptoms are often present in the prodromal phase of schizophrenia. We hypothesized that male adolescents diagnosed as suffering from major affective disorder (MAD) at age 17 would be at increased risk for later schizophrenia.

Method: Results of the medical and mental health assessments on 828,342, 16–17 year old male adolescents screened by the Israeli draft board were cross-linked with the national psychiatric hospitalization case registry, which contains data on all psychiatric hospitalizations in the country, enabling a 1–22 year follow-up.

Results: The prevalence of MAD in the population was 0.3%.

Having a diagnosis of MAD increased the risk of later hospitalization for schizophrenia, RR=10.0, chi square=231.78, P<0.001. The risk for schizophrenia in adolescents with MAD was greatest at age 18–19, and decreased gradually with the increase in age.

Discussion: In males, having a diagnosis of MAD in adolescence greatly increases risk for schizophrenia. These adolescents should be followed closely, to enable early intervention for those who begin to suffer from the symptoms of schizophrenia.

References:

NR522 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Affective Disorders in Adolescence Increase Risk of Later Schizophrenia
Gad Lubin, M.D., Department of Mental Health, IDF, PO Box 1476, Shoham 73142, Israel; Mark Weiser, M.D., Ross Yazvitsky, B.A., Avi Reichenberg, Ph.D., Naama Haron, B.A., Haim Knobler, M.D., Daniela Nahon, M.S.C.

Educational Objectives:
At the conclusion of this session, the participant should recognize that depressive symptoms in adolescents may be a precursor of later schizophrenia.
Conclusion: Aripiprazole was significantly more effective than haloperidol for reduction in negative symptoms during long-term therapy of patients with schizophrenia.

References:

NR524 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Rivastigmine Tartrate for the Treatment of Cognitive Impairments and Negative Symptoms in Schizophrenia
Michael J. Reinstein, M.D., Department of Psychiatric Research, Forest Foundation, 4755 North Kenmore Avenue, Chicago, IL 60640; John G. Sonnenberg, Ph.D., Sangarapillai C. Mohan, M.D., Maxim A. Chasanov, M.D., Shephali A. Patel, M.D., Rad Gharavi, M.D.

Educational Objectives:
At the conclusion of this session, the participant should enhance his/her understanding of negative symptoms and cognitive impairments in schizophrenia, emphasizing the discrete and separate nature of the symptoms. The importance of treating cognitive and negative symptoms, and the potential usefulness of cholinergic enhancing therapies, is presented.

Summary:
Introduction: The negative symptoms of schizophrenia often include cognitive deficits and, like Alzheimer's Disease, are associated with fronto lobe deficits in cholinergic activity. Rivastigmine tartrate, an Alzheimer's therapy that enhances cholinergic activity in the frontal cortex, may decrease symptom acuity by countering cognitive deficits and/or the negative symptoms of schizophrenia.

Methods: Twenty schizophrenic subjects (12M/8F; mean age 53.1, SD 6.6, range 41–63) showing long-standing cognitive impairments not associated with a known dementia were treated with Rivastigmine. At baseline, subjects received the CGI-Severity scale, MMSE, and PANSS. The CGI Improvement scale, MMSE, and PANSS were repeated at four weeks. The PANSS was tallied for the BPRS and the Negative Symptom Subscale.

Findings: At baseline, the mean CGI-Severity score was 4.6 (SD=0.9), indicating subjects were typically assessed in a range from moderately to markedly ill. At four weeks, the mean CGI Improvement score was 1.4 (SD=0.5), falling between much and very much improved. The mean MMSE score rose from 21.2 (SD=4.4) to 24.6 (SD=3.0), indicating a 15% increase from baseline. The mean PANSS score decreased from 64.7 (SD=7.6) to 51.6 (SD=6.4), indicating a 20% reduction. The mean Negative Symptom score decreased from 30.4 (SD=5.7) to 22.15 (SD=4.2), indicating a 27% reduction.

Discussion: Rivastigmine appeared useful in treating cognitive and negative symptoms associated with schizophrenia. Alzheimer's medications of the cholinesterase inhibitor class may warrant further consideration for the treatment of cognitive impairments and negative symptoms within the schizophrenic population.

References:

NR525 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Ziprasidone Versus Risperidone in Schizophrenia: 52 Weeks of Comparative Data
Supported by Pfizer Inc.
Donald E. Addington, M.D., Department of Psychiatry, University of Calgary, 1403 29th Street, NW, Calgary, AB T2N 279, Canada; Christos Pantelis, M.B., Mary Dineen, M.D., Isma Bernattia, M.D., Steven J. Romano, M.D., Stephen R. Murray, M.D.

Educational Objectives:
At the conclusion of this presentation, participants should be able to discuss the findings of the reported 8-week randomized, double-blind trial and subsequent 44-week, double-blind continuation study comparing the efficacy and tolerability of ziprasidone and risperidone in patients with schizophrenia or schizoaffective disorder.

Summary:
Objective: To compare the efficacy and tolerability of ziprasidone 40–80 mg BID and risperidone 3–5 mg BID in acute exacerbation of schizophrenia or schizoaffective disorder.

Methods: In an eight-week, randomized, double-blind trial, primary efficacy evaluations were PANSS Total and CGI-S scores; secondary variables included PANSS Negative Subscale score, BPRS Total and Core scores, and Global Assessment of Functioning (GAF). Primary efficacy analyses were based on evaluable patients (≥14 days of treatment). Completers could enter a 44-week, double-blind continuation study.

Results: On the basis of a predetermined equivalency criterion, evaluable ziprasidone (n=124) and risperidone (n=132) patients demonstrated equivalent efficacy improvements in primary and secondary measurements. Ziprasidone had a significantly lower mean Movement Disorder Burden Score (MDBS) and lower incidences of prolactin elevation and weight gain ≥7%. In the 44-week continuation, ziprasidone (n=59) and risperidone (n=76) groups exhibited comparable, sustained improvement in efficacy variables from baseline of the eight-week study. MDBS and incidences of prolactin elevation and weight gain ≥7% remained lower with ziprasidone.

Conclusion: Patients receiving 52 weeks of double-blind ziprasidone or risperidone demonstrated comparable symptom improvement; patients on ziprasidone had a lower movement disorder burden and lower incidences of prolactin elevation and clinically significant weight gain.

References:

NR526 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Drug Abuse in First-Episode Nonaffective Psychosis
Supported by the Norwegian National Research Council
Tor K. Larsen, M.D., Rogaland Psychiatric Institute, Armaker Hansensv20, P O Box 1163, Stavanger 4011, Norway; Svein Fris, M.D., Fan O. Fohannessen, M.D., Thomas H.
NR528  Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Core Symptom Remission in Patients With Schizophrenia Receiving Long-Acting Risperidone Supported by Janssen Pharmaceutica Products, L.P.
Robert Lasser, M.D., Janssen Pharmaceutica Products, L.P., 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200; Stephen Rodriguez, M.A., Cynthia Bossie, Ph.D., Georges Gharabawi, M.D., John M. Kane, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to assess the effects of long-acting risperidone on remission in patients with schizophrenia.

Summary:
Introduction: DSM-IV defines the essential features of schizophrenia as the presence and persistence of characteristic signs and symptoms. These include delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, and negative symptoms. The objective of this analysis was to assess the effect long-acting risperidone on these core disease features, exploring the concept of disease remission.

Method: Expert-defined essential disease features (via Positive and Negative Syndrome Scale) defined remission: delusions (P1) conceptual disorganization (P2), hallucinations (P3), suspiciousness (P6), blunted affect (N1), emotional withdrawal (N2), and conceptual disorganization (G9). Remission was defined as a score of ≤3 (mild or less) on each item for ≥2 consecutive visits. Data were derived from an open-label 50-week study of long-acting risperidone in stable patients with schizophrenia or schizoaffective disorder.

Results: Although patients were clinically stable at study entry, 397 did not meet remission criteria at baseline (≤3, each item). PANSS total scores decreased significantly for these patients (baseline 74.7, endpoint 64.1; p<0.0001). Of these patients, 144 (36.3%) met remission criteria during the study.

Conclusion: A substantial number of patients treated with long-acting risperidone reached the defined level of remission, supporting the need for further attention to the symptomatic and functional definition of remission in schizophrenia.

References:

NR529 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Lifestyle Program Reduces BMI for Inpatients on Atypical Antipsychotics
Supported by Eli Lilly and Company
Jack J. Kettler, M.D., Selkirk Mental Health Centre, Box 9600 825 Manitoba, Selkirk, MB R1A 237, Canada; Susan L. Holm, Ph.D., Roxie B. Eyer, R.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to treat weight gain that results from atypical antipsychotic use.

Summary:
Objective: To investigate the effectiveness of a diet change on the body mass index (BMI) of patients receiving clozapine and other atypical antipsychotics.

Method: A Healthy Lifestyle Program was initiated at the Selkirk Mental Health Centre, a 268-bed provincial psychiatric facility. A program-wide diet change was introduced, whereby a 2200 kcal diet, representing a 10% reduction in energy, was provided. BMIs of patients in an inpatient rehabilitation program were obtained by chart review for six months pre-, time of, and six months post-diet change. A total of 57 patients (male = 42, female = 15, M age = 42) on atypical antipsychotics (clozapine = 32, other atypical = 25) who had BMIs on chart were identified.

Results: BMI did not change from six months pre-diet change (M = 30.2) to time of diet change (M = 30.1; F < 1, ns). Six months post-diet change, BMI decreased significantly (M = 29.0; F < 1, ns). Six months post-diet change, BMI decreased significantly (M = 29.0; F < 1, ns). Six months post-diet change, BMI decreased significantly (M = 29.0; F < 1, ns). Six months post-diet change, BMI decreased significantly (M = 29.0; F < 1, ns).

Conclusion: This research demonstrates that with a diet change, weight reduction is possible for patients on clozapine or other atypicals.

References:

NR531 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Efficacy of IM Ziprasidone Without Adjunctive Benzodiazepines
Supported by Pfizer Inc.

NR530 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
A Comparison of the Efficacy and Safety of Quetiapine and Risperidone
Supported by AstraZeneca Pharmaceuticals, L.P.

References:

Summary:
Objectives: To compare the efficacy, safety, and tolerability of quetiapine and risperidone in patients with schizophrenia.

Methods: Multicenter, double-blind, randomized, eight-week noninferiority study in patients with schizophrenia flexibly dosed BID with quetiapine (200−800mg/day) or risperidone (2−8mg/day). Primary outcome was change from baseline on PANS total scores. Secondary outcomes were changes in PANS subscales, EPS, and safety.

Results: 328 patients were randomized to quetiapine and 320 to risperidone; mean daily doses were 480mg and 5.2mg, respectively. There were no statistical or clinically relevant differences between treatment groups on change from baseline to end-point in PANS total scores. Similar percentages of patients in each group (risperidone, 26.9%; quetiapine 26.5%) showed ≥30% reduction in PANS total. Approximately 40% of patients in each group were rated as "much" or "very much" improved. Adverse events (AEs) related to EPS were 12.7% for quetiapine and 21.9% for risperidone. Sexual side effects occurred more frequently with risperidone than with quetiapine. Changes in glucose, weight, and other vital signs were similar between groups.

Conclusions: Although quetiapine and risperidone were similarly efficacious in treating schizophrenia, risperidone-treated patients were more likely to experience EPS and sexual AEs than quetiapine-treated patients. Changes in weight and glucose were similar in both groups.

References:
S scores significantly improved with 20 mg ziprasidone (n=40) versus 2 mg ziprasidone (n=37) (P<0.001). Among patients in the three-day IM treatment phase trial who did not receive benzodiazepines, ziprasidone (n=262) produced significantly greater improvement in BPRS Total score (P<0.0002) than haloperidol (n=77). In this study, incidence and severity of adverse events in ziprasidone-treated patients receiving benzodiazepines (n=167) were comparable to those in patients not receiving benzodiazepines.

Conclusions: IM ziprasidone improved agitation and psychotic symptoms without benzodiazepines, but coadministration with benzodiazepines was well tolerated.

References:

NR532 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Orbitofrontal Cortex in Schizophrenia: A Pilot Study With the Gambling Task
Serge M. Sevy, M.D., Psychiatric Research Department, Zucker Hillside, 266th Avenue & 76th Avenue, Glen Oaks, NY 11004; Hema Visweswaraiah, B.A.; Marjorie McMeniman, Ph.D., Antoine Bechara, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to explore the orbitofrontal cortex in schizophrenia using a computerized version of the Gambling Task.

Summary:
Objective: The purpose of this pilot study is to investigate the orbitofrontal cortex in schizophrenia using a computerized version of the Gambling Task (GT; Bechara et al, 1994).
Methods: Subjects were ten outpatients with DSM-IV diagnosis of schizophrenia or schizoaffective disorder who participated in this study after signing an informed consent form. Patients were matched for age and sex with ten normal controls. The GT is a decision-making task in which subjects must choose one card at a time from four decks on a computer screen. They have 100 trials and may win or lose hypothetical money with each trial. Two of the decks are higher risk (higher rewards and higher losses) than the other two decks (lower rewards and lower losses). The goal of the task is to maximize profit. Data were analyzed in five blocks of 20 trials each. Statistics: mixed model repeated measures analysis.
Results: All patients were able to complete the GT. Compared with normal controls, results for schizophrenia patients differ significantly (p<0.01) for blocks 3 to 5, but were not significant for the first two blocks.
Conclusion: Contrary to a previous study (Wilder et al, 1998), our results suggest a dysfunction of the orbitofrontal cortex in schizophrenia. While schizophrenia patients understand and are able to complete the GT, they seem insensitive to the long-term consequences of their decision and favor immediate reward. The lack of difference between patients and normal controls for the first two blocks suggest that our findings are not related to a global frontal deficit.

References:

NR533 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Stroop Interference and Processing Speed in Childhood Psychotic Disorders
Joyce W. Yuan, B.A., McLean Hospital, East House 322, 115 Mill Street, Belmont, MA 02478; Anthony J. Giuliano, Ph.D., Vamsi K. Koneru, B.A., Sandra M. DeJong, M.D., Jean A. Frazier, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that apparent selective attention deficits in psychotic youth could be attributed to a more fundamental deficit in processing speed. Further research is needed to clarify the nature of attentional deficits in childhood psychotic disorders, as well as the relation of these deficits to adult schizophrenia.

Summary:
Objective: Although selective attention deficit in adults with psychotic disorders has often been studied using the Stroop Test, results have yet to reach a consensus. Little study has been done on selective attention in psychotic youth. We therefore examined Stroop Test performance in psychotic youth, in relation to selective attention and other cognitive abilities.
Method: Twenty youth with a primary psychotic disorder (schizophrenia, schizoaffective disorder, or bipolar disorder with psychotic features) and 23 controls participating in a brain imaging study completed the Stroop Test, WISC-III, and WRAT-3. T-test comparisons and ANCOVA (with WISC-III and WRAT-3 scores as covariates) were conducted to analyze differences between groups on Stroop performance.
Results: T-test comparisons of age-corrected T-scores showed that psychotic youth scored significantly lower than controls in all conditions of the Stroop Test (p<.05). T-scores for Stroop interference were also significantly lower for the psychotic group than for controls (p<.05). ANCOVA comparisons using processing speed as a covariate eliminated group differences.
Conclusions: Stroop performance and results of the ANCOVA suggest a fundamental processing speed deficit in psychotic youth. This finding is consistent with slow processing speed reported in studies of adult schizophrenia. Further comparisons between youth and adults affected by psychosis are warranted.

References:

NR534 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Semantic Association to Heard Words in Schizophrenia: Evidence of Abnormal Network With an Open Response Task
Almut F. Engeliien, M.D., Department of Psychiatry, Cornell University, 525 East 68th Street, Box 140, New York, NY 10021; Hong Pan, David A. Silbersweig, M.D., Oliver Tiescher, M.D., Emily Stern, M.D.
Educational Objectives:

At the conclusion of this session, the participant should understand important cognitive deficits in schizophrenia.

Summary:

Objective: Abnormalities of semantic processing have recently been demonstrated in schizophrenia. Most tasks used to date were cognitive semantic tasks, such as priming and judging semantic distance, and used visual stimulus material. Given these abnormalities and studies from our group and other laboratories indicating impairment of auditory processing in schizophrenia, we wanted to assess the internal organization of the semantic network in schizophrenia activated to spoken words.

Methods: 30 healthy subjects and 15 patients with a DSM-IV diagnosis of schizophrenia or schizoaffective disorder, treated as outpatients at the time of testing, identified 43 spoken English words and wrote down one related word. The responses were classified into seven categories: (1) superordinate—general; (2) superordinate—specific; (3) other item of same semantic range—level of hypernymy; (4) frequent context association; (5) subordinate—hyponym; (6) synonym; or (7) “other”—loose or strange association. Paired t-tests were performed for number of responses per category between groups.

Results: Significant between-group differences were found for response categories 1 (N1.<Pt., p=0), 3 (N1.<Pt., p=0.049), 4 (N1.<Pt., p=0), 5 (N1.<Pt., p=0.007), and 7 (N1.<Pt., p=0).

Conclusions: Free semantic association to spoken words is abnormal in schizophrenic patients—they have more general, loose, and strange associations. The overall most frequent type of association in all subjects is frequency of context association (e.g. “earthquake” San Francisco).

References:


NR536 Wednesday, May 21, 12:00 p.m.-2:00 p.m.

The Efficacy of Aripiprazole in Patients With Schizoaffective Disorder

Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co, Ltd.

Mary J. Kujawa, M.D., Medical Department, Bristol-Myers Squibb Company, 777 Scudders Mill Road, Plainsboro, NJ 08538; Joseph Stringfellow, M.S., Sterling Hardy, M.S., Mirza Ali, Ph.D., Ronald R. Marcus, M.D., Elyse G. Stock, M.D.

Educational Objectives:

At the conclusion of this session, the participant should understand the role of aripiprazole in the treatment of patients with schizoaffective disorder.

Summary:

Objective: To examine the efficacy of aripiprazole for treatment of patients with schizoaffective disorder.

Methods: The present analysis was performed on data from a subsample of patients with schizoaffective disorder who participated in two four-week, multicenter, double-blind studies comparing aripiprazole (n = 117) with placebo (n = 54). Daily doses of aripiprazole ranged from 15 mg/d to 30 mg/d.

Results: The mean reduction in PANSS total score was significantly greater among patients treated with aripiprazole than among those randomized to placebo (−12.5 vs −2.3, P = 0.016). These reductions were similar to those observed for patients with schizophrenia enrolled in the two trials. Reduction in PANSS positive score among patients with schizoaffective disorder was also significantly greater with aripiprazole than with placebo (−3.6 vs −0.7, P = 0.017). The changes in Simpson Angus, Barnes Akathisia, and Abnormal Involuntary Movement scales scores in this patient population were comparable to those with placebo and the overall incidence of adverse events was similar in the two treatment groups.

Conclusion: In four-week trials, aripiprazole was effective, safe, and well tolerated for treatment of symptoms in patients with acute exacerbation of schizoaffective disorder.

References:

NR537  Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Aripiprazole Versus Perphenazine in Treatment-Resistant Schizophrenia
Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd.

John M. Kane, M.D., Department of Psychiatry, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11040-1150; William H. Carson, Jr., M.D., Mary J. Kujawa, M.D., Joseph Stringfellow, M.S., Ronald N. Marcus, M.D., Raymond Sanchez, M.D., Herbert Y. Meltzer, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will have a better understanding of the efficacy and safety of aripiprazole compared with perphenazine in patients with treatment-resistant schizophrenia.

Summary:
Objective: To assess the efficacy and safety of aripiprazole compared with perphenazine in treatment-resistant schizophrenia.
Methods: In a multicenter, double-blind study, eligible patients entered a four- to six-week, open-label, atypical antipsychotic treatment phase (olanzapine or risperidone) to confirm treatment resistance. Patients were then entered into a 2-10-day, single-blind, placebo washout phase, then randomized to the six-week, double-blind treatment phase of aripiprazole, 15 or 30 mg/d (n=154) or the typical neuroleptic, perphenazine, 6-84 mg/d (n=146). Assessments of PANSS, CGI, safety, and the quality-of-life scale (QLS) were done.
Results: Failure on olanzapine or risperidone, patients treated with either aripiprazole or perphenazine showed improvement in PANSS Total (−9.8 and −10.5, respectively), negative and positive subscale scores, and CGI Improvement Scores. Overall, 27% and 26% of patients responded to aripiprazole and perphenazine, respectively, based on CGI-I Score of 1 or 2 or >30% decrease in PANSS Total. Aripiprazole-treated patients demonstrated more improvement in the QLS Total Score than perphenazine-treated patients but these differences were not statistically significant. Fewer aripiprazole-treated patients experienced EPS, ECG abnormalities, or elevations in plasma prolactin levels. There were no clinically significant differences in weight.
Conclusions: Aripiprazole and perphenazine produced significant improvement in schizophrenia patients resistant to olanzapine or risperidone.

References:

NR539  Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Managing Weight Gain in Patients With Schizophrenia: Twelve Months of Data on the Healthy Living Program
Supported by Eli Lilly and Company
Matthew A. Menza, M.D., Department of Psychiatry, RWJ Medical School, 675 Hoes Lane, Room D207A, Piscataway, NJ 08854; Betty Vreeland, A.P.N., Shula Minsky, Ed. D., Michael Gara, Ph.D., Tobert G. Stem, M.D., Maria Sakowitz, R.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the importance of longitudinal re-evaluation of diagnosis in first-episode psychoses.

Summary:
Introduction: Diagnostic stability is the degree to which an illness remains the same when re-evaluated at a later point. There are few studies that have looked at diagnostic stability of psychiatric illnesses. This study aimed to prospectively evaluate diagnostic stability in first-episode psychotic patients, and seven for delusional disorder.

Results: All 49 subjects initially diagnosed with schizophrenia retained the diagnosis after one year (PPV=100%). Eleven of the schizophreniform subjects were re-diagnosed as schizophrenia (PPV=8.3%); all five psychosis NOS patients remained the same (PPV=100%). One schizo-affective disorder (PPV=90.9%), one mood disorder (PPV=94.1%) and one delusional disorder (PPV=85.7%) subject were re-diagnosed as schizophrenia at follow-up.

Conclusions: The most frequent shifts in diagnosis of the categories were to schizophrenia, and not the other way, suggesting that this category may evolve later in some cases of psychosis. Thus, a longitudinal re-evaluation of diagnosis is critical for appropriate management in first episode psychotic patients, especially in those not originally diagnosed with schizophrenia.

References:
Introduction/Hypothesis: We hypothesize that the Weight Watchers (WW) program may promote weight loss in overweight patients who take antipsychotic medications.

Methods: Naturalistic study of outpatients diagnosed with schizophrenia, schizoaffective disorder or bipolar disorder taking antipsychotic medications and, in some cases, mood stabilizers recruited from the CMHC Psychosis Program or the CMHC Clozapine Clinic. Weights were obtained before and after a 10 week WW class by two experienced WW counselors assisted by CMHC clinical staff. Patients learned to quantitate calories from food and activity by assigning points. Paired t-tests were performed on weights before and after WW in 19 patients completing the 10-week program.

Results: 18 of the 19 patients lost weight, one patient gained 1 lb. Mean weight before WW=236.6±67.2 lbs., mean weight after WW=231.31±65.5 lbs. Mean weight loss=5.5±3.5 lbs (p < .01).

Conclusions/Discussion: Our results support the hypothesis that patients on antipsychotic medications may lose weight by completing a widely available program. Weight loss was gradual but consistent across patients. This finding has significant implications for protecting the health of patients taking antipsychotic medications. These results need to be confirmed in a controlled, prospective, follow-up study to determine whether 1/2 pound/week weight loss will be sustained over longer periods of time.

References:

NR541 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
A Pilot Study to Reduce the Health Risks of Antipsychotic Medications
Supported by Eli Lilly and Company: CMHC Foundation Weltner Fellowship

Steven H. Madonick, M.D., Department of Psychiatry, Yale University, 34 Park Street, 2nd floor, New Haven, CT 06519; Geraldine Adeski-Cameron, R.G.N., Victoria M. Dreisbach, D.O., Scott W. Woods, M.D., Bruce E. Wexler, M.D., Jeanne L. Steiner, D.O.

Educational Objectives:
- Weight gain is a serious side effect of most antipsychotic medications. Relatively straightforward modifications of behavior through the available Weight Watchers program may significantly reduce this problem.

Summary:
- Introduction/Hypothesis: We hypothesize that the Weight Watchers (WW) program may promote weight loss in overweight patients who take antipsychotic medications.
- Methods: Naturalistic study of outpatients diagnosed with schizophrenia, schizoaffective disorder or bipolar disorder taking antipsychotic medications and, in some cases, mood stabilizers recruited from the CMHC Psychosis Program or the CMHC Clozapine Clinic. Weights were obtained before and after a 10 week WW class by two experienced WW counselors assisted by CMHC clinical staff. Patients learned to quantitate calories from food and activity by assigning points. Paired t-tests were performed on weights before and after WW in 19 patients completing the 10-week program.
- Results: 18 of the 19 patients lost weight, one patient gained 1 lb. Mean weight before WW=236.6±67.2 lbs., mean weight after WW=231.31±65.5 lbs. Mean weight loss=5.5±3.5 lbs (p < .01).
- Conclusions/Discussion: Our results support the hypothesis that patients on antipsychotic medications may lose weight by completing a widely available program. Weight loss was gradual but consistent across patients. This finding has significant implications for protecting the health of patients taking antipsychotic medications. These results need to be confirmed in a controlled, prospective, follow-up study to determine whether 1/2 pound/week weight loss will be sustained over longer periods of time.

References:

Jose M. Canive, M.D., Department of Psychiatry, VA Medical Center, 1501 San Pedro SE, Albuquerque, NM 87108; Gregory A. Miller, Ph.D., Lawrence E. Adler, M.D., Daniel Ricker, Jessica Irwin, B.A., Natalie Sanchez, Robert J. Thoma, Ph.D., Faith M. Hanlon, M.S., Sandra N. Mosesi, M.S., Christopher J. Edgar, Ph.D., Michael P. Weishend, Ph.D., Mingxiong Huang, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize the basic methodology underlying sensory gating deficit in schizophrenia and how related to positive and negative symptoms.

Summary:

Although a P50 sensory gating deficit has long been considered characteristic of schizophrenia, clinical correlates of the deficit have not been well documented. While the standard EEG P50 sensory gating measure does not foster differential assessment of left- and right-hemisphere contributions, its analogous MEG measured M50 component may be better suited to explore hemispheric differences. The present investigation sought to determine how schizophrenia’s P50/M50 sensory gating deficit relates to positive and negative symptoms. A standard paired-click paradigm was used during simultaneous EEG and MEG data collection in a group of 27 patients with schizophrenia. Sensory gating ratios were determined by measuring the 50 ms response of the second divided by the first click (S2/S1), and symptoms assessed with the Schedule for the Assessment of Negative Symptoms (SANS), the Positive and Negative Symptoms Scale (PANSS). There was a significant positive correlation between the magnitude of negative symptoms and MEG right hemisphere sensory gating ratio, but not with MEG left hemisphere or EEG sensory gating ratio. There was a significant quadratic effect of left M50 ratio on PANSS Positive score, those with either higher or lower left M50 gating ratios demonstrating a greater magnitude of positive symptoms.

References:


NR543 Wednesday, May 21, 12:00 p.m.-2:00 p.m.

Auditory Sensory Grating Deficit and Symptoms in Schizophrenia

Jose M. Canive, M.D., Department of Psychiatry, VA Medical Center, 1501 San Pedro SE, Albuquerque, NM 87108; Gregory A. Miller, Ph.D., Lawrence E. Adler, M.D., Daniel Ricker, Jessica Irwin, B.A., Natalie Sanchez, Robert J. Thoma, Ph.D., Faith M. Hanlon, M.S., Sandra N. Mosesi, M.S., Christopher J. Edgar, Ph.D., Michael P. Weishend, Ph.D., Mingxiong Huang, Ph.D.

Educational Objectives:

At the conclusion of this session, the participants should be able to diagnose the metabolic syndrome in patients with schizophrenia. Metabolic syndrome, a constellation of truncal obesity, dyslipidemia, disturbed insulin and glucose metabolism, and hypertension, is associated with the development of type 2 diabetes mellitus and cardiovascular disease. In this pilot study we determine the prevalence of metabolic syndrome in patients with schizophrenia.

Method: Cross-sectional study of 31 female and 32 male patients recruited from an outpatient psychiatric clinic. Metabolic syndrome was defined using the ATP III criteria.

Results: The prevalence of metabolic syndrome was 60% in patients with schizophrenia. In patients with metabolic syndrome, the mean age was 42.16 ± 11.53 years, 54% were female, 87% had abnormal waist circumference, 84% had increased triglycerides, 78% had abnormal high density lipoprotein, 73% had hypertension, and 24% had abnormal glucose.

Conclusion: In this pilot study, 60% of schizophrenic patients had metabolic syndrome. This is far greater than the 22% prevalence reported in the general population. Data suggest that patients with schizophrenia may be at an increased risk to develop metabolic syndrome which is associated with the development of type 2 diabetes and cardiovascular disease. Early identification of metabolic syndrome in patients with schizophrenia may provide opportunities for prevention of cardiovascular disease and type 2 diabetes. Further prospective studies are needed to corroborate our findings.

References:


There were no significant differences in the DUP among men and women. There were no significant differences in the GAF, PANSS (although poor impulse control was assessed to be significantly higher in men [p = 0.009]) or QOL-BREF scores at baseline. Men had significantly more readmissions (p = 0.03) in the one-year follow-up period; however response to treatment did not vary within the groups.

Conclusions: Gender differences in patients with first-episode psychosis were similar to those of chronic patients. Rehospitalization rates also followed a similar pattern with men having significantly more hospitalization and longer stays.

References:

**NR545 Wednesday, May 21, 12:00 p.m.-2:00 p.m.**

**Risk of Weight Gain and Diabetes Among People Taking Antipsychotics**

Supported by Bristol-Myers Squibb Company

Wildon R. Farwell, M.D., Indiana University, 3504 Idlewood Parkway, Apartment 507, Indianapolis, IN 46214; Timothy E. Stump, M.A., Jane Wang, Ph.D., Eskinder Tafesse, Ph.D., Gilbert L'Italien, Ph.D., William M. Tierney, M.D.

**Educational Objectives:**

At the end of this session, the participant should be able to describe the relationship among antipsychotic exposure, weight gain, and the development of diabetes among people using antipsychotic agents.

**Summary:**

*Introduction:* Atypical antipsychotics are safer than conventional agents but have been associated with weight gain and other metabolic events. We assessed the risk of weight gain and new-onset diabetes among adults taking olanzapine or risperidone, controlling for prior history and intensity of care.

*Methods:* A comprehensive clinical data repository yielded 3,115 patients treated with antipsychotic drugs. Cases who gained ≥7% body weight or had new-onset diabetes in the first year of treatment were matched with up to four controls by age, sex, and race. Conditional logistic regression models assessed the odds of ≥7% weight gain or diabetes, controlling for comorbidity and prior outpatient visits.

*Results:* Subjects’ mean age was 43 years; 58% were women. Olanzapine (OR 2.3, p = 0.02) and risperidone (OR 1.8, p = 0.05) were significant independent risk factors for ≥7% weight gain. Olanzapine use was significant (OR 2.65, p = 0.01) independent risk factor for diabetes, but not risperidone (OR 0.8, p = 0.3). Weight gain was not associated with developing diabetes.

*Conclusion:* Controlling for comorbidity and care intensity, both olanzapine and risperidone increased patients’ risk of significant weight gain in the first year of treatment, olanzapine more so. Weight gain was not associated with developing diabetes, but taking olanzapine (but not risperidone) was.

**References:**

**NR546 Wednesday, May 21, 12:00 p.m.-2:00 p.m.**

**Optimal Dosing of Oral Ziprasidone: Analysis of Clinical Trial Data**

Supported by Pfizer Inc.

Stephen R. Murray, M.D., Pfizer Incorporated, 235 East 42nd Street, New York, NY 10017; Cynthia O. Slu, Ph.D., Steven J. Romano, M.D.

**Educational Objectives:**

At the conclusion of this presentation, the participant should be able to discuss the reported findings on dosing, symptom improvement, and tolerability in clinical trials of ziprasidone.

**Summary:**

*Objective:* To elucidate optimal dosing of oral ziprasidone through analysis of clinical trial data.

*Methods:* We analyzed pooled efficacy (BPRS Total score), discontinuation, and adverse event data from four 4–6 week, fixed-dose, placebo-controlled trials in which 569 patients received 20–80 mg BID, and reviewed dosing and discontinuation data from three six- to eight-week flexible-dose (maximum 80 mg BID) active-comparator trials (n = 706).

*Results:* In analyses of placebo-controlled trials, early and sustained improvement was demonstrated for doses ≥ 120 mg QD (p < 0.001 at Week 1; p < 0.05, Week 6). Doses ≤80 mg QD did not demonstrate significant changes until Week 3. Improvement was generally dose-related. Discontinuation rate within first 14 days of treatment was lower for 60 and 80 mg BID (5.2%) than for 20 and 40 mg BID (11.5%). Incidence of adverse events was comparable across dosing groups. Among the three flexible-dose trials, mean daily dose during flexible periods was 123 to 136 mg; discontinuation due to inadequate response was less common in two studies allowing faster titration.

*Conclusions:* The superior, more rapid BPRS Total score improvement observed in placebo-controlled trials and the dosing results from flexible-dose studies support titration of ziprasidone to ≥ 60 mg BID in patients with acute schizophrenia.

**References:**

**NR547 Wednesday, May 21, 12:00 p.m.-2:00 p.m.**

**Features of OCD With Schizophrenia or Schizoaffective Disorder**

Masayuki Ohta, M.D., Department of Neuropsychiatry, Hyogo College of Medicine, 1-1 Mukogawa, Nishinomiya, HY 663-8501, Japan; Masahiro Kokai, M.D., Yoshio Morita, M.D.

**Educational Objectives:**

At the conclusion of this session, participants will be able to recognize obsessive-compulsive disorder (OCD) comorbid with schizophrenia or schizoaffective disorder frequently and to under-
stand a possibility to distinguish schizophrenic patients with OCD based on their motor symptoms.

Summary:

Objective: It is difficult to diagnose obsessions among patients with schizophrenia or schizoaffective disorder. For better diagnosis of obsessions among schizophrenic patients, we investigated differences in the neuropsychiatric features between schizophrenic patients with or without obsessive-compulsive disorder (OCD).

Methods: Eighty-two subjects with the DSM-IV diagnosis of schizophrenia or schizoaffective disorder were evaluated by the Structured Clinical Interview for DSM-IV Axis I Disorders, the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), and the Positive and Negative Syndrome Scale. To assess their motor symptoms, the Abnormal Involuntary Movements Scale (AIMS), the Barnes rating scale for drug-induced akathisia (BAS) and the Simpson and the Angus extrapyramidal symptoms rating scale (SAEPS) were used.

Results: The 16 subjects with OCD (19.5%) had significantly more severe motor symptoms than the non-OCD subjects on the AIMS and the SAEPS. The mean Y-BOCS score of the subjects with OCD was nearly twice as high as that of the subjects without OCD. The average age of the subjects, age at onset of psychosis, duration of psychosis, total amount of neuroleptics and duration of exposure to neuroleptics did not differ between the two groups.

Conclusion: In schizophrenic patients, we may be able to distinguish these patients with OCD based on their motor symptoms.

References:


NR549 Wednesday, May 21, 12:00 p.m.–2:00 p.m.

Short-Term Efficacy of Aripiprazole on Depression and Anxiety in Schizophrenia

Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co, Ltd.

William H. Carson, Jr., M.D., Otsuka America Pharmaceutical Company, 100 Overlook Drive, Princeton, NJ 08540; Donald G. Archibald, M.Phil., George Manos, Ph.D., Ronald N. Marcus, M.D., Dusan Kostic, Ph.D., Elyse G. Stock, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the short-term effects of aripiprazole on the depression and anxiety symptoms associated with schizophrenia.

Summary:

Objective: To examine the short-term effects of aripiprazole on the depression and anxiety symptoms associated with schizophrenia.

Methods: Pooled data from five four- to six-week, double-blind studies of aripiprazole in patients with schizophrenia or schizoaffective disorder were used in the analysis. Changes in the depression/anxiety cluster, determined using factor analysis of PANSS scores, among patients treated with aripiprazole (n=885) were compared with those randomized to placebo (n=405). The same analysis was additionally performed on two fixed-dose trials that included haloperidol as an active control.

Results: The mean reduction in PANSS depression/anxiety factor was significantly greater among patients treated with aripiprazole than among those randomized to placebo (P=0.001). The effect was particularly pronounced among patients with baseline scores above the median value (~3.18 vs ~1.88, P<0.001). Reduction in the PANSS depression item (G6) was also significantly greater among patients randomized to aripiprazole (P=0.008). In the two trials including a haloperidol arm, the change in the depression/anxiety factor was similar in the haloperidol and placebo arms (P=0.368), while significant improvement over placebo was seen in the aripiprazole arm (P=0.013).

Conclusion: In short term trials, aripiprazole was effective for amelioration of the depression and anxiety symptoms of schizophrenia, as determined by PANSS factor analysis.

References:

1. Kane JM, Carson WH, Saha AR, McQuade RD, Ingenito GC, Zimbroff DL, Ali MW: Efficacy and safety of aripiprazole and


NR550 Wednesday, May 21, 12:00 p.m.-2:00 p.m. Insulin Resistance and Syndrome X Among Patients With Schizophrenia


Educational Objectives:

At the conclusion of this session, the participant should be able to identify the prevalence of insulin resistance and syndrome X among schizophrenia patients.

Summary:

Objective: The primary study objective was to assess the prevalence of insulin resistance and syndrome X among individuals with schizophrenia. Secondary objectives were to evaluate the prevalence of dyslipidemia and overweight and obesity.

Method: This multi-center, investigator-initiated, naturalistic study enrolled 125 inpatients and outpatients (75 M, 50 F) meeting DSM-IV criteria for schizophrenia or schizoaffective disorder. Ninety-eight outpatients from the United States and 27 inpatients from Taiwan were included. Patients were taking a variety of conventional and atypical antipsychotic medications as well as mood stabilizers, and antidepressants. All subjects were evaluated for insulin resistance and syndrome X using laboratory and clinical assessments. Patients were instructed to withhold food and beverages (except water) after midnight and any morning medications prior to their laboratory assessments. Patients’ usual medication regimes were not changed during the study.

Results: 70.3% of outpatients (HOMA-IR = 3.0, SD = 1.9) and 44.4% of inpatients (HOMA-IR = 2.1, SD = 2.0) met criteria for insulin resistance alone. 51.0% of outpatients and 22.2% of inpatients met the criteria for syndrome X. Seven previously undiagnosed outpatients met criteria for diabetes mellitus. Lipid and weight data were also analyzed.

Conclusions: This preliminary study indicates that patients with schizophrenia have a higher prevalence of insulin resistance and syndrome X than the general population.

References:


NR551 Wednesday, May 21, 12:00 p.m.-2:00 p.m. Ethnicity and Schizophrenia Medication Choice Supported by Eli Lilly and Company

Jayme L. Opolka, 3154 Tinkersfield Lane, Indianapolis, IN 46214; Karen Rascati, Ph.D., Carolyn M. Brown, Ph.D., Joseph P. Gibson, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize that ethnicity is a significant predictor of the type of antipsychotic patients with schizophrenia are prescribed.

Summary:

Objective: To demonstrate associations between hyperprolactinemia and sexual dysfunction in schizophrenic patients treated with prolactin (PRL)-elevating antipsychotic drugs, and that sexual function improves after switching to olanzapine (OLZ).

Methods: Schizophrenia patients (N=402), treated in the community with conventional antipsychotics or risperidone (RISP) for at least three months, participated in a one-day prevalence trial to estimate hyperprolactinemia and associated morbidity. A sub-sample of hyperprolactinemic patients, entered a four month prospective, open-label study, and were randomized to remain on current antipsychotic therapy (N=27), or switch to OLZ (5–20 mg/day) (N=27). Sexual morbidity was assessed with the Global Im-

NR552 Wednesday, May 21, 12:00 p.m.-2:00 p.m. Sexual Dysfunction Associated With Neuroleptic-Induced Hyperprolactinemia Improves With Reduction in Prolactin Levels Supported by Eli Lilly and Company

Bruce J. Kinon, M.D., Lilly Research Lab, Eli Lilly And Company, Lilly Corporate Center, Indianapolis, IN 46285; Hong Liu, Ph.D., Jonna Ahl, Ph.D.

Educational Objectives:

At the conclusion of this session, participant should be able to recognize that sexual dysfunction may be associated with hyperprolactinemia, and that switching patients to an antipsychotic that is prolactin-sparing may reduce serum prolactin and improve sexual dysfunction.

Summary:

Objective: Patients with schizophrenia may respond better to 2nd generation antipsychotics versus older antipsychotics due to superior efficacy and safety profiles. However, there is a reduced likelihood of ethnic minorities receiving newer antipsychotics. The purpose of this study was to examine if ethnicity helped predict whether patients with schizophrenia were prescribed (1) haloperidol versus risperidone or olanzapine, and (2) risperidone versus olanzapine, when controlling for other factors.

Methods: Texas Medicaid claims were analyzed for persons, age 21 to 65, diagnosed with schizophrenia or schizoaffective disorder, initiating treatment with olanzapine (N=1875), risperidone (N=982), or haloperidol (N=726) between 1/1997 and 8/1998. The association between antipsychotic prescribing and ethnicity (African American, Mexican American, or Caucasian) was assessed using logistic regression. Covariates included other patient demographics, region, comorbid mental health conditions, and prior medication and health care resource use.

Results: The results of the haloperidol versus risperidone or olanzapine analysis indicated that African Americans were significantly less likely than Caucasians to receive second-generation antipsychotics (odds ratio = 0.657; 95% CI = 0.539, 0.801). Ethnicity was not associated with significant differences in use of risperidone versus olanzapine.

Conclusions: When other factors are controlled for, African Americans were significantly less likely to receive the newer antipsychotics. Among those who did receive the newer antipsychotics, ethnicity did not affect medication choice.

References:

pressures of Sexual Functioning scale, and the Changes in Sexual Functioning Questionnaire.

Results: The prevalence of hyperprolactinemia in males and females was 42.4% and 59.2%, respectively. Increased PRL was significantly associated with decreased sexual interest in females (p=0.0523), and ejaculatory dysfunction in RISP-treated males (p=0.039). After switching to OLZ, PRL levels normalized in greater than 90% of the patients, and overall sexual functioning improved significantly (p=0.028). Male patients experienced significant improvement in erectile function (p=0.028), and female patients were significantly less likely to experience painful intercourse (p=0.046).

Conclusions: Sexual dysfunction may improve with reduced PRL levels in patients switched from treatment with PRL-elevating antipsychotics to OLZ.

References:

NR553 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Longitudinal Effects of Olanzapine on Fasting Serum Lipids: A Randomized, Prospective, Four-Month Study
Supported by Eli Lilly and Company
Bruce J. Kinon, M.D., Lilly Research Lab, Eli Lilly And Company, Lilly Corporate Center, Indianapolis, IN 46285; Hong Liu, Ph.D., Jonna Ahl, Ph.D., Robert W. Baker, M.D.

Educational Objectives:
- At the conclusion of this session, participant should be more familiar with the chronic effects of antipsychotics on fasting serum lipids, and how lipid levels may transiently change upon switching medications.

Summary:
- Objective: To compare lipid profiles of clinically stable schizophrenic patients treated with conventional antipsychotics or risperidone to those of patients switched to olanzapine.

Methods: Fasting serum lipids were measured in subjects participating in a study of the effect of switching antipsychotic medications on serum prolactin. Patients were randomized to: remain on current conventional antipsychotic or risperidone (N=27) or switch to olanzapine (OLZ) 5–20 mg/day, (N=27). Total cholesterol, high density lipoproteins (HDL), low density lipoproteins (LDL), and triglycerides were collected monthly.

Results: All mean baseline serum lipids were at, or exceeded, the upper limit of normal except for HDL. In patients switched to olanzapine, there was no significant within-group change baseline to endpoint in total cholesterol (p=0.69) or triglycerides (p=0.81). These changes were comparable to those in patients continuing on conventional antipsychotics or risperidone (between-group: total cholesterol, p=0.69; triglycerides, p=0.81). Visit-wise cholesterol and triglyceride levels increased within the first month of olanzapine treatment and returned to baseline levels by months two and three, respectively.

Conclusion: Longitudinal measures reveal that patients switched to olanzapine may experience an initial rise in fasting serum lipids that returns to pretreatment levels, which are not significantly different from those in patients on conventional antipsychotics or risperidone.

References:

NR554 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Differential Rate of Weight Gain Present Among Patients Treated With Olanzapine Supported by Eli Lilly and Company
Bruce J. Kinon, M.D., Lilly Research Lab, Eli Lilly And Company, Lilly Corporate Center, Indianapolis, IN 46285; Matthew D. Rotelli, Ph.D., Christopher Kaiser, Ph.D., Sara Kolack-Walker, Ph.D.

Educational Objectives:
- At the conclusion of this session, participant should be able to understand the patterns of weight gain and their prevalences after olanzapine treatment of schizophrenia and schizoaffective disorder. This will aid in targeting interventions to patients likely to gain significant weight during olanzapine treatment.

Summary:
- Objective: Previous studies demonstrated varied weight response in olanzapine-treated patients: some patients gain little to no weight, others gain modestly, and others gain excessive weight. In patients gaining weight, increases occur early in treatment, plateauing after thirty-three weeks.

Methods: A retrospective analysis of weight gain was performed in patients with schizophrenia or schizoaffective disorder treated with olanzapine over fifty-two weeks (HGAJ study, 1191/1336 patients with complete data; average olanzapine dose 13.2 mg).

Results: Patients were dichotomized by percentage of weight gained during the first six weeks of treatment: 1) patients gaining >7% (Rapid Weight Gain Group, RWG), and 2) patients gaining <7% of body weight (NonRapid Weight Gain Group, NRWG).

Conclusion: By measuring weight during the first weeks of olanzapine treatment and assessing appetite change, clinicians may predict patients likely to gain weight rapidly and benefit most from interventions limiting overall weight gain.

References:

NR555 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Incidence of Presumptive Tardive Dyskinesia in Elderly Patients Treated With Olanzapine or Conventional Antipsychotics Supported by Eli Lilly and Company
Bruce J. Kinon, M.D., Lilly Research Lab, Eli Lilly And Company, Lilly Corporate Center, Indianapolis, IN 46285;
Virginia L. Stauffer, Pharm.D., Christopher Kaiser, Ph.D., Sara Kollack-Walker, Ph.D.

**Educational Objectives:**

At the conclusion of this session, participant should be able to understand the relative risk of developing tardive dyskinesia during antipsychotic drug therapy in elderly patients who are at greater risk for developing this abnormal movement disorder.

**Summary:**

Background: Incidence rates of presumptive tardive dyskinesia (TD) were compared in acutely psychotic or agitated elderly patients treated with olanzapine (OLZ) or conventional antipsychotic (CNV) drug therapy.

Methods: Patients without TD were randomized to OLZ (2.5–20 mg/day; n=150) or CNV (dosed per label; n=143) therapy, and underwent a six-week drug tapering/drug initiation period, followed by reassessment of TD. Patients remaining without TD after six weeks were treated with OLZ or CNV for up to one year. Primary analysis was time-to-TD incidence, defined as rating on the Abnormal Involuntary Movement Scale (AIMS) of either: A) moderate severity (≥3) in one body region or mild severity (≥2) in two or more body regions, or B) moderate severity (≥3) in one body region.

Results: Patients in CNV group were at a greater risk for presumptive TD than patients in OLZ group (criteria A or B, p<.05). Incidence of presumptive TD that persisted for at least one month was lower and differed between treatments only for criterion B (moderately severe symptoms; p<.05).

Conclusions: In elderly patients who are at a greater risk for developing TD, these data revealed a lower risk of developing dyskinetic symptoms in patients treated with olanzapine versus conventional antipsychotics.

**References:**


**NR556 Wednesday, May 21, 12:00 p.m.-02:00 p.m.**

**Osteopenia Associated With Increased Prolactin and Aging in Psychiatric Patients Treated With Prolactin-Elevating Antipsychotics Supported by Eli Lilly and Company**

Bruce J. Kinon, M.D., Lilly Research Lab, Eli Lilly And Company, Lilly Corporate Center, Indianapolis, IN 46285; Hong Liu, Ph.D., Jonna Ahl, Ph.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to recognize that patients with elevated prolactin may be at risk for developing osteopenia when they are treated with prolactin-elevating antipsychotics.

**Summary:**

Objective: To determine the prevalence of osteopenia in schizophrenic patients treated with prolactin (PRL)-elevating antipsychotics (APD), and to identify factors influencing bone density.

Methods: Schizophrenia patients (N=402) treated in the community with conventional APD or risperidone for at least one month, participated in a one-day trial to estimate hyperprolactinemia, and associated morbidity. Bone density (T-score) was determined by ultrasonography of the calcaneus; bone metabolism by serum osteocalcin (OCN) levels. Logistic regression analyzed the effect of age, length of APD treatment, and PRL on T-scores and OCN separately for males and females.

Results: The frequency of osteopenia (T-scores<−1) was 20.4% in females and 28.6% in males. Decreased T-scores were significantly associated with increased age for males (p=0.07) and females (p=0.001). In males, but not females, age and decreased T-scores were significantly associated with increased PRL (p=.05). Increased OCN was significantly associated with increased PRL (p<.01) and increased age (p=.03) in females, but increased PRL (p=.05) and lower age (p=.01) in males.

Conclusions: Osteopenia was prevalent in a psychiatric population treated with PRL-elevating APDs. Risk factors appear to be increased age and increased PRL across gender. Bone demineralization may be a common comorbidity in psychiatric patients treated with PRL-elevating APDs.

**References:**


**NR557 Wednesday, May 21, 12:00 p.m.-02:00 p.m.**

**Long-Term Effects on Negative Symptoms in Patients Treated With Clozapine or Olanzapine Supported by Novartis Pharmaceuticals Corporation**

Vinod Kumar, M.D., Department of Clinical Research, Florida Institute of Neurology, 530 South Nokomis Avenue, Suite 14, Venice, FL 34285; Jonathan Salem, B.Sc., Chanchieh Hsu, Ph.D., Rocco M. Zaninelli, M.D., Rajinder A. Judge, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant will be able to discern the difference of effects between olanzapine and clozapine on schizophrenic patients with negative symptoms who are not depressed.

**Summary:**

Objective: To evaluate the long-term effects of clozapine and olanzapine on negative symptoms.

Method: Data from a two-year prospective study of 980 patients with schizophrenia or schizoaffective disorder were analyzed to compare the long-term effects of clozapine and olanzapine on negative symptoms. Baseline Calgary Depression Scale scores were classified into four groups: not depressed, mildly depressed, moderately depressed, and severely depressed.

Results: The overall mean change from baseline on the PANSS negative subscale (PANSS-N) showed a statistically significant improvement for clozapine- and olanzapine-treated patients. For clozapine- and olanzapine-treated patients, the mean change from baseline on the PANSS-N was significant for all four severity subgroups. Patients classified as severely depressed at baseline had a higher baseline PANSS-N score than the other three groups and showed a higher reduction in negative symptom scores. The differences between the mean change from baseline for patients classified as not, mildly or moderately depressed were not significant for the clozapine group (p=0.715). In the olanzapine group, those patients classified as not depressed experienced less reduction in negative symptoms than those classified as mildly or moderately depressed. After two years, improvement in negative symptoms for patients classified as not depressed was greater for the clozapine group than for the olanzapine group (−5.85 and −3.37 respectively).

Conclusion: Clozapine and olanzapine have long-term effects on the reduction of negative symptoms. The data indicate that...
clozapine-treated patients with no depression experience a greater reduction in negative symptoms than olanzapine-treated patients.

References:

**NR558** Wednesday, May 21, 12:00 p.m.-2:00 p.m.

**Long-Term Effects of Aripiprazole on Affective Symptoms of Schizophrenia**

**Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd.**

Elyse G. Stock, M.D., Bristol-Myers Squibb Company, 5 Research Park, Wallingford, CT 06492-7660; Donald G. Archibald, M.Phiil., Stavros Tourkodimitris, Ph.D., Mary J. Kujawa, M.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 long-term impact of aripiprazole and haloperidol on affective symptoms in patients with schizophrenia.

**Summary:**
*Objective:* To compare long-term effects of aripiprazole and haloperidol on the affective symptoms of schizophrenia.

*Methods:* Data from a 52-week trial comparing aripiprazole with haloperidol for maintenance of response in 1,283 patients with acute exacerbation of chronic schizophrenia were used in the analyses. The affective symptoms were assessed using the PANSS depression item (G6), the depression/anxiety PANSS cluster derived by factor analysis, and the MADRS score.

*Results:* The improvements in PANSS depression item score and the PANSS depression/anxiety cluster score were greater in the aripiprazole group than in the haloperidol group at week 8. This effect was maintained through week 52; mean treatment difference was 0.14 (P<0.027) for the depression item and 0.52 (P=0.015) for the depression/anxiety cluster. The difference in the depression/anxiety cluster was particularly pronounced among patients in the upper tertile after stratification by baseline scores (treatment difference 1.10, P=0.02). Similar results were obtained for MADRS scores; among patients with pronounced depressive symptoms (MADRS >16), the reductions in MADRS score were 6.0 with aripiprazole and 3.5 with haloperidol (P=0.029).

*Conclusion:* Long-term therapy with aripiprazole is more effective than haloperidol for reduction of affective symptoms in patients with schizophrenia, as measured by changes in MADRS and relevant PANSS items scores.

References:

**NR559** Wednesday, May 21, 12:00 p.m.-2:00 p.m.

**Ziprasidone Negative Symptom Efficacy in Long-Term Clinical Trials**

**Supported by Pfizer Inc.**

Nina R. Schooler, Ph.D., Psychiatric Research Department, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004; Stephen R. Murray, M.D., Cynthia O. Siu, Ph.D., Steven J. Romano, M.D.

**Educational Objectives:**
At the conclusion of this presentation, the participant should be able to discuss results from ziprasidone clinical trials that suggest it has long-term efficacy in treating negative symptoms of schizophrenia.

**Summary:**
*Objective:* We reviewed ziprasidone’s efficacy in treating negative symptoms in long-term, double-blind trials and in extension studies of patients switched to ziprasidone from other antipsychotics.

*Methods:* Changes in PANSS negative subscale scores were evaluated in four randomized, double-blind studies of ziprasidone versus placebo (52 weeks), haloperidol (28 weeks), olanzapine (>6 months), and risperidone (52 weeks), using analysis of covariance (ANCOVA). In three open-label extension studies (>215 days) evaluating improvement following switch to ziprasidone from conventional agents, olanzapine, or risperidone, changes in PANSS negative subscale scores were analyzed using paired t-tests.

*Results:* Ziprasidone was superior to placebo (LOCF, p<0.05) in improving negative symptoms. Change in PANSS negative was not significantly greater than haloperidol, but percentage of PANSS negative responders (≥20% decrease) was higher (P<0.05). Ziprasidone’s treatment effect was comparable to olanzapine’s (95% CI: −2.3, 2.8) and risperidone’s (95% CI: −3.2, 2.4). In the switch studies, improvement was observed for patients switched from conventional agents (p<0.01), olanzapine (p<0.05), and risperidone (p<0.01).

*Conclusions:* In long-term treatment of negative symptoms of schizophrenia, ziprasidone showed efficacy superior to placebo’s and comparable to olanzapine’s and risperidone’s and a responder rate higher than haloperidol’s. Significant long-term improvement was also observed in patients switched from other antipsychotics.

References:

**NR560** Wednesday, May 21, 12:00 p.m.-2:00 p.m.

**Mortality Associated With Sertindole: Review of Epidemiological Studies**

Monther Tourmi, M.D., Lunderbeck SA, 37 Ave PierrelerdeSerbe, Paris 750086, France; Ron Mann, Ph.D., Gillian Hall, Ph.D., Miriam Sturkenboom, Nicholas Moore, Ph.D.
Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the results of the reported pharmacokinetic/pharmacodynamic study, which demonstrate that ziprasidone's effects on QTc prolongation at 320 mg/day, twice the maximum recommended daily dose, are slightly greater than those observed at a dosage of 160 mg/day.

Summary:

Objectives: To characterize QTc effects of oral ziprasidone and haloperidol at three steady-state dose levels.

Methods: After tapering and washout of existing antipsychotic therapy, subjects with schizophrenia or schizoaffective disorder were randomized to escalating doses of ziprasidone (40, 160, and 320 mg/day) or haloperidol (2.5, 15, and 30 mg/day) administered over 16 days to attain steady-state dose levels. ECGs were collected at baseline (drug-free condition) and during study drug administration on steady-state days 4, 10, and 16, at estimated T_max and one hour before and after. Samples for pharmacokinetic measurements were collected at estimated T_max, and telemetry was performed throughout high-dose period.

Results: Mean ziprasidone concentrations (n=25) increased ~6-fold across the 40–320 mg/day dose range, reaching 327 ng/mL at the 320 mg/day dose level. Mean ΔQTc from baseline were 4.5 msec at 40 mg/day, 19.5 msec at 160 mg/d, and 22.5 msec at 320 mg/day. For haloperidol (n=23), mean ΔQTc were −1.2, 6.6, and 7.2 msec at the three respective dose levels. No telemetric abnormalities or QTc ≥500 msec were observed.

Conclusions: At twice the recommended daily dose, oral ziprasidone showed marginal QTc increase from 160 mg/day, with no significant cardiovascular symptoms or QTc ≥500 msec.

References:


NR561 Wednesday, May 21, 12:00 p.m.-2:00 p.m.

High-Dose Ziprasidone Is Associated With Marginal Additional QTc Increase Supported by Pfizer Inc.

Jeffrey J. Miceli, Ph.D., Global Rod, Pfizer Inc., 50 Pequot Ave MS 6025-B223, New London, CT 06320, Thomas M. Shiovitz, M.D., Rachel H. Swift, Richard J. Anziano, Thomas Tensfeldt

Educational Objectives:

At the conclusion of this presentation, participants should be able to discuss the results of the reported pharmacokinetic/pharmacodynamic study, which demonstrate that ziprasidone's effects on QTc prolongation at 320 mg/day, twice the maximum recommended daily dose, are slightly greater than those observed at a dosage of 160 mg/day.

Summary:

Objectives: To characterize QTc effects of oral ziprasidone and haloperidol at three steady-state dose levels.

Methods: After tapering and washout of existing antipsychotic therapy, subjects with schizophrenia or schizoaffective disorder were randomized to escalating doses of ziprasidone (40, 160, and 320 mg/day) or haloperidol (2.5, 15, and 30 mg/day) administered over 16 days to attain steady-state dose levels. ECGs were collected at baseline (drug-free condition) and during study drug administration on steady-state days 4, 10, and 16, at estimated T_max and one hour before and after. Samples for pharmacokinetic measurements were collected at estimated T_max, and telemetry was performed throughout high-dose period.

Results: Mean ziprasidone concentrations (n=25) increased ~6-fold across the 40–320 mg/day dose range, reaching 327 ng/mL at the 320 mg/day dose level. Mean ΔQTc from baseline were 4.5 msec at 40 mg/day, 19.5 msec at 160 mg/d, and 22.5 msec at 320 mg/day. For haloperidol (n=23), mean ΔQTc were −1.2, 6.6, and 7.2 msec at the three respective dose levels. No telemetric abnormalities or QTc ≥500 msec were observed.

Conclusions: At twice the recommended daily dose, oral ziprasidone showed marginal QTc increase from 160 mg/day, with no significant cardiovascular symptoms or QTc ≥500 msec.

References:


NR562 Wednesday, May 21, 12:00 p.m.-2:00 p.m.

Treatment-Emergent EPS Symptoms During Treatment With Olanzapine or Risperidone Supported by Eli Lilly and Company

Sara Kollack-Walker, Ph.D., Department of Neuroscience, Eli Lilly & Company, Lilly Corporate Center, DC, Indianapolis, IN 46285; Illya Lipkovich, Ph.D., Saeeduddin Ahmed, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to learn about scales to measure EPS in clinical trials and how EPS is related to two commonly prescribed atypical antipsychotic agents.

Summary:

Background: This study examines the dynamic expression of extrapyramidal symptoms (EPS) in patients treated with olanzapine (OLZ) or risperidone (RIS).

Methods: Data from a double-blind, parallel group, controlled 28-week study in psychotic patients comparing OLZ (10–20 mg/d; n=172) and RIS (4–12 mg/d, n=167) were analyzed posthoc using longitudinal repeated measures analysis. EPS were evaluated at baseline and during 28-week treatment period using standard measurement scales and spontaneously reported adverse events. Data were analyzed for all patients, and subgroups of patients with and without EPS at baseline. RIS patients were divided into > or ≤ 6 mg/d modal dose subgroups.

Results: Longitudinal analysis revealed greater reduction in Barnes Global (p=.023) and Simpson-Angus (p<.001) scores following treatment with OLZ compared with RIS. Patients with pre-existing EPS at baseline (>0 score) showed less improvement in Barnes Global (p=.026) and Simpson-Angus (p=.007) scores with RIS. Patients with no EPS at baseline showed greater increases in Simpson-Angus score (p=.020) during treatment with RIS. Improvement in Simpson-Angus score was greater with OLZ compared with RIS at either low or high modal dose.

Conclusions: Olanzapine treatment led to significantly greater improvement in EPS compared to risperidone. Furthermore, olanzapine had a lower liability for treatment-induced parkinsonian symptoms.

References:


NR563 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Clinical Correlates of Weight Gain In First-Episode Patients on Olanzapine
Supported by Eli Lilly and Company
Robert B. Zipursky, M.D., Department of Psychology, University of Toronto Clarke Institute, 250 College Street, Room 732, Toronto, ON M5T 1R8, Canada; Gu Hongbin, Ph.D., Alan I. Green, M.D., Franca Centorrina, M.D., Ira D. Glick, M.D., Jeffrey A. Lieberman, M.D.

Educational Objectives:

At the conclusion of this session, the participant should understand that the weight gain associated with the use of olanzapine in patients with a first-episode of psychosis cannot be predicted on an individual basis.

In order to fully understand the predictors and clinical correlates of antipsychotic-induced weight gain, it is ideal to study patients receiving treatment for a first episode of psychosis. We evaluated 262 patients meeting criteria for schizophrenia, schizoaffective disorder, or schizoaffective disorder who were treated with olanzapine, 5–20mg/day (n=130) or haloperidol, 2–20mg/day (n=132) during the 12-week acute treatment phase of a two-year randomized, double-blind study. Weight gain on olanzapine was not predicted by age, sex, race, previous neuroleptic treatment, or pre-treatment BMI. Using change in BMI as a time-dependent covariate, a hierarchy of survival analysis revealed that greater BMI increase on olanzapine was associated with a higher likelihood of remaining in the study (\chi^2=6.77, p<0.01). Greater clinical improvement at each study visit was also associated with an increased likelihood of remaining in the study (\chi^2=29.4, p<0.001). After controlling for the association between clinical improvement and study continuation, the effect of change in BMI on study continuation was no longer statistically significant (\chi^2=2.34, p=0.13 for change in BMI, \chi^2=12.56, p<0.001 for change in PANSS total score). These results suggest that in patients treated with olanzapine, clinical improvement is a better predictor of study continuation than weight gain.

References:


NR564 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Time of Dosing and Food Effects on Aripiprazole Pharmacokinetics
Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co, Ltd.
Suresh Mallikarajan, Ph.D., Otsuka Maryland Research Institute, 2440 Research Boulevard, Rockville, MD 20850; Daniel E. Salazar, Ph.D., Steven L. Bramer, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to determine that the time of dosing and a high fat meal does not impact on the pharmacokinetics of aripiprazole.

Summary:

Objective: To determine if the time of dosing or a high-fat meal impact aripiprazole pharmacokinetics.

Methods: Data from two studies are presented. In one study, healthy subjects received a single, 20 mg dose of aripiprazole in the morning (AM, n=16) or in the evening (PM, n=16) using an open-label, parallel group design. In another study, subjects received 15 mg aripiprazole in a fasted condition or within five minutes of consuming a high-fat breakfast using a two treatment, three period, replicate cross-over design (N=39) at least 21 days washout between each treatment. In both studies, blood samples were collected and pharmacokinetic parameters determined.

Results: Aripiprazole Cmax was lower and Tmax was delayed following PM dosing compared to AM dosing. However, since total exposure (AUC=\infty) and oral clearance (C1/F) were not statistically significantly different, small changes in Cmax are not considered to be clinically relevant. A high-fat meal did not significantly affect the Cmax or AUC of aripiprazole or its active metabolite, dehydroaripiprazole.

Conclusion: Aripiprazole may be dosed regardless of time of day and without regard to meals.

References:


NR565 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Definitive Evidence That Aripiprazole Is a D2 and 5HT 1A Partial Agonist
Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co, Ltd.
Shaun Jordan, Ph.D., Otsuka Maryland Research Institute, 2440 Research Boulevard, Rockville, MD 20850; Yushihiro Tadori, B.S., Robert D. McQuade, Ph.D., Frank Yocca, Ph.D., Tetsuro Kikuchi, D.V.M.

Educational Objectives:

At the conclusion of this session, the participant should have a better understanding of the partial agonism of aripiprazole at cloned D2 and 5HT1A receptors.

Summary:

Objective: To provide alternative biochemical readouts to support published in vitro evidence that aripiprazole has a mechanism of action at D2 and 5HT1A receptors distinct from other effective antipsychotic drugs.

Methods: The study used [3H]arachidonic acid release and [35S]GTP\gamma S binding assays to estimate the in vitro functional profile of aripiprazole at cloned human D2L and native rat hippocampal 5-HT1A receptors, respectively.

Results: Aripiprazole displayed a potent, partial agonist activity (pEC50 = 8.13 ± 0.23) in stimulation of [3H]arachidonic acid release in CHO cells stably expressing cloned human D2L receptors; this effect was blocked in a concentration-dependent fashion by the selective D2L antagonist raclopride. In comparison, haloperidol,
olanzapine, ziprasidone, clozapine, and risperidone did not stimulate D₂ receptor-mediated increases in [³H]arachidonic acid release. At the 5HT₁₆A receptor, aripiprazole also stimulated [³⁵S]GTPγS binding to rat hippocampal membranes with a potent partial agonist profile. Ziprasidone, but not clozapine, risperidone, or olanzapine, displayed a similar potent, partial agonist profile to that of aripiprazole.

**Conclusion:** The present study provides additional support to existing evidence that aripiprazole is a potent, partial agonist at D₂ and 5-HT₁₆A receptors. Furthermore, the in vitro functional profile of aripiprazole at D₂ and 5-HT₁₆A receptors was distinct from all other antipsychotic drugs tested.

**References:**


**NR567** Wednesday, May 21, 12:00 p.m.-2:00 p.m.

Changes in Clinical Indicators Between Olanzapine and Risperidone Initiators

**Boston University School of Public Health, Center for Health Quality, Outcomes, and Economic Research, and Eli Lilly and Company**

Xinhua S. Ren, Ph.D., Department for Health Quality Outcomes and Economic Research, 200 Springs Road, Bedford, MA 01730; Lewis Kazis, Sc.D., Yu-Hui Huang, M.P.H., Austin Lee, Ph.D., Donald Miller, Sc.D.

**Educational Objectives:**

At the conclusion of this session, the participant should recognize the differential effects of the initiation of olanzapine compared with risperidone on patient outcomes such as patient physical and mental health status and use of health services.

**Summary:**

**Objective:** To compare changes in clinical characteristics of patients with schizophrenia who were initiated on one of two widely prescribed atypical antipsychotics, olanzapine and risperidone.

**Methods:** The study used VA national data on ICD-9-CM codes, health care use, and prescriptions. Changes were measured by clinical characteristics before and after the initiation of each target drug during 1999 and 2000.

**Key Findings:** Compared with olanzapine initiators (N=9,739), patients starting on risperidone (N=8,760) had a 30% greater increase in the overall use of medications for psychiatric conditions (p < 0.001), but greater decrease in the number of non-psychiatric hospitalizations (17%, p < 0.01) and hospitalization days (18%, p < 0.05). For both drugs, patients who were initiated on higher doses (> 20mg for olanzapine; > 6mg for risperidone), as compared with those initiated on lower doses, had a greater increase in the use of other drugs for psychiatric conditions, such as typical antipsychotics, mood stabilizers, and drugs for treating extrapyramidal symptoms.

**Conclusion:** The study suggests that, following initiation, olanzapine initiators have greater improvements in indicators related to mental health (e.g., psychiatric hospitalizations) than risperidone initiators. Whereas risperidone initiators have greater improvements in indicators related to medical health (e.g., non-psychiatric hospitalizations).

**References:**


**NR568** Wednesday, May 21, 12:00 p.m.-2:00 p.m.

Optimal Titration for Quetiapine: A Pilot Study

**Supported by AstraZeneca Pharmaceuticals, L.P.**

Mark A. Smith, M.D., Department of CNS, AstraZeneca Pharmaceuticals, 1800 Concord Pike, Post Office Box 15437,
NR569 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Antipsychotic-Induced Hyperlipidemia Among People With Schizophrenia
Supported by Bristol-Myers Squibb Company
Bruce Lambert, Ph.D., Pharm Admin, University of Illinois, 833 South Wood Street, Chicago, IL 60612-7231; Eskinder Tafessse, Ph.D., William H. Carson, Jr., M.D.

Educational Objectives:
At the end of this session, the participant should be able to describe the relationship between atypical antipsychotic exposure and the development of hyperlipidemia among people with schizophrenia.

Summary:
Introduction: Recent research suggests that certain atypical antipsychotics increase the risk of hyperlipidemia.
Methods: Using Medi-Cal data (1997–2000), a matched case-control study quantified the risk of hyperlipidemia among schizophrenics exposed to antipsychotic drugs (clozapine, olanzapine, risperidone, and quetiapine versus various typicals). Cases (n=4,371) had schizophrenia (ICD9 295), were 18 years or older, were diagnosed with hyperlipidemia (ICD9 272.0–272.4) subsequent to schizophrenia, and were exposed to only one antipsychotic during 12 weeks prior to hyperlipidemia diagnosis. Cases were matched to n=6,052 controls (i.e., non-hyperlipidemic schizophrenic patients on antipsychotic monotherapy, matched on gender and age +/- 8 years). Conditional logistic regression modeled the risk of exposure controlling for age, gender, ethnicity, and exposure to other hyperlipidemia-inducing medications.
Results: Exposure to olanzapine (OR = 1.27, 95% CI 1.15–1.39) and clozapine (OR = 1.17, 95% CI 1.01–1.38) significantly increased the risk of developing hyperlipidemia compared with typicals. Exposure to risperidone (OR = 1.06, 95% CI 0.95–1.18) & quetiapine (OR = 1.13, 95% CI 0.89–1.43) did not. Hypothesis tests comparing the four atypicals to one another revealed that the odds ratio for olanzapine was greater than that for risperidone (p=0.002).
Conclusion: Compared with typical antipsychotics, exposure to olanzapine or clozapine increases the risk of hyperlipidemia among schizophrenia patients.

References:

NR571 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Impact of Comorbid Diabetes and Schizophrenia on Health Care Resource Use
Supported by Pfizer Inc.
Joan Mackell, Ph.D., Pfizer Inc, 235 East 42 Street, New York, NY 10017; Lewis Warrington, M.D.

Educational Objectives:
At the completion of this presentation, the participant will be able to discuss the reported findings from a survey of patients on the impact of comorbid diabetes and schizophrenia on the use of healthcare resources.

Summary:
Introduction: We compared use of health care resources in patients with schizophrenia alone, comorbid diabetes and schizophrenia, and diabetes alone.

Methods: In June 2002, 850 people with schizophrenia, identified through NAMI and CMHCs, completed self-administered questionnaires. Of these, 109 (12.8%) reported comorbid diabetes. For comparison, a random sample of 1,000 type 2 diabetics (18–64 years old) was generated from a similar study of 4,721 people with diabetes. Data on ER visits and hospitalization during the past six months were collected for all respondents. Costs were calculated based on Statistical Abstracts of the United States: 2000 (ER $320/visit; hospitalizations $1,126/day). Gender, age, and race were controlled using multiple regression analysis.

Results: Patients with schizophrenia averaged 3.3 days more hospitalized (p=0.004) than patients with diabetes alone (additional cost, $3,700). Patients with comorbid schizophrenia and diabetes averaged 1.2 ER visits more (p<0.001) and 11.3 days more hospitalized (p<0.001) than patients with diabetes alone (additional costs, $396 and $12,800, respectively), and 1.0 ER visit more (p=0.001) and 8.1 days more hospitalized (p<0.001) than respondents with schizophrenia alone (additional costs, $319 and $9,100, respectively).

Conclusion: Comorbid schizophrenia and diabetes are associated with significantly greater health care resource use and costs of care than diabetes or schizophrenia alone.

References:

NR572 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Assessment of Patients in Use of Haloperidol and Risperidone
Valeria B. Souza, M.P.H., Department of Medicina Clinica, Universidade Federal, Rua Mael Jesuono, 974 Varjota, Fortaleza-Ceara, CE 60175-270, Brazil; Manuela Carvalho, M.D., Ana R. Guedes, Alexandra F. Camdelo, Maria C. Martins, Fabio G. Souza, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate that there was no statistical differences in clinical nor in social status between patients in use of typical (haloperidol) and atypical (risperidone) antipsychotics, but haloperidol cause more extrapyramidal symptoms than risperidone.

Summary:
Objective: This transversal study aims to compare social behaviour, cognitive performance and clinical state of schizophrenic patients treated with typical (haloperidol) and atypical (risperidone) antipsychotics.

Method: The sample consisted of 19 patients taking haloperidol and 29 patients taking risperidone for, at least, six months. Patients met the DSM-IV criteria for schizophrenia. Cognitive assessment was made through the subtests of Wechsler Adult Intelligence Scale (WAIS) battery. The current clinical state was assessed by the Brief Psychiatric Rating Scale (BPRS) and the Abnormal Involuntary Movements Scale (AIMS). For the evaluation of the social behaviour, the Social Behaviour Schedule (SBS) was used. Data were analyzed by the Statistical Package for Social Sciences (SPSS).

Results: There were statistical significances only in the following subtests of the WAIS: digit span backward (t=−2.33; p=0.02) and digit symbol (t=−2.49; p=0.02). According to AIMS, patients treated with haloperidol had more involuntary movements than those treated with risperidone (t=2.67; p=0.01). There were no statistical differences in the BPRS and SBS scores.

Conclusion: In cognitive tests that required more attention, concentration and better psychomotor capacity, patients in use of risperidone had a better performance. However, this drug does not seem to be sufficient to promote changes in the social behaviour.

References:

NR573 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Cognitive Assessment of Patients in Use of Antipsychotics
Valeria B. Souza, M.P.H., Department of Medicina Clinica, Universidade Federal, Rua Mael Jesuono, 974 Varjota, Fortaleza-Ceara, CE 60175-270, Brazil; Manuela Carvalho, M.D., Ana R. Guedes, Alexandra F. Camdelo, Maria C. Martins, Fabio G. Souza, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to differentiate the cognitive effects of typical and atypical antipsychotics in schizophrenia and also to verify that there are no significant differences in cognition among atypical antipsychotics.

Summary:
Objective: This transversal study aims to compare cognitive performance of schizophrenic patients treated with typical (haloperidol) and atypical (risperidone, clozapine and olanzapine) antipsychotics.

Method: The sample consisted of 114 patients, 36 taking haloperidol and 78 taking atypical antipsychotics (risperidone, n=30; clozapine n=32 and olanzapine n=16) for at least, six months. Patients met the DSM-IV criteria for schizophrenia. The assessment of cognitive function was made through subtests of Wechsler Adult Intelligence Scale (WAIS) battery, that analyzes attention, concentration, perceptive activity, motor response, and concep-
tual formation. Data were analyzed by the program Statistical Package for Social Sciences (SPSS).

Results: Tests that differentiated the typical and atypical groups were: similarities \( t=3.82; p=0.00 \), digit span forward \( t=2.42; p=0.02 \), digit span backward \( t=2.88; p=0.00 \) and digit span total \( t=3.24; p=0.00 \), digit symbol \( t=2.60; p=0.01 \) and object assembly \( t=2.70; p=0.01 \). When comparing the three atypical antipsychotics, there were no statistical significances in none of the tests.

Conclusion: Atypical antipsychotics probably contribute to a better cognitive performance of patients treated with them.

References:


NR574 Wednesday, May 21, 12:00 p.m.–02:00 p.m.

Quality of Life of Patients With Schizophrenia: A Randomized, Naturalistic, Controlled Trial Comparing Olanzapine With Typical Antipsychotics in Brazil Supported by Eli Lilly and Company

Mauricio S. Lima, M.D., Dept de psiqui, Federal University, P.O. Box 354, Pelotas 96015-000, Brazil; Jair de Jesus Mari, Ph.D., Anna M.N. Costa, M.D., Neusa Alexandrini, M.D., Salomao R. Filho, M.D., Irismar R. de Oliveira, M.D., Matthew Hotopf, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate that olanzapine’s clinical profile leads to social functioning and quality of life improvement superior to that achieved with conventional treatment.

Summary:

Objectives: (1) To assess the effectiveness of olanzapine for treating schizophrenia; (2) to test the hypothesis that patients on olanzapine have better quality of life than those on typical antipsychotics (APs).

Method: This was a multicenter, naturalistic, randomized, open study that compared olanzapine with conventional APs, at hospitalization and during a nine-month follow-up. Outcome assessors were blind to the allocated drug and to the objectives of the study. The daily dose of APs was determined by the doctors according to their clinical practice routine.

Results: A total of 198 patients were randomly assigned to olanzapine \( n=104 \) and typical antipsychotics \( n=94 \). Patients on olanzapine showed higher improvements on PANSS negative and general psychopathology subscales. When compared with patients on typical APs, patients treated with olanzapine showed higher improvements in most of the SF-36 domains, with statistically significant differences in the following domains; physical functioning, role physical, and role emotional.

Conclusion: Compared with typical antipsychotics, olanzapine has advantages in a naturalistic setting for treating patients with schizophrenia and improving relevant clinical outcomes, such as negative symptoms and quality of life. These findings are highlighted by the naturalistic approach adopted in this trial, as olanzapine was compared with real-world practices in the use of typical APs.

References:


NR575 Wednesday, May 21, 12:00 p.m.-02:00 p.m.

Neuropsychiatric and Neuropsychological Profile of Treatment-Resistant Schizophrenia

Jesus Ezcurra, Ph.D., H. Psiquiatrico Alava-UPR, Alava 43, Vitoria 01006, Spain; Edorta Elizagarate, M.D., Pedro Sanchez, M.D., Ana Blanca Yoller, M.D., Esther Ibarrola, M.D., Natalia Ojeda, Ph.D., Marta Arrasate, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize the neuropsychiatric and cognitive variables that correlate with refractory symptoms in schizophrenia.

Summary:

Introduction: Studies of pathology suggest that cognitive decline is related to the evolution of Schizophrenia. Some authors have even attempted to define clinical subtypes of Schizophrenia according to the neuropsychological type of deficits (mainly confirmed with patients with negative symptoms). The relation has not been described in patients with treatment-resistant schizophrenia.

Methods: Seventy patients with schizophrenia (both criteria DSM-IV and CIE-10) who met Kane’s criteria (1988) for refractory Schizophrenia were evaluated and compared with 70 normal controls. Neuropsychiatric evaluation included the administration of PANNS, BPRS, DAS-WHO, GAF-EEAG, Mania Young Scale, Insight Evaluation—David, Social Premorbid Adjustment (Canada-Spoor), Substance abuse-Likert Scale, and CGI. Cognitive assessment included tests of attention/concentration, memory, language, executive functions, motor abilities, AVD’s, and general intellectual capacity.

Results: Patients obtained significant low levels of cognitive functioning in all neuropsychological measures, except personal orientation. Additionally, the neuropsychiatric profile of the sample, describes three subgroups of patients which authors named: positive, negative (most often) and mixed subgroups, depending on the clinical predominance of symptoms. The three clinical subtypes correlated with a differential cognitive decline profile, stressing attentional deficits; learning, memory, and executive functioning; global cognitive decline.

Among all variables, premorbid general functioning resulted into one of the best predictors for early diagnosis of refractory in the illness.

Discussion: Implications for treatment and rehabilitation are included.

References:


NR576  Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Neurocognition After Two Years Olanzapine or Low-
Dose Haloperidol in FE Psychosis
Supported by Eli Lilly and Company
Richard S. Keefe, Ph.D., Department of Psychiatry, Duke
University, Box 3270, Durham, NC 27710; Larry J. Seidman,
Ph.D., Robert M. Hamer, Ph.D., Deborah Yurgelun-Todd,
Ph.D., Bruce Christensen, Ph.D., Margriet M. Sitskoorn, Ph.D.,
Jeffrey A. Lieberman, M.D.

Educational Objectives:
At the conclusion of this session, the participant should learn
the neurocognitive effects of olanzapine versus low doses of halo-
peridol in patients with first-episode psychosis.

Summary:
Patients in the first episode of psychosis manifest severe neuro-
cognitive deficits, which are correlated with occupational and so-
cial skills and quality of life. The treatment of neurocognitive defi-
cits at the onset of psychosis may have a tremendous impact on
patients’ lifetime level of functioning. Previous work has suggested
that 12 weeks of treatment with olanzapine improves cognitive
function to a greater degree than low dose haloperidol in a first-
episode sample, especially on a measure of vigilance. In this
double-blind study of olanzapine (OLZ) and haloperidol (HAL),
246 (of 263 randomized) first-episode patients were assessed on
a range of neurocognitive tests at baseline. Patients were also
assessed after 12 (N=189), 24 (N=126), 52 (N=89), and 104 (N=
46) weeks of treatment. The mean modal doses of HAL and OLZ
were 4.8 and 10.2 mg/day, respectively. A neurocognitive principal
component comprised of measures of verbal fluency, motor func-
tions, working memory, verbal memory and vigilance improved
more following treatment with OLZ than with HAL at 12 weeks
(P<.05), 24 weeks (P<.05) and 104 weeks (P<.10). OLZ particu-
larly improved vigilance and digit-symbol performance compared
to HAL. The relationship of cognitive change with symptom
change, extrapyramidal symptoms and anticholinergic use in this
trial will be detailed.

References:
1. Keefe RSE, Mohs RC, Bilder RM, Harvey PD, et al: Neurocog-
nitive assessment in the CATIE Project schizophrenia trial:
Development, methodology and rationale. Schizophrenia Bul-
letin, in press.

NR577  Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Safety of Aripiprazole in Patients With Schizophrenia
Supported by Bristol-Myers Squibb Company and Otsuka
Pharmaceutical Co., Ltd.
William B. Lawson, M.D., Department of Psychiatry, Howard
University Hospital, 2041 Georgia Avenue, NW, Washington,
DC 20061; William H. Carson, Jr., M.D., Shirley Lam,
Pharm.D., Neveen Abou-Gharbia, Pharm.D., Ronald N.
Marcus, M.D., Stephen Kaplita, M.S.

Educational Objectives:
At the conclusion of this session, the participant should under-
stand the safety and tolerability profile of aripiprazole in patients
with different racial backgrounds.

Summary:
Objective: To examine the safety and tolerability profile of aripi-
prazole in patients with different racial backgrounds.
with diagnosed anxiety disorders, with normal controls, and to examine this effect on autonomic tone.

References:

NR579 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Glycemic Control and Plasma Lipids in Long-Term Aripiprazole Treatment
Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co., Ltd.
Stephen R. Marler, M.D., Department of Psychiatry, Veterans Administration Greater LA HCCTR, 11301 Wilshire Boulevard, Building 210A, Los Angeles, CA 90073-1003; Stephen Kaplita, M.S., Anutosh R. Saha, Ph.D., William H. Carson, Jr., M.D., Anne Torbeys, Ph.D., Elyse G. Stock, M.D.

Educational Objectives:
At the conclusion of this session, the participant should better understand the effects of metabolic parameters during long-term treatment with aripiprazole.

Summary:
Objective: To examine the effects on metabolic parameters during long-term treatment with aripiprazole, an antipsychotic associated with minimal weight gain.
Methods: Levels of glucose, plasma lipids, and glycosylated hemoglobin (A1C) were determined from fasting blood samples collected in a 26-week trial comparing aripiprazole with placebo for prevention of relapse in patients with chronic stable schizophrenia.
Results: Changes from baseline to endpoint in mean fasting plasma glucose were minimal with both aripiprazole (0.1 mg/dL) and placebo (2.1 mg/dL). A1C decreased by 0.17% and 0.11% in the placebo and aripiprazole groups, respectively. Small decreases in levels of fasting total and LDL cholesterol were observed with aripiprazole and placebo, while plasma HDL cholesterol levels increased slightly in both arms of the study. Median fasting plasma triglyceride levels were reduced by 12 mg/dL and 4 mg/dL in the aripiprazole and placebo groups, respectively.
Conclusion: Aripiprazole was not associated with adverse metabolic changes during long-term therapy. Effects on glycemic control and plasma lipid profile were similar to those of placebo.

References:

NR580 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Cognitive, Affective, and Prosocial Improvement After Switch to Ziprasidone
Supported by Pfizer Inc.
Philip D. Harvey, Ph.D., Department of Psychiatry, Mt. Sinai Medical Center, 1425 Madison Avenue, New York, NY 10029; Antony D. Loebel, M.D., Cynthia O. Siu, Ph.D., Steven J. Romano, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will understand the relationships between improvement in cognitive impairment, affective symptoms, and social engagement in patients with schizophrenia treated with ziprasidone.

Summary:
Introduction: We studied changes in cognition and affective symptoms, their interrelationships, and possible correlative improvement in social engagement in patients switched to ziprasidone.
Methods: In three six-week open-label trials, outpatients were switched from conventional antipsychotics (n=108), olanzapine (n=104), or risperidone (n=58) to ziprasidone (40–160 mg/day) due to suboptimal efficacy or tolerability. Assessments included PANSS and a cognitive battery. Relationships between cognition and improvement in affective symptoms were explored using multiple regression and path analysis methods. The potential role of these variables as mediators of prosocial outcome was also assessed.
Results: All three groups improved significantly on a global score derived from factor analysis of the cognitive battery. On the PANSs cognitive subscale and anxiety-depression cluster, patients switched from conventional and risperidone demonstrated significant improvement from baseline. All three groups improved on the PANSs prosocial subscale, a measure of social engagement. Prosocial symptom improvement was related to changes in cognition and affective symptoms.
Conclusion: Patients switched to ziprasidone from other antipsychotics demonstrated significant improvement in cognition and affective symptoms, which influenced prosocial outcome.

References:

NR581 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Clinical Status of Patients With Schizophrenia in a Naturalistic Setting
Supported by Eli Lilly and Company
Sheila S.M. Assuncão, M.D., Instituto de Psiquiat, Universidade de Sao Paulo, Sao Paulo, IN 46285, Brazil; Beatrice A. Lepine, Ph.D., Anna M.N. Costa, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the actual effectiveness of olanzapine in a naturalistic setting.

Summary:
Objective: Response to antipsychotic treatment among patients with schizophrenia is becoming more important than ever due to the wider range of treatment options. This observational study aims to assess and compare effectiveness of olanzapine with other antipsychotics (APs).
Method: According to the participating psychiatrists, 1,072 Brazilian outpatients with schizophrenia (initiating or changing an antipsychotic) were randomly assigned to two groups: olanzapine and other APs.
Results: Seventy-two percent of patients received olanzapine. All patients were followed for a period of six months, and comparisons regarding psychopathologic and functional status were made between the two groups. Olanzapine-treated patients had a signifi-
cant improvement of total, negative, and depressive symptoms on the Clinical Global Impressions scale (CGI). The number of hospitalizations of olanzapine-treated patients decreased significantly (between baseline and month 3, compared with patients treated with risperidone and typical antipsychotics). Regarding body weight, the body mass index of olanzapine-treated patients did not differ from that of patients treated with other antipsychotics.

Conclusion: Data on olanzapine effectiveness in a naturalistic setting are consistent with findings based on clinical trials. Compared with patients treated with both risperidone and typical antipsychotics, olanzapine-treated patients showed better clinical outcome in a real world.

References:

NR582 Wednesday, May 21, 12:00 p.m.–2:00 p.m.
Effects of Aripiprazole on Excitement and Hostility: Symptoms of Schizophrenia
Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co, Ltd.
Ronald N. Marcus, M.D., Bristol-Myers Squibb, Department of Neurosciences, 5 Research Parkway, Wallingford, CT 06492; Dusan Kostic, Ph.D., Joseph Stringfellow, M.S., Sterling Hardy, M.S.; William H. Carson, Jr., M.D., Elyse G. Stock, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the effect of aripiprazole on the excitement and hostility symptoms associated with schizophrenia.

Summary:
Objective: To examine the effects of aripiprazole, a new antipsychotic with low potential for sedation, on the excitement and hostility symptoms associated with schizophrenia.
Methods: The excitement/hostility cluster was derived by factor analysis of PANSS scores from short- and long-term studies. Analyses were performed on pooled data from patients with schizophrenia or schizoaffective disorder randomized to aripiprazole (n = 885) and placebo (n = 405) in five short-term randomized trials. Long-term data are based on a 52-week study comparing aripiprazole (n = 853) with haloperidol (n = 430) in patients with schizophrenia.
Results: The mean excitement/hostility factor score in five short-term trials increased by 1.29 with placebo and decreased by 0.94 aripiprazole-treated patients (P<0.001). In two fixed-dose trials that included haloperidol arms, the excitement/hostility score was significantly (P<0.001) reduced by both aripiprazole and haloperidol (−1.17 and −1.11, respectively) compared with placebo (+1.48). In the long-term trial, both aripiprazole and haloperidol reduced the excitement/hostility score during the first 8 weeks of therapy (by 2.56 and 2.43, respectively) and the effect was maintained throughout the 52-week trial.

Conclusion: Aripiprazole was more effective than placebo and comparable to haloperidol for reduction of the excitement and hostility symptoms associated with schizophrenia.

References:

NR583 Wednesday, May 21, 12:00 p.m.–2:00 p.m.
A Wellness Education Class for Psychiatric Inpatients
Donna A. Wirshing, M.D., Department of Psychiatry, Greater Los Angeles Healthcare, 11301 Wilshire Boulevard, Building 210, B151, Los Angeles, CA 90073; Rebecca A. Smith, B.A., Stephen R. Marder, M.D., Jennifer L. Churg, B.A., William C. Wirshing, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the impact of an educational intervention on psychiatric inpatients’ knowledge of nutrition and exercise.

Summary:
Objective: To determine the baseline state of nutritional understanding and to assess the learning potential of a heterogeneous group of psychiatrically hospitalized veterans (predominantly middle-aged males with schizophrenia).
Method: Psychiatric inpatients attended one 30-minute interactive presentation addressing the importance of maintaining a healthy weight, proper food choices, managing hunger, and beginning an exercise program. A 12-item knowledge quiz covering the material from the class was administered before and after the session. Information about patients’ eating behaviors and demographics was also collected.
Results: 28 patients completed both pre- and post-tests. The mean score on pre-tests was 84.8% and on post-tests was 89.8% (p = 0.04). 70% percent of respondents expressed a desire to lose weight. 33% of respondents ate meals in their own home or at fast-food restaurants (30%). Most did not prepare their own meals: nearly 60% said they cooked never or rarely.
Conclusions: Psychiatric inpatients can recall material from a brief educational intervention. Future research will be focused upon patients’ ability to apply this knowledge and utilize additional classes to prevent obesity.

References:

NR584 Wednesday, May 21, 12:00 p.m.–2:00 p.m.
Olanzapine Versus PBO for the Schizophrenic Prodrome: One-Year Results
Supported by Eli Lilly and Company; NIMH
Thomas H. McGlashan, M.D., Department of Psychiatry, Yale University, 301 Cedar Street, P O Box 208098, New Haven, CT 06520-8098; Robert B. Zipursky, M.D., Diana O. Perkins, M.D., Jean M. Addington, Ph.D., Scott W. Woods, M.D., Stacy Lindborg, Ph.D., Alan F. Breier, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the potential advantages and disadvantages of
atypical neuroleptic treatment of patients who appear to be at risk of onset of psychosis.

Summary:

**Aim:** This is the first multi-site, randomized, double-blind, placebo-controlled clinical trial testing the safety and efficacy of olanzapine in the treatment of the pre-onset, prodromal phase of schizophrenia. Patients meeting study prodromal symptom and syndrome criteria receive drug or placebo for one year and no pills for a second year. Aims are to test whether drug delays or prevents psychosis onset (conversion), reduces prodromal symptoms, and produces minimal side effects. The one-year results of 60 patients have been unblinded.

**Results:** Fifteen patients developed psychosis according to the study's criteria. Of these, 10 patients were placebo and five were drug (p=0.139). The majority (8 of 15) converted within the first month from baseline. There were no differences between drug and placebo on vital signs or EPS. Weight gain (in kg) was higher for drug (8.0 vs. 0.3, p<0.012). Severity of prodromal symptoms (Scale of Prodromal Symptoms), psychotic symptoms (PANSS), depression (MADRS), and mania (YMS) were compared at 12 weeks, six months, and one year. PANSS, MADRS, and YMS symptom levels were low at baseline and stayed low. Prodromal symptoms were reduced in severity from baseline in the olanzapine arm for all three time points.

**Significance:** At one year olanzapine appears effective in treating prodromal symptoms and is associated with weight gain but not EPS. It reduces conversion to psychosis by 50%, a difference suggestive but not significant. Two-year data are still blinded. Implications for treatment and research will be discussed.

**References:**


**NR585 Wednesday, May 21, 12:00 p.m.-2:00 p.m.**

External Validity of the SQLQ Versus Quality of Life Supported by Lilly Laboratories, A.A., Madrid, Spain

Jose Giner, M.D., Psychiatry, Virgen Macarena, Doctor Fedrani, 3, Seville, ES, Spain; Julio B. Bobes, M.D., Salvador Cervera, M.D., Enrique Baca-Garcia, M.D., Carmen Leal, M.D., Elena Ibanez, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to recognize the factors that influence the quality of life in schizophrenics and will know the Seville Quality of Life Questionnaire.

**Summary:**

**Introduction:** Traditionally, controlling psychotic symptoms was the primary goal of schizophrenia treatment. However, progresses in conceptualization of quality of life (QoL), as a comprehensive measure of patients’ subjective experience, and introduction of atypical antipsychotics have allowed considering more ambitious goals, including control of less psychotic reactive affective symptoms like depression and anxiety, which influence QoL. This presents results of long-term olanzapine treatment in a number of schizophrenics where QoL, affective symptoms, and psychopathology were measured.

**Methods:** One-year prospective study comprising 372 schizophrenics after switching to olanzapine. Seville Quality of Life Questionnaire and Lehman’s structured interview. Simple product-moment correlation coefficients and ordinary least squares regression models were used to evaluate relationship between both instruments.

**Results:** there was a significant improvement in QoL. Moment correlation was moderate in some items and high in others. Regression showed significant contribution of SQLQ for changes in Lehman’s domains, with up to 52% of explanation through the global score. Occupation, place of residence, finances, and legal/safety domains of the Lehman’s interview could be removed without impact on the percentage of explanation. Overall satisfaction, daily activities, family, and social relations domains had important weight, being significant by themselves.

**Conclusions:** The SQLQ has demonstrated a good external validity given the high correlation with the other QoL instrument. Factors influencing QoL in schizophrenics were identified.

**References:**

performance, and consequently reduce reactive affective symptoms. These facts are included in the conceptualization of QoL.

References:

NR587 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Risk Factors for Occurrence of Manic Episodes in Bipolar Patients in the United Kingdom
Supported by Eli Lilly and Company
Henrik Finnern, Ph.D., Lilly Research, Eli Lilly & Company, Er1 Wood Manor, Sunninghill Road, Windlesham GU20 6PH, England, Michael Lothgren, Ph.D.

Educational Objectives:
At the conclusion of this session, the audience will have a better understanding of different risk factors that potential influence the occurrence of manic episodes in patients with bipolar disorder in the U.K.

Summary:
Objectives: To estimate potential risk factors for occurrence of manic episodes in patients with bipolar I disorder (BPDI) in the U.K.
Methods: A retrospective chart review was conducted covering 19 months of observations on a sample of 134 UK patients aged 18 years or over (average age 48.4 years) diagnosed with bipolar disorder.

Results: The annual average of manic episodes were 0.5 for all n=89 BPDI patients in the study compared with 0.92 for patients experiencing a an episode during the study period. Patients in the age group 48–57 had more frequent manic episodes than any other age group with an annual average of 0.86 manic episodes (compared with an average of 1.07 episodes for patients experiencing an episode during the study period). Male patients were found to suffer more frequent manic episodes once they experienced an episode with an annual average of 1.06 compared with a female average of 0.82. On average, 55% of the patients experiencing manic episodes were hospitalised.

Conclusion: Previous manic episode, age, and gender were identified as potential risk factors for occurrence of manic episodes in BPDI patients. Further studies need to assess if these risk factors hold true in larger study samples.

References:

NR588 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Impaired Glucose Regulation in Patients With Schizophrenia
Michael B. Sheikman, M.D., Center for Mental Health Research, University of Massachusetts Medical School, PO Box 528, Shrewsbury, MA 01545-0528

Educational Objectives:
At the conclusion of this course, the participant should be able to identify some risks of developing diabetes in patients with schizophrenia during the treatment.

Summary:
Accumulating evidence in recent literature suggests that the prevalence of Diabetes Mellitus (DM) and weight gain in patients with schizophrenia is greater than expected in the general population and the hospitalized population is particularly at a greater risk. Some antipsychotic medications further increase the chance of developing hyperglycemia, along with weight gain that may cause a long-term medical morbidity. Hyperglycemia is not dose dependent and is reversible on cessation of treatment with clozapine or olanzapine. The mechanisms underlying this glucose dysregulation are not fully understood. It occurs with most atypical antipsychotic drugs, albeit at different degrees. According to the literature, clozapine and olanzapine are more likely to cause these effects, while ziprasidone is least likely. In our study, the incidence of DM in a group of hospitalized patients with schizophrenia treated with clozapine was found to be two of 38 (5.3%). Similarly, three of 42 patients (7.1%) with schizophrenia who were receiving olanzapine, and three of 35 patients (8.6%) with schizophrenia receiving risperidone, were also diagnosed with DM. This is higher than what to be expected in general population.

References:
Conclusions: Social adaptation is a new dimension and target for treatment of schizophrenic patients, which improves following switch from conventional antipsychotics to risperidone.

References:

NR590 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Application of a Medical Clearance Protocol
Leslie Zun, M.D., Emergency YD EPT, Mount Sinai Hospital, 1500 S California, Chicago, IL 60608; Lavonne Downey, Ph.D.

Educational Objectives:
A medical clearance protocol, clinically driven and non-routine-based, has been presented for use in the emergency department to standardize the evaluation of psychiatric patients with behavioral complaints. The objective of the study was to determine if the use of a medical clearance protocol reduce costs and the throughput times for ED psychiatric patients undergoing medical clearance.

Summary:
A medical clearance protocol, clinically driven and non-routine-based, has been presented for use in the emergency department to standardize the evaluation of psychiatric patients with behavioral complaints. The objective of the study was to determine if the use of a medical clearance protocol reduce costs and the throughput times for ED psychiatric patients undergoing medical clearance.


NR591 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Community-Based Detoxification Program Evaluation
James R. Westphal, M.D., Department of Psychiatry, University of California, San Francisco, Box 0852 SFGH Adm, San Francisco, CA 94143; Shelley Johnson, B.S.N.

Educational Objectives:
To evaluate a community-based, residential, medical-assisted detoxification (MAD) program serving an urban, public-sector, triply-diagnosed population using an inpatient program as a control.

Summary:
Background: Detoxification provided by the acute inpatient program was terminated in 6/00, due to budget cuts. The MAD started in July 2001 to continue to meet community need at a lower cost.

Methods: A retrospective review of males utilizing the fifty, first admissions to the MAD in 7/01 and the inpatient program in 7/99. Using an administrative database these variables were collected: age, educational level, marital status, ethnicity, living situation, service utilization for six-month pre and six-month post detoxification.

Results: Demographics reflected a slightly younger more homeless population was served in the community-based program. Other demographic information was not significantly different between the programs. Cost for detoxification services is significantly less when provided in the community. Inpatient utilization decreased after detoxification in the community setting.

Conclusion: Providing medically assisted detoxification in the community effectively decreased cost for initial service to a demographic similar population. When services are provided in the community there is a further shift in health care utilization away from short-supply, costly inpatient services, to less costly community based healthcare services.

NR592 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Community Perception of Schizophrenia in the City of Sao Paulo, Brazil
FAPESP, Sao Paulo Brazil
Erica T.P. Peluso, M.A., Department of Psychiatry, UNIFESP, Rua Dom Paulo Pedrosa 668 AP41, Sao Paulo, SP 05687-001, Brazil; Sergio L. Blay, D.R.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the important differences between the lay perception of schizophrenia and the professional vision on this topic in the city of Sao Paulo, Brazil.

Summary:
Introduction: There is very little information about public perception of schizophrenia in Latin America.

Objectives: to evaluate community recognition of schizophrenia and beliefs about its causes, severity and frequency.

Methods: A representative community survey (n=2000) was undertaken in the city of Sao Paulo (Brazil) using face-to-face structured interviews. A vignette depicting a person suffering from schizophrenia was presented to 500 respondents. They were asked questions about identification of the problem depicted in the vignette, its causes, severity and frequency.

Results: The most frequent answers to the recognition question were depression (23%), psychological problems (13%), mental disorder (11%) and spiritual problems (9%). Only 2% mentioned schizophrenia. Using a ranking approach, the main causes endorsed by the respondents were drug use (22%), isolation (21%), lack of faith in God (9%) and unemployment (8%). Almost half of the respondents (45%) thought it was a very severe problem.
More than half of the respondents (56%) thought schizophrenia was very frequent in the population.

**Conclusion:** There is lack of information about schizophrenia in our population and the level of knowledge must be raised.

**References:**


**NR593 Wednesday, May 21, 12:00 p.m.-2:00 p.m.**

**Galantamine Reduces Caregiver Time for Alzheimer's Patients Living in the Community**

**Supported by Janssen Pharmaceutica Products, L.P.**

Dennis M. Meletiche, Pharm.D., Janssen Pharmaceutica Products, L.P., Titusville, NJ 08560; Gary W. Small, M.D., Susan Bolge, M.A.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to describe the effects of galantamine treatment on caregiver time of patients with Alzheimer's disease living in the community.

**Summary:**

**Objective:** To determine differences in caregiving time between caregivers of Alzheimer's disease (AD) patients receiving galantamine and those receiving no treatment.

**Methods:** The analysis was based on data from the AD Caregiver Project survey. Data were collected using a self-administered questionnaire distributed (December 2001) to a large national sample of unpaid caregivers. Caregiver time was the number of hours spent by the primary caregiver during a typical week. Using linear regression, caregiving times for galantamine and untreated patients were compared. Covariates included patient and caregiver demographics, including employment status and income level, and patient disease severity, functional status, and living situation.

**Results:** Galantamine patients (N=97) differed from untreated patients (N=803) with regard to gender (61% vs 35% males), age (74.1 vs 79.6), and living situation (1% vs 6% living alone). Caregivers of galantamine patients were significantly older (66.3 vs 59.2 years) and more likely to be a spouse (77% vs 33%). After controlling for differences between groups, caregivers of galantamine patients provided 18 fewer hours of care per week than caregivers of untreated patients (95% CI: 3.3-32.5, p=0.016).

**Conclusion:** Relative to untreated patients, galantamine treatment is associated with significantly less caregiving time.

**References:**


**NR594 Wednesday, May 21, 12:00 p.m.-2:00 p.m.**

**Transforming Mental Health Services: Its Impact on Group Home Providers in Montreal, Canada**

Myra Piat, Ph.D., Ultra Specialized Department, Douglas Hospital, 6875 La Salle Boulevard, Verdun, Qb H4H 1R3, Canada; Nicole Ricard, Ph.D., Alain D. Lesage, M.D.

**Educational Objectives:**

At the conclusion of this session participants will (1) learn about the new responsibilities that group home providers have taken on, (2) gain insight into the role that group home providers have in supporting people in the community, and (3) learn about the specific recommendations for improving services to this population.

**Summary:**

**Statement of Problem:** Over the past four decades mental health professionals have used group homes (foster homes) to place deinstitutionalized persons into the community. However, as services evolved, and new forms of housing emerged, group homes and providers have taken on a peripheral role. During the recent re-organization of mental health services (1997-2001) psychiatric hospitals downsized considerably, and discharged patients into group homes. However, group home providers were not informed nor consulted.

**Objectives:** The purpose of this study was to examine the impact of this re-organization on group home providers and their work with severe and persistent mentally ill persons in Montreal, Canada. The fundamental research question was: How do group home providers perceive their role and responsibilities, the type of clientele they care for, and the demands being put on them since the restructing of services? Ultimately, this study would give a "voice" to group home providers, which in turn would improve services.

**Methods:** Thirty semi-structured, in-depth interviews were conducted with group home providers of two major psychiatric hospitals in Montreal. The sampling universe included a total of 1,346 persons with severe mental illness living in 261 group homes. Group home providers were selected according to: (1) the number of years of experience as a provider, and (2) the size of the group home. Interviews were tape recorded and transcribed verbatim. Data analysis was inductive and used a constructivist approach.

**Results:** Group home providers identified both positive and negative impacts resulting from the re-structuring in services. However more negative than positive consequences emerged. Respondents report that patients now being discharged and placed into group homes are inappropriate and require 24-hour supervision. Group home providers argued that their workload has increased and that they are now doing the work previously done by professionals. They also noted the lack of support services as well as unrealistic expectations from professionals.

**Conclusion:** Findings from this study have important implications for supporting group home providers. Specific recommendations are put forth to improve working relationships between providers and mental health professionals.

**References:**


**NR595 Wednesday, May 21, 12:00 p.m.-2:00 p.m.**

**Legal Complications of Substance Use Disorders In Bipolar Disorder**

**Supported by the National Institute of Mental Health**

Joseph R. Calabrese, M.D., Department of Psychiatry, University Hospital of Cleveland, 11400 Euclid Avenue, Suite 222
Memantine Enhances Autonomy in Patients With Alzheimer’s Disease
Supported by H. Lundbeck A/S
Pierre-Michel Llorca, M.D., CMPB-CHU, BP69 Cedex, Clermont-Ferrand 63003, France; B. Rive, Mondher Toumi, M.D.

Objective: Alzheimer’s disease (AD) is characterized by a progressive deterioration of mental and physical functions reducing patient autonomy, which is associated with a decrease in quality of life and predicates institutionalization and additional costs of care. This study sought to assess the impact of memantine on autonomy by using the Activities of Daily Living (ADL) scales.

Method: Autonomy was assessed from the results of a six-month, double-blind randomized trial. Clustering methods (K-means) using basic and instrumental ADL scales (ADCS-ADL) were used to categorize patients into autonomous and dependent groups. The validity of this classification was tested by comparing socio-demographic, clinical, and economic characteristics. In order to estimate the impact of memantine on autonomy, a logistic model controlling confounding factors (age, sex, duration of illness, severity, and autonomy at baseline) was applied.

Results: Dependent patients (n=106) had longer disease duration (p<0.05), poorer MMSE, NPI, SIB scores (p<0.001), and higher total societal cost (p<0.001) than autonomous patients (n=146). For patients who were autonomous before randomization to either memantine or placebo, fewer memantine patients became dependent compared with placebo patients (OR=1.95, p<0.05).

Conclusion: Memantine enhances autonomy in moderately severe and severe AD patients, which could explain the lower societal costs for memantine-treated patients.
Educational Objectives:
At the conclusion of this session, participants should understand basic principles and capabilities of webcam digital recording in a clinical setting.

Summary:
Introductory: Computer video plus webcam technology offers new teaching possibilities. Radiologists collect teaching images; psychiatrists could collect teaching interviews. Conventional video is cumbersome, but now, personal computers, even laptops, can store and edit video. Pocketbook-sized webcams (<$100) can capture audio and medium resolution video. Patient interviews could be recorded with common hardware and small webcams. 

Objective—determine if webcam recording produces teaching quality videos.

Methods: Design—open label. Setting—urban university teaching hospital emergency service. Patients—six week convenience sample of unrestrained patients able to understand a photography consent form. Interventions—webcam and laptop computer were running on a desk during interviews. Outcome measures—patient acceptance, recording intelligibility, storage requirements.

Results: Five of six patients agreed; four of five recordings were of sufficient quality for teaching purposes; recording generates about 10 megabytes a minute. Key findings—only refusal was related to a child custody dispute; only unintelligible recording was due to a quiet patient and a loud fan; one recording fits on a CD-R disk;

Conclusions: Teaching quality videos are feasible using webcams and personal computers. Patients are willing to be recorded, at least in a teaching hospital. Main limitation is webcam audio—separate patient microphones could help.

References:

NR600 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
The Impact of Chronic Illness on Risk of Developing Depression
Anupama A. Krishnan, M.S., Health Outcomes, GSK, 5 Moore Dr., Durham, NC 27709, Li-Ling Chang, Ph.D., Susan Hogue, Pharm.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the association between common chronic illnesses and risk of developing comorbid depression.

Summary:
Depression imposes a significant economic burden and is frequently comorbid with several chronic illnesses. The US Preventive Services Task Force recommends screening adults for depression in clinical practice.

Objective: To determine the association between common chronic illnesses and risk of developing comorbid depression.

Methods: Incident cases of depression (between 7/95 and 12/96) were identified among continuously enrolled members in a national managed care claim and were age and gender-matched to controls without depressive illness in the study period. Exposure of interest was a diagnosis for any one of the following chronic illnesses: Anxiety, Irritable Bowel Syndrome (IBS), fatigue, migraine, asthma and diabetes in the six-months prior to diagnosis of depression.

Results: The odds ratio for the risk of developing depression was statistically significant (p<0.0001) for all associations and highly clinically relevant in patients with anxiety (OR=9.01, 95% CI=1.43, 1.86). The odds ratios and 95% CI for other chronic illnesses were: Diabetes: 1.64 (1.43, 1.86); Asthma: 1.86 (1.65, 2.09); Migraine: 2.61 (2.26, 3.02); IBS: 2.86 (2.27, 3.61); Fatigue: 3.69 (2.36, 4.05)

Conclusions: Presence of a chronic condition increases the likelihood that the person has a depressive disorder. Hence patients with chronic illnesses should be screened regularly for depression.

References:
The Impact of Augmentation and Switching on Costs of Treatment of Depression

Anupama A. Krishnan, M.S., Health Outcomes, GSK, 5 Moore Dr., Durham, NC 27708; Li-Ling Chang, Ph.D., Susan Hogue, Pharm.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to understand the impact of switching/augmentation on the costs of treatment of depression.

Summary:

Treatment of depression frequently requires the use of combination therapy or necessitates a switch between alternative antidepressants.

Objective: To estimate the impact of switching/augmentation on costs in the treatment period and one-year post-treatment period.

Methods: 2655 patients diagnosed with depression between 6/95–12/96, prescribed an SSRI within thirty days of diagnosis and enrolled in a national managed care plan were followed up for one year after discontinuation of anti-depressant treatment. A treatment algorithm based on prescription refill patterns was used to identify completers, switchers and augmenters. Log-transformed linear regression controlling for demographics, comorbidities at baseline was the primary method of analysis.

Results: 21% of the patients required use of a second antidepressant during course of treatment. The adjusted mean one-year post treatment costs for switchers, augmenters and completers were $3415, $4938 and $2728 respectively (F=40.29, p=0.000). The costs/month during the treatment period for switchers, augmenters and completers were $531, $592 and $421 respectively (F=194.37, p=0.000).

Conclusion: Switchers and augmenters incurred higher costs in the treatment and post-treatment period as compared to completers. There is a need for new antidepressants that are effective in a heterogenous population reducing the need to switch/augment antidepressant therapy.

References:


Factors Affecting Rehospitalization Amongst Psychiatric Patients in Singapore

Rathi Mahendran, M.B.B.S., Gen Psychiatry, Int of Mental Health, 10 Buangkok View, Singapore 539747, Singapore; Mythili Subramaniam, M.B.B.S., Siow A. Chong, M.B.B.S.

Educational Objectives:

At the conclusion of this session, the participant should recognize factors affecting rehospitalization in schizophrenia patients.

Summary:

Objective: To study the patterns of readmission in a cohort of first admission schizophrenia patients and to identify demographic and clinical factors that influence frequent readmissions.

Methods: A retrospective analysis of case records was done of first-admission schizophrenia patients during one year (1993) to the hospital. Patients’ records were examined to gather data on clinical, demographic characteristics, and referral to the Community Psychiatry Nursing (CPN) programme. Patients who had only one admission during follow up were compared with those who were defined to be "revolving door patients," i.e., those with four or more admissions in the five years following their initial admission.

Results: The cohort comprised 264 patients of which 78 patients (33.3%) had one admission to the hospital while 56 (23.9%) fulfilled the revolving door criteria. On performing a logistic regression, we found male gender (p = 0.02), shorter duration of illness (p = 0.01), and community psychiatric nurse referral (CPN) (p = 0.006) to be significantly associated with revolving door phenomena.
Conclusions: Our study identified male gender, self harm, short duration of illness and referral to CPN services to be risk factors for “revolving door” phenomena. This may suggest a subgroup of patients whose illness may take a more serious form and where specific interventions may be necessary.

References:

NR604 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Involuntary Commitment and Dangerousness in Veterans With PTSD
National Institute of Mental Health

Marion I. Butterfield, M.D., Department of Psychiatry, Duke-Durham VAMC, 508 Fulton Street, Suite 116A, Durham, NC 27705; Patrick S. Calhoun, Ph.D., Hayden B. Bosworth, Ph.D., Karen M. Siechuchak, M.A., Jeffrey Swanson, Ph.D., Marvin S. Swartz, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to 1) Recognize the high rates of involuntary commitment in veterans with PTSD. 2) Discuss the risks of involuntary commitment and dangerousness in persons with PTSD as compared to other severe mental illnesses.

Summary:
Objective: To examine rates and risks of involuntary commitment in veterans with PTSD compared to other severe mental illnesses (SMIs).

Methods: Veterans (n=399) with PTSD, schizophrenia, schizoaffective or bipolar disorder were consecutively enrolled from a psychiatric inpatient unit. Involuntary commitment and risks of dangerousness to self (e.g., suicidality) or others (e.g., assaultive violence), lifetime trauma exposure, and substance use were assessed.

Results: 152 veterans with PTSD (38%) and 247 (62%) with other SMIs were enrolled. Most were male (91%) and black (55%) mean age, 48. Combat exposure was higher in the PTSD group (90% vs. 34%, p<0.001), but no differences in other lifetime trauma variables were observed. Rates of involuntary commitment were 32% for the PTSD group vs. 56% for the SMI group (p<0.001). The PTSD group was more likely than the SMI group to report a recent history of suicidal ideation (71% vs. 53%, p<0.001), suicide attempts (28% vs. 11%, p<0.01), and self-harm (16% vs. 9%, p=0.05). High rates of dangerousness to others were reported, but the differences were not significant between PTSD and other SMIs; physical fights (39% vs. 36%), number of people physically fought in past year (median=2 for both groups), and recent weapon use (16% vs. 11%). High rates of comorbid alcohol (41%) and drug use disorders (26%) were observed, with no significant differences between groups.

Conclusions: Veterans hospitalized for PTSD are at high risk for involuntary commitment, suicidal ideation, suicide attempts, self-harm, assaultive violence, and dangerousness. Comorbid alcohol or drug use do not fully explain these findings.

References:

NR605 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Item Characteristics and Responses to a Self-Report System Measure
National Institute of Mental Health

Martha Shumway, Ph.D., Department of Psychiatry, UCSF/ SFGH, 1001 Potrero Avenue, Room 7M-W21, San Francisco, CA 94110; George J. Unick, M.S.W., Wynne Bamberg, Tetine Sentell, M.A.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify item characteristics that may negatively impact response accuracy in self report symptom measures.

Summary:
Objective: Standardized symptom measures are central to research and practice. Survey research documents that question characteristics, like length and complexity, affect responses to standardized questions. This study tested the hypothesis that item characteristics are associated with similar effects in symptom measures.

Method: Brief Symptom Inventory (BSI) data from 721 outpatients treated in a psychosocial medicine clinic were analyzed. In regression analyses examining impact of item characteristics on responses, the 52 BSI items were the analysis unit; dependent variables were response effects (choosing the first, last or middle response, repeating the previous response) and response distribution characteristics (mean, standard deviation, item-total correlation with BSI scale).

Results: Item characteristics were significantly predictive of response effects (p=.01). Effects were sufficient to shift mean responses downward and reduce item-total correlations (p=.05).

Conclusions: The BSI, a standardized self-report symptom measure, appears susceptible to the same response effects seen in opinion surveys. With long, complex items, respondents appear to take cognitive “short cuts”, choosing the first or last response, repeating their last response, or leaving the item blank. These effects shift response distributions and could reduce the accuracy, reliability and validity of self-report measures.

References:

NR606 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Psychiatric Comorbidities Among Veterans Treated for Depression

Karen Austin, M.P.H., HSR&D, Veteran's Affairs, 2215 Fuller Road, Ann Arbor, MI 48105; Kiran Khanuja, M.D., Kristen L. Barry, Ph.D., Richard R. Owen, Jr., M.D., Marcia T. Valenstein, M.D.

Educational Objectives:
At the conclusion of this session, participants will appreciate that clinicians frequently recognize and diagnose co-morbid psychiatric conditions among their patients with depression. They will also understand which co-morbidities are diagnosed most frequently. In addition, participants will understand the impact of diagnosed comorbidities on depressed patients’ health care utilization.
Summary:

Objectives: We examined the prevalence of clinicians’ diagnosis of co-morbidities among patients treated for depression, and the association between co-morbid diagnoses and healthcare use.

Methods: We obtained fiscal year 2001 (FY01) data from the VA National Registry for Depression and compared service use among patients diagnosed with depression alone, patients with depression plus one psychiatric comorbidity, and patients with depression and two or more comorbidities.

Results: The majority (54%) of depressed veterans had an additional psychiatric diagnosis; 36% had one co-morbid diagnosis and 17% had two or more co-morbid diagnoses. PTSD and substance abuse were the most commonly diagnosed co-morbid conditions among veterans. Patients with one comorbidity had 1.6 times as many outpatient visits as did patients with depression alone (p<0.0001) and patients with two or more comorbidities had 2.6 times as many outpatient visits (p<0.0001). Patients with psychiatric comorbidities were more likely to have a psychiatric hospitalization than patients with depression alone (p<0.0001).

Conclusions: Consistent with the epidemiological literature, clinicians frequently recognize and diagnose comorbid psychiatric disorders among patients with depression. Comorbidities are associated with higher services use, suggesting greater disease burden. Since comorbid depression is the norm, guideline developers should consider emphasizing the treatment of comorbid conditions among patients with depression.

References:

NR607 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
The Pharmacological Treatment of Veterans With PTSD and Depression
Frederic C. Blow, Ph.D., HSR&D, Veteran’s Affairs, 2215 Fuller Road, Ann Arbor, MI 48105; Kiran Khanuja, M.D., Marcia T. Valenstein, M.D., Karen Austin, M.P.H., Israel Liberzon, M.D.

Educational Objectives:
At the conclusion of this session, participants will understand the similarities and differences in the pharmacological treatment of patients with depression alone and patients with comorbid PTSD and depression in clinical settings. Participants will also be able to evaluate these treatment differences in the context of current guidelines and research evidence.

Summary:
Objectives: We examined differences in the pharmacological management of patients with comorbid depression and PTSD and patients with depression alone.

Methods: Fiscal year 2001 data were obtained from the VA National Registry for Depression for patients with comorbid depression and PTSD (n=45,834) and patients with depression alone (n=141,955). We examined the use of psychotropic medications, including antidepressants, antipsychotics, and benzodiazepines among these groups of patients.

Results: Comparable percentages of patients with depression alone (85%) and patients with comorbid depression and PTSD (91%) were treated with antidepressants. However, patients with comorbid depression and PTSD were much more likely to receive antipsychotic medication. Twenty percent of patients with PTSD and depression, but only 8.8% of patients with depression alone received antipsychotic medications. Most comorbid patients receiving antipsychotics (>80%) were treated with an atypical agent, and most treatment was long term (average of 249 days).

Conclusions: Antipsychotic medications appear to be widely used among patients with comorbid PTSD and depression despite their high costs and potentially problematic side effects. Only one published randomized controlled trial supports the efficacy of this approach. Additional research examining the efficacy of this widespread practice is urgently needed.

References:

NR608 Wednesday May 21, 12:00 p.m.-2:00 p.m.
Patterns of Health Resource Use in Subjects With Bipolar Disorders
Supported by GlaxoSmithKline
Mark A. Frye, M.D., Department of Psychiatry, University of California at Los Angeles, 300 UCLA Medical Plaza, Suite 1544, Los Angeles, CA 90095; Joseph R. Calabrese, M.D., Robert M.A. Hirschfeld, M.D., Michael L. Reed, Ph.D., Karen D. Wagner, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the health resource utilization patterns associated with a positive MDQ screen for bipolar disorder.

Summary:
Objective: To evaluate consultation, diagnostic, and treatment patterns associated with bipolar disorders (BPD) in the U.S.

Method: 3059 subjects identified from a large prevalence study of BPD were surveyed and matched to scores on the Mood Disorders Questionnaire (MDQ) and 2000 U.S. Census data. Health resource utilization data, including medical consultation, diagnostic patterns, and medication and alternative remedy use were collected.

Results: Survey response rate was 80% (1167 MDQ+, 1283 MDQ-). Although significantly more subjects who screened positive for BPD had consulted a healthcare provider for their symptoms compared with MDQ subjects (54% vs 26%, p=0.016), 46% had never consulted a provider. Among MDQ+subjects, 18% had received a diagnosis of BPD from a healthcare provider, 41% were diagnosed with another disorder, and 41% had no psychiatric diagnosis. Subjects who screened positive and received a diagnosis of BPD used the following medications alone or in combination: antidepressants (52%), mood stabilizers (32%), and/or atypical antipsychotics (15%).

Conclusions: Large proportions of subjects who screened positive for BPD had not consulted healthcare providers for their bipolar symptoms and many had not received treatment for possible BPD, regardless of consultation. Use of screening instruments and appropriate diagnostic and treatment strategies for BPD may improve access to psychiatric care.

References:

NR609 Wednesday May 21, 12:00 p.m.-2:00 p.m.

Health Resource Utilization in Bipolar Depression Compared to Unipolar Depression and Healthy Controls

Supported by GlaxoSmithKline

Mark A. Frye, M.D., Department of Psychiatry, University of California at Los Angeles, 300 UCLA Medical Plaza, Suite 1544, Los Angeles, CA 90095; Joseph R. Calabrese, M.D., Robert M.A. Hirschfeld, M.D., Michael L. Reed, Ph.D., Karen D. Wagner, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to compare and contrast the health resource utilization patterns associated with bipolar depression to that of unipolar depression and healthy controls.

Summary:

Objective: To examine the patterns of health resource utilization in bipolar depression (BP-D), unipolar depression (UP-D), and healthy controls.

Methods: A self-administered survey was completed by a sample of subjects who had previously participated in a general population survey. Subjects who screened positive for bipolar disorder (MDQ+) or reported a diagnosis of bipolar disorder and depression were considered BP-D (n=395). The UP-D (n=794) group reported a diagnosis of depression, were MDQ-, and did not report a diagnosis of bipolar disorder. The healthy control group (n=1612) consisted of those reporting no psychiatric conditions. Results were adjusted for demographic differences among groups.

Results: Depression severity was significantly (p<0.01) worse in BP-D vs UP-D. Compared to UP-D subjects, BP-D subjects consulted a healthcare provider earlier (age 25 versus 33, p<0.01), were more likely to report a psychiatrist or psychologist consult, psychiatric hospital admission, PC visit, EF/urgent care use and social service use (p=0.01 for all). Those with BP-D were also more likely to report drug or alcohol abuse (p<0.01) and other comorbid psychiatric conditions (anxiety, panic, eating disorder, all p<0.01).

Conclusions: BP-D is associated with more severe depression, medical comorbidities, and emergency/urgent care use than UP-D or healthy controls.

References:

NR610 Wednesday, May 21, 12:00 p.m.-2:00 p.m.

Comparison of Olanzapine Versus Quetiapine in the Treatment of Hospitalized Patients With Schizophrenia

Supported by Eli Lilly and Company

Peter F. Wang, M.D., Pharm Research, Premier Healthcare, 2320 Cascade Point Boulevard, Charlotte, NC 28266; Zhongyun Zhao, Ph.D.

Educational Objectives:

At the conclusion of the presentation, participants should be able to recognize the relative cost and effectiveness of olanzapine versus quetiapine in the treatment of inpatients with schizophrenia.

Summary:

Objective: To compare pharmacotherapy patterns and treatment outcomes for olanzapine versus quetiapine-treated hospitalized patients with schizophrenia.

Methods: Hospitalized olanzapine- and quetiapine-treated patients discharged with schizophrenia (ICD-9: 295.xx) between 01/1999 and 09/2001 were identified using Premier's Perspective database, the largest U.S. hospital drug utilization database. Outcome measures include use of other antipsychotics, mood stabilizers, antidepressants, anxiolytics, and hypnotics; length of stay (LOS); and total treatment costs were analyzed by regressions, controlling diagnoses, illness severity, and patient and institution characteristics.

Results: Of 9,433 patients (54.8% male, mean age 41.5 years), 6,699 were olanzapine treated and 2,734 quetiapine treated. After adjusting for confounding factors, olanzapine-treated patients used fewer psychotropic agents (~0.36, p<0.0001) and were less likely to switch to or augment with other atypical antipsychotics (odds ratio (OR)=0.71, 95% confidence interval (CI)=0.62-0.81). Olanzapine-treated patients were less likely to be treated with typical antipsychotics (OR=0.77, CI=0.70-0.85), mood-stabilizers (OR=0.84, CI=0.77-0.93), anxiolytics (OR=0.67, CI=0.60-0.74), or anti-Parkinsonian agents (OR=0.87, CI=0.79-0.98). There was no between-group difference in antidepressant or hypnotic use. Total costs for olanzapine-treated patients were lower (~$678, p<0.0001) as the result of shorter LOS (~11.4%, p<0.0001).

Conclusions: Compared with quetiapine, olanzapine treatment for hospitalized patients with schizophrenia was associated with more favorable pharmacotherapy patterns, shorter LOS, and lower costs.

References:

NR611 Wednesday, May 21, 12:00 p.m.-2:00 p.m.

Changes in Health Care Utilization for Patients With Major Depression and a Comorbid Anxiety Disorder After Treatment With Sertraline, Fluoxetine, or Paroxetine

Supported by Pfizer Inc.

James M. Russell, M.D., Department of Psychiatry, University of Texas at Galveston, 404 University Boulevard, Galveston, TX 77555-0197; David Harrison, M.A., Roma Trelia, M.H.A.

Educational Objectives:

At the conclusion of this session, the participant should recognize that comorbid anxiety symptoms associated with depression may affect healthcare utilization patterns and have implications regarding treatment choices.

Summary:

Background: Previous studies have shown a decrease in emergency room utilization in patients with panic disorder treated with
Benzodiazepine Use Among Veterans Treated for Depression

Marcia T. Valenstein, M.D., Marcia T. Valenstein, M.D., HSR & D. Veterans Affairs, 2215 Fuller Road, Ann Arbor, MI 48105; Karen Austin, M.P.H., Helen C. Kales, M.D., Karen Austin, M.P.H., Helen C. Kales, M.D., Frederic C. Blow, Ph.D., Frederic C. Blow, Ph.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to recognize predictive factors for being satisfied by the evaluation in patients and GP.

Summary:
- Introduction: A central task for the specialist service in psychiatry is to make evaluations of patients referred from the general practitioners (GP). A study from England showed that evaluations within a short time and continuity of follow-up, lead to high ratings of patients' satisfaction. The Collaborative Working Group on Shared Mental Health Care in Canada have summarised three opportunities for better collaboration as seen from GP point of view. The aim of this study is mapping change in mental symptom load and predictive factors for being satisfied by the evaluation in patients and GP.
- Methods: From a rural area of 80,000 inhabitants in Norway all patients referred from GP during 1997–1999 who received four or fewer sessions (N=160) were eligible. Ninety-one (57%) patients completed and returned a questionnaire and a SCL-90-R form. Thirty-eight (79%) GP gave their opinions on 128 (80%) patient evaluations. Analyses were performed by means of paired t-test (changes in SCL-90-R from evaluation to follow-up) and logistic regression (predictor factors for being satisfied).
- Results: A mean reduction in Global Symptom Index (GSI) from 1.6 at evaluation to 1.1 at follow-up (95% CI: 0.29 – 0.66, p < 0.001) Patients' work/sick leave status was found as single predictor factor for the patients experience of the evaluation to be "of great/very great use" (OR 4.43, 95% CI: 1.78 – 10.99, p = 0.001). No predictive factors were found for being satisfied by the evaluation in GP.

Conclusion/Discussion: When treatment capacity is limited, patients being at work may benefit from an evaluation.
References:

NR614 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Psychiatric Reform in Brazil
Universidade Federal do Ceara—Brasil
Fabio G. Souza, M.D., Department of Medicina Clinica, Universidade Federal do Ceara—UFC, Rua Manoel Jesusino, 974 Varjota, Fortaleza Ceara, CE 60175 270, Brazil; Maria C. Martins

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate how the Brazilian psychiatric system evolved since the publication of the first state law in 1992.

Summary:
Objective: This study sets out to evaluate the ongoing psychiatric reform in Brazil.
Method: The number of hospitals, beds, rate of beds per 1,000 inhabitants, hospital admissions, length of hospitalization and the availability of alternative services in Psychiatry from 1992 to 2001 were chosen to be the parameters of analysis of the psychiatric care in Brazil.
Results: It is observed that in Brazil, from 1992 to 2001, there was a steady decrease in the following parameters: psychiatric beds (from 90,160 to 68,891), rate of psychiatric beds per 1,000 inhabitants (from 0.61 to 0.41), psychiatric hospital admissions (from 428,600 to 357,538) and length of hospitalization in psychiatric hospitals (from 62.3 days to 30.1 days). The number of psychiatric hospitals also declined (from 313 in 1991 to 260 in 2001), while there was a parallel increase in psychiatric day-hospitals admissions (from 99 in 1994 to 22,183 in 2001) and in the number of centers for psychological and social attention (from 167 in 1998 to 315 in 2001).
Conclusion: The reduction in the number of hospitals in Psychiatry has reached higher proportions than the development of community-based services and programs for the rehabilitation and resettlement of patients in the community.

References:

NR616 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
A Simple Qualitative Procedure for Qualitative Outpatient Satisfaction Assessment
Regie Regionale de la Sante et des Services de Montreal. Fonds de la Recherche du Quebec
Michel Perreault, Ph.D., Department of Psychiatry, Douglas Hospital, 6875 Boulevard Lasalle, Montreal H4H 1R3, Canada

Educational Objectives:
At the conclusion of this session, the participant should be able to (1) recognize strength and weaknesses of standard assessment procedures used for patient satisfaction evaluation, (2) identify basic aspects of content analysis, (3) apply the procedure that will be described for patient satisfaction assessment.

Summary:
Standardized scales present a number of limitations for patient satisfaction assessment: limited usefulness of global scores, content not always suited for the services to evaluate, and tendency to generate high satisfaction scores. Perreault et al. (1993) have suggested a qualitative method based on personal interviews to address these limitations. In a context of limited resources, the objective of this study is to validate the same procedure with self-administered questionnaires.

Method: survey design with a random sampling of 243 patients from two outpatient psychiatric clinics of the Douglas Hospital, in Montreal. A five-category content analysis grid was used. Comments were also categorized to create a trichotomized satisfaction score, for parametric analysis. Convergent validity was tested with the OQOS (Perreault et al., 2001), a multidimensional satisfaction scale.
Results: As expected, open-ended questions have generated significantly lower scores than the standardized scale. In comparison with personal interviews, the number of comments emitted to open-ended questions was less than a half and answers were shorter. Scores generated were strongly correlated with the QOQS.

Conclusion: The procedure appears useful for the identification of the main sources of patient dissatisfaction. It can also generate indicators comparable to the scores of standardized scales.

References:

NR617 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Prevalence of Hepatitis-A, Hepatitis-B, and HIV Among Hepatitis-C Seropositive State Hospital Patients: Screening Results From Oregon State Hospital
Jonathan M. Meyer, M.D., Psychiatry, VA SDH S, 3350 La Jolla Village Dr. 116-A, San Diego, CA 92161

Educational Objectives:
At the conclusion of this session, the participant should be able to appreciate the high prevalence of hepatitis C virus (HCV) and HIV among chronically mentally ill inpatients, and the need to screen for hepatitis A and B viruses among HCV positive patients.

Summary:
Background: Multiple studies have shown that individuals with severe mental illness are at increased risk for acquired infection with human immunodeficiency virus (HIV), hepatitis B (HBV) and hepatitis C (HCV) viruses. Moreover, patients with chronic HCV infection are at risk for fulminant hepatitis from concurrent infection with hepatitis A virus (HAV) or HBV; “but there is no data on the prevalence of HIV, HAV or HBV in chronically hospitalized US psychiatric patients without mental retardation who have HCV seropositive.” To address this issue, a comprehensive screening program was commenced at Oregon State Hospital beginning in 1999.

Method: The computerized records of all nongeriatric adult inpatients at Oregon State Hospital on April 23, 2001 were reviewed to assess physician compliance with screening, and the prevalence of infection with HIV, HAV, HBV, and HCV.

Results: Of the 535 patient records reviewed, 95% were screened for HCV, of which 20.3% were seropositive. Among HCV seropositive patients, only 1.9% were not screened for HAV and HBV, but 23.3% were not tested for HIV. In the HCV seropositive group, 35.9% were HAV positive, 49.5% HBV positive and 1.9% HIV positive.

Conclusions: High physician compliance rates can be achieved with voluntary screening programs for hepatitis viruses in state hospital settings, but more effort is needed to improve HIV testing rates. Chronic inpatients have high HCV prevalence rates, and may be at risk for complications unless vaccinated for HAV and HBV.

References:

NR618 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Impact of Antidepressant Use on Utilization of Medical Services in Obesity
Tanis L. Adey, M.D., Psychiatry Department, Health Sciences Center, 300 Prince Philip Drive, St John’s, NF A1B 3V6, Canada; Samra Mian, B.S.C., Tamar El-Tahan, B.S.C., Caroline MacCallum, Yvonne Tobin, R.N., Proton Rahman, M.D.

Educational Objectives:
Our objective is to create awareness of the increased utilization of general medical services among obese subjects with coexisting depressive/anxiety symptoms as assessed by current antidepressant use.

Summary:
Objective: To determine if coexistent depressive/anxiety symptoms as assessed by current antidepressant use, contributed to increased utilization of general medical services.

Method: Consecutive subjects enrolling for a population based genetic study in obesity (defined as BMI > 30) were used in our study. All subjects were assessed using a standardized protocol. Subjects were asked specifically about current antidepressant use. Demographic information, physical activity level, and coexisting medical conditions were recorded. Utilization of health care services was assessed by having subjects recall visits to family physicians, specialists, diagnostic tests, and hospitalizations over the preceding three months and systematically recorded.

Results: Of the 750 obese subjects enrolled, 21% were on antidepressants. When comparing 161 subjects on antidepressants versus 589 without, those on antidepressants were more likely to be females (p=0.005), sedentary (p=0.015), obese (p=0.004), hypertensive (p=0.004), and experience arthralgias (p=0.0003). They also encountered more visits to family doctors (p=0.0002), specialist (p=0.003), diagnostic tests (p=0.04), and hospitalizations (p=0.02). The increase in health care costs in those on antidepressants remained significant after adjusting for differences in age, sex, BMI, and concurrent medical illness by ANCOVA (p=0.015).

Conclusion: Antidepressant use in obese subjects is common and associated with significant increase in general medical services.

References:

NR619 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Antipsychotic Treatment Patterns and Costs Following New Onset of Diabetes Mellitus Among Medicaid Schizophrenic Patients
Supported by Bristol-Myers Squibb Company
Daniel E. Casey, M.D., P3 MireCC, Portland VA Medical Center, 3710 SW, U.S. Veterans Hospital Road, Portland, OR 97239; Hong Li, Ph.D., Allan Z. Safierman, M.D., Reg Waldeck, Ph.D., Mary J. Kujawa, M.D., Patricia Hines, Taro Iwamoto, Ph.D.
Summary:

Objectives: Diabetes has been associated with the use of certain antipsychotics. We examined antipsychotic treatment patterns and costs for six months pre- and post new-onset diabetes mellitus (NODM) among adult schizophrenic California Medicaid patients.

Methods: The following entry criteria were defined: (1) primary diagnosis of schizophrenia followed by single-agent use of clozapine, olanzapine, risperidone, or haloperidol for six months prior to NODM; (2) continuous eligibility six months pre- and post NODM. Antipsychotic treatment patterns and costs pre- and post NODM were compared.

Results: Monotherapy regimens among 829 eligible patients were: clozapine (15.7%), haloperidol (24.4%), risperidone (24.2%), and olanzapine (35.7%). During the first three months post NODM, ≥ 65% of all patients remained on antipsychotic monotherapy. In the following three months, 85.4% of clozapine, 54.9% of haloperidol, 65.2% of risperidone, and 64.9% of olanzapine remained on monotherapy. Mean costs pre- and post NODM were: $1,532 to $1,643 for clozapine, $2,170 to $2,592 for olanzapine, $2,104 to $2,305 for risperdone, and $1,550 to $2,173 for haloperidol. Cost increases were attributed to increased hospitalization, physician, and anti-diabetic use.

Conclusion: NODM alters antipsychotic monotherapy treatment patterns and direct medical costs in the first six months following NODM. Regimens not associated with NODM are desirable.

References:

NR620 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Inadequate Antidepressant Use Predicts Premature Statin Discontinuation

Jeffrey B. Weilburg, M.D., Department of Psychiatry, Massachusetts General Hospital, 55 Forest Street, Boston, MA 02114; Richard W. Grant, M.D., Kathleen M. O’Leary, B.A., James B. Meigs, M.D., Randall S. Stafford, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the potential impact of antidepressant treatment adequacy on adherence to statin medications.

Summary:

Background: Patients with depression have lower rates of adherence to treatment regimens for co-morbid medical disorders than do patients without depression.

Objective: We hypothesized that patients who receive antidepressant treatment that is inadequate are more likely to have poor adherence to treatment regimens for other co-morbid medical disorders.

Methods: Persistence in statin therapy was assessed using pharmacy claims (7/1/99–6/30/02) from patients in an HMO and cared for by physicians affiliated with Partners Community Health Care. Antidepressant trials were defined as inadequate if they were below minimum guideline standards for dose and duration. We determined persistence in statin therapy for six months and 12 months after initial prescriptions, comparing patients receiving adequate vs. inadequate antidepressant treatment.

Results: Persistence with statin treatment for > 6 months was greater among patients with adequate vs. inadequate antidepressant treatment (76% vs. 66%, N = 1028, p < .001). Persistence for > 12 months was also greater among adequately vs. inadequately treated patients (59% vs. 47%, N=902, p < .001).

Conclusions: Failure to meet minimum guideline standards for antidepressant use (i.e. inadequate antidepressant treatment) has a negative impact on the treatment of elevated cholesterol with statins. Antidepressant treatment adequacy may be a factor that influences patient adherence to treatment for other medical disorders and should be further evaluated.

References:

NR621 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Effectiveness of Fluoxetine Weekly Compared to Fluoxetine Daily in General Practice

Tulio R. Ortega, M.D., Department of Pharmacy, Suny at Buffalo, 36 Forest Meadow, Rochester, NY 14624; Terrance J. Bellnier, M.P.A., Kashinath B. Patil, M.D., Adam Decatur, Ph.D., Shyam D. Karki, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify the importance of improving medication compliance by reducing doses administered.

Summary:

Objective: All chronic diseases have adherence as an obstacles to treatment. Consequences can include relapse, suicide, and comorbid illnesses. These consequences can have significant economic burden on society. We evaluated the effectiveness and compliance of Fluoxetine 180 mg (2 x 90 mg tablets) once a week compared to Fluoxetine 40 mg daily in general practice.

Method: Thirty patients stabilized on fluoxetine 40 mg daily for six months were evaluated in a mirror image design. They were switched to fluoxetine 180 mg (2 x 90 mg tablets) once a week. Serum drug concentration, Clinical Global Impression-Severity (CGI-S), compliance and patient attitude survey were obtained one month before and after the switch.

Results: Subject Characteristics: 41.7 ± 11.7 years, 8 males, DSM IV criteria for major depression, duration of illness was 8±3 years.

Fluoxetine/Norfluoxetine (ng/ml) 261±185 295±206 P= .11 (t=1.71, df=29)
CGI-S 2.6±0.7 2.8±0.7 P= .26 (t=1.14, df=29)
Compliance 73.6% 91% P=.0001 (t=7.86, df=29)

95% of the patients agreed that weekly dosing was preferred over daily.

Conclusion: Our evaluation indicates that once a week dosing is equally effective as a daily dose in the management of major depression. Significant improvement in compliance can only have a positive impact on health outcome and costs.

References:
NR622  
Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Use of the Duke Psychiatric Common Data Repository for Clinical Research
Supported by Wyeth Research

Kenneth R. Gersing, M.D., Psychiatric Informatics Program, Duke University, 3525 Hospital South, Durham, NC 27710

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the use of a clinical data repository for clinical research; and understand how frequently clinicians enter tolerability issues into this automated clinical information system.

Summary:
Objective: The psychiatric common data repository (PCDR) at Duke Medical Center was evaluated to understand how frequently clinicians entered antidepressant tolerability issues into this information system.

Methods: Patients with major depressive disorder (MDD) treated with venlafaxine or selective serotonin reuptake inhibitors (SSRIs) between 8/9>7/02 were retrospectively identified using ICD-9 codes (296.2x, 296.3x) and prescription claims. Clinicians were required to enter patient diagnosis, medication administered, and tolerability issues into the PCDR within two weeks for reimbursement purposes. The frequency of tolerability issues represents the proportion of patients in each group for whom ≥ 1 report of a given issue was entered.

Results: A total of 137 patients were treated with venlafaxine (15 immediate-release, 122 extended-release [XRI]) and 399 with SSRIs (134 sertraline, 100 fluoxetine, 95 citalopram, 62 paroxetine, eight fluvoxamine). Tolerability issues entered by clinicians included sexual dysfunction (5.8% vs. 7.8%), weight gain (0.73% vs. 2.0%), dry mouth (2.2% vs. 2.0%), headache (0.73% vs. 1.3%), nausea (2.2% vs. 1.6%), sedation (2.9% vs. 1.5%), or tremor (2.2% vs. 0.5%) for the VEN/VEN XR and SSRI groups, respectively.

Conclusions: Our results suggest areas for future research and inquiry as the PCDR evolves. Clinicians entered tolerability issues infrequently for patients treated with VEN/VEN XR or SSRIs.

References:

NR624  
Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Pain-Related Diagnoses and Treatment in Patients With Anxiety Disorders
Supported by Wyeth Research

George J. Wan, Ph.D., Health Outcomes, Wyeth Research, 555 East Lancaster Avenue, St. Davids, PA 19087; Erika C. Geissler, Trent McLaughlin, Ph.D.

Educational Objectives:
To understand that pain-related diagnoses are commonly associated with anxiety disorders and to learn that treatment of physical and emotional symptoms is an important consideration in management of anxiety disorders.

Summary:
Objective: To describe pain-related diagnoses and treatment in patients with anxiety disorders.

Methods: Retrospective analysis was conducted using medical and pharmacy data (n=6,647; 26 US health plans) from the PharoMetrics Integrated Outcomes database. Data were collected for 12 months before and after the first anxiolytic prescription date during the index period (1/1/98-12/31/00). Sample included patients with an ICD-9 diagnosis of anxiety disorder, and their original anxiolytic prescription refill within 120 days. ICD-9 codes, medical and prescription data identified the existence of pain-related diagnoses and treatment.

Results: Most common anxiety diagnoses were anxiety not otherwise specified (67%), panic disorder (14%), and generalized anxiety disorder (13%). The most prescribed anxiolytics were benzodiazepines including alprazolam (43%) or lorazepam (27%). Chest pain (21%) was the most common pain-related diagnosis comorbid with anxiety disorders followed by abdominal pain (18%), joint pain (14%), headache (11%), and dyspnea (11%). More than half of all patients with anxiety disorders (53%) had at least one of these pain-related diagnoses. Nearly half of all patients with anxiety disorders received codeine-containing products (30%) or non-narcotic analgesics (16%).
Conclusions: Pain-related diagnoses are commonly associated with anxiety disorders. Treatment of physical and emotional symptoms is an important consideration in management of anxiety disorders.

References:

NR625 Wednesday, May 21, 12:00 p.m.-2:00 p.m.

Creativity Related to Dislike of Simplicity and Symmetry Rather Than Like of Complexity and Asymmetry
National Alliance for Research on Schizophrenia and Depression
Connie M. Strong, Ph.D., Department of Psychiatry, Stanford University, 401 Quarry Road, Room 2124, Stanford, CA 94305-5723; Jean-Frederic Aboudarham, Ph.D., Terence A. Ketter, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that enhanced creativity in bipolar disorders patients and creative subjects may be more related to the ability to express dislike rather than like during artistic evaluations, perhaps due to negative affective traits.

Summary:

Objective: To investigate the relative contributions to creativity of negative (disliking simplicity and symmetry) compared with positive (liking complexity and asymmetry) artistic discriminations.
Method: 49 euthymic bipolar disorder patients (BP), 25 euthymic (unipolar) major depressive disorder patients (UP), 47 healthy controls (HC), and 32 creative discipline graduate student controls (CC) completed the Barren-Welsh Art Scale (BWAS). Negative (BWAS-DISLIKE) and positive (BWAS-LIKE) discrimination subscales were examined in relationship to five personality/temperament factors, and across groups.
Results: BWAS-DISLIKE correlated with negative affective traits (r = 0.39, p < 0.0001), and was 88% to 90% (p < 0.001) higher in BP and CC (but not UP) than HC. In contrast, BWAS-LIKE correlated with openness to experience (r = 0.26, p < 0.002), but was only 9% to 17% (p = NS) higher in BP and CC than HC.
Conclusion: The ability to express dislike (of simplicity and symmetry) and like (of complexity and asymmetry) in the BWAS may be related to negative affective traits and openness to experience, respectively. However, enhanced creativity in BP and CC appeared more related to ability to express dislike than like, consistent with our prior observation that negative affective traits contribute importantly to enhanced creativity in BP and CC.

References:

NR626 Wednesday, May 21, 12:00 p.m.-2:00 p.m.

Effect of Medical Student Attitudes of a One-Week Addiction Site Rotation
George W. Christison, M.D., Psychiatry Department, Loma Linda University, 11374 Mountain View Avenue, Loma Linda, CA 92354; Mark G. Haviland, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to explain the need for positive addiction treatment experiences in medical education, and discuss the effect one week on an addiction site has on students' regard for patients with alcoholism.

Summary:

Introduction: Medical students need positive clinical experiences with substance-abusing patients to counteract medical education's usual effect of increasing the stigma associated with addiction diagnoses. In previous work (that established the reliability and validity of a new attitude scale, the Medical Condition Regard Scale [MCRS]), we reported that students with no exposure to addiction treatment in a psychiatry clerkship showed no change in regard for patients with alcoholism. In contrast, three weeks of exposure produced significant increases in regard for such patients, with a medium effect size. We hypothesized that one week of exposure would produce a similar-sized improvement in attitudes toward alcohol-dependent patients.
Method: Using the MCRS, attitudes toward patients with alcoholism were examined in 134 third-year medical students on the first and last clerkship day. All students spent one of the clerkship's six weeks on an addiction treatment site.
Results: Students' ratings of regard for patients with alcoholism (mean MCRS scores) increased significantly (p < .05), with a small-to-medium effect size (d = .37).
Conclusions: Spending even one week of a six-week psychiatry clerkship on an addiction treatment site increases regard for patients with alcoholism. We have previously shown this effect to be absent in students who receive no such exposure.

References:

NR627 Wednesday, May 21, 12:00 p.m.-2:00 p.m.

Do Personal Stories Improve Media Depictions of Mental Illness?
John H. Coverdale, M.D., Baylor College of Medicine, One Baylor Plaza, Houston, TX 77005; Raymond Nairn, M.D., Donna Claassen

Educational Objectives:
At the conclusion of this section, the participant should know how patients with mental disorders portray themselves and their condition, and appreciate the potential of these depictions for challenging the predominant negative stereotypes in print media.
Summary:

Objective: Because there are no published studies evaluating whether psychiatric patients speaking directly in the print media challenge the stigma of mental illness, we set out to determine the frequency of such stories in a national, prospectively collected sample of print media depictions of mental illness, and to analyze how these stories portrayed the speaker.

References:
Method: A commercial clipping bureau was contracted to provide cuttings of all print items with any mental health or illness aspect in all publications in New Zealand over a four-week period. Six hundred items were identified ranging from news briefs to full-page newspaper articles. We identified all items in which a person who had been a psychiatric patient or who had a mental disorder either described their experiences or was quoted directly by the reporter. Discourse analysis of these items through repeated readings enabled the identification and classification of patterns or themes in the construction of mental illness.

Results: Five articles (0.8%) were found in which a person with a mental disorder spoke directly in the media. Within these items five themes predominated: Ordinariness/Living Well; Vulnerability; Stigma; Crisis; and Disorder/Treatment. Ordinariness/Living Well, which included the personal strengths required for everyday living well, and coping with the effects of stigmatizing beliefs, were central to emphasizing how the persons with mental disorders were ordinary, human, and understandable.

Conclusions: These preliminary findings demonstrate the importance of directly reporting the stories of persons with mental disorders when challenging the predominantly negative stereotypes of print media depictions of mental illness.

References:

NR628 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Perception of Stigma Among Patients With Schizophrenia
Aygun Ertugrul, M.D., Psychiatry Department, Hacettepe University, Sihhiye, Ankara 06100, Turkey; Berna D. Ulug, M.D.

Educational Objectives:
Participant will recognize the relation between symptoms and perception of stigma in schizophrenic patients. This study shows how symptoms and stigma reinforce each other.

Summary:
Many individuals with schizophrenia are stigmatized by society. It is necessary to understand the factors contributing to stigma (Link et al., 1997; Dickerson et al., 2002). This study investigated the relation of symptoms and other patient characteristics with perceived stigmatization in patients with schizophrenia. Sixty patients with schizophrenia were included in the study. Symptomatology was assessed by Positive and Negative Syndrome Scale. Perceived stigmatization was measured by several questions which were included in World Health Organization-Disability Assessment Schedule II (WHO-DAS-II). Patients were grouped as positive or negative for perceived stigmatization. Characteristics of patients and severity of symptoms were compared between the two groups. The results showed that patients who reported to perceive stigmatization had more severe symptoms than the patients who did not perceive stigmatization. Positive symptoms and general psychopathology scores were significantly higher in the previous group. Patients reporting stigmatization were significantly more disabled than the group negative for perceived stigmatization. Demographic variables were not different between the two groups. Stepwise regression analysis showed that depression and active social avoidance were the items which could predict the perception of stigmatization. The relation between perception of stigmatization and symptoms is a vicious cycle in which the elements reinforce each other. Interruption of this cycle will increase the adaptive abilities and decrease the disability of these patients.

References:

NR629 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Assessment of Stigmatizing Perceptions of Disease in the Workplace
Blagovest G. Nikolov, M.D., Neurology Department, Weill Cornell Medical Center, 525 East 68th Street, K615, New York, NY 10021; Cynthia L. Harden, M.D., Susanne M. Vera, Martin A. Goldstein, M.D., Douglas Labar, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to determine which aspects of neuropsychiatric disease impact the perception that job performance will be adversely affected, but that this is not related to the perception that the afflicted person is to some degree “at fault” for his/her illness.

Summary:
Objective: To evaluate perceptions that coworkers have of three chronic illnesses: multiple sclerosis, epilepsy and depression.
Methods: We distributed a 31 question survey to employees in two New York City companies. Three vignettes were presented describing new employees who eventually revealed that they had either depression, multiple sclerosis, or epilepsy. Multiple sclerosis was the only visible illness. Perceptions were assessed by a three to four degree scale.

Results: Seventy-four out of two hundred surveys were returned (37% response). Forty-four percent of respondents reported that they realized the subject of the vignette had MS before it was revealed to them, compared with 28% with depression and 12% with epilepsy. Forty-three percent of respondents reported that they thought epilepsy would have no effect on job ability, compared with 32% for depression, and 15% for MS. Ten percent of respondents thought that the depressed subject could “very much” have job performance, compared with 5% for MS and 7% for epilepsy.

Conclusions: Visibility of a neurologic illness such as multiple sclerosis in the workplace is associated with the impression that the job is at risk for being performed inadequately. Depression is associated with more “blame” than the other two illnesses.

References:

NR630 Wednesday, May 21, 12:00 p.m.-2:00 p.m.
Emotional Reaction of Coworkers to Neuropsychiatric Disease
Cynthia L. Harden, M.D., Department of Neurology, Weill Cornell Medical Center, 525 East 68 Street, Room K-615, New York, NY 10021; Susanne M. Vera, Martin A. Goldstein, M.D., Douglas Labar, M.D.
Educational Objectives:
At the conclusion of this presentation, the participant should be able to identify several emotional responses leading to avoidance in the workplace produced by finding out that a coworker has depression, epilepsy or multiple sclerosis. Further, the severity of emotions elicited can be ranked according to illness.

Summary:
Objective: This study evaluated the emotional reactions produced upon finding out that a coworker has either epilepsy, depression, or multiple sclerosis.

Methods: We distributed a 31 question survey entitled “Perceptions of Medical Conditions in the Workplace” to employees in two New York City companies. Three vignettes were presented in the survey, describing new employees who eventually revealed that they had either depression, multiple sclerosis or epilepsy. Emotional reactions to the subject of each vignette were assessed by a 3 to 4 degree scale.

Results: Seventy-four surveys out of 200 were returned (37% response). Fifteen percent of respondents reported “much more anxiety” at the idea of interacting with the person with epilepsy, compared to 11% with depression and 5.4% with MS. Twenty percent of respondents reported that they were “very worried” that the person with epilepsy would have sudden, unpredictable behavior, compared with 11% for depression, and 5.4% for MS. Forty percent of respondents had “very comfortable” spending time with the MS subject after working hours, compared with only 38% for depression and epilepsy.

Conclusions: Epilepsy and depression produce a greater degree of social discomfort than multiple sclerosis and this may contribute to stigma of these illnesses in the workplace.

References:

NR631 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Morning Cortisol Levels in Chronic, Heavy Drinkers Department of Veteran Affairs
Thomas P. Beresford, M.D., Department of Psychiatry, VAMC/University of Colorado, 1055 Clermont Street, Suite 116, Denver, CO 80220; Brandon K. Martin, B.A., Julie L. Alfers, B.A., Laura E. Mangum, M.S.W., David B. Arciniegas, M.D., Mark Laudenslager, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant will appreciate the significance of sustained hypercortisolemia and its potential neuro-psychiatric effects in heavy drinkers.

Summary:
Objective: studies note that ethanol given acutely stimulates adreno-corticotrophic hormone production resulting in high circulating levels of serum cortisol. We showed that the hippocampal to pituitary volume ratio distinguished a group of chronic, heavy drinkers from a light drinking control group. Because this shift may be mediated, in part, by sustained, elevated cortisol levels, we hypothesized that morning cortisol concentration would characterize chronic, heavy, current drinkers.

Method: we collected morning saliva samples (1) from nine male subjects who drank at least three standard drinks at least four days weekly during the previous three months and whose last drink was within 24 hours, and (2) from 13 male controls with no alcohol in the last day and no episodes of three or more standard drinks during the previous three months. Saliva samples were taken on specially treated paper strips. Extracted cortisol was measured by enzyme immunoassay.

Results: The drinkers showed significantly higher mean levels of morning cortisol when compared to the non-drinkers (t-test, p<.02). Their diurnal pattern presented higher levels overall.

Conclusions: These results suggest that sustained heavy alcohol use is associated with higher circulating levels of cortisol that may, in turn, lead to hippocampal damage and pituitary hypertrophy.

References:
NR633 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Disulfiram Treatment for Hepatitis-C Alcoholic Patients
Department of Veteran Affairs
Thomas P. Beresford, M.D., Department of Psychiatry, VAMC/University of Colorado, 1055 Clermont Street, Suite 116, Denver, CO 80220; Brandon K. Martin, B.A., Julie L. Alfers, B.A., Loraine K. Clapp, M.S., Diana Bialkowski, M.S., Clark Kulig, M.D.

Educational Objectives:
- At the conclusion of this session, the participant will be able to recognize disulfiram as a potentially viable treatment option for alcohol dependent patients who are HCV seropositive.

Summary:
- Objective: Hepatitis C (HCV) is epidemic among alcohol-dependent (AD) persons. Despite the advantages of immediate abstinence, clinicians are reluctant to prescribe disulfiram for fear of liver injury. From clinical experience, we hypothesized that aminotransferase levels would not rise in AD/HCV cases given disulfiram treatment, 500 mg. p.o., three times weekly. The discontinuation.
- Method: We retrospectively collected alanine aminotransferase (ALT) levels in HCV-seropositive alcoholics undergoing supervised disulfiram treatment, 500 mg. p.o., three times weekly. The test group included 28 consecutive HCV-positive patients; the control group consisted of 20 randomly selected HCV-negative patients receiving supervised disulfiram at the same dose and frequency. Mean change in ALT from baseline was examined. Despite the advantages of immediate abstinence, clinicians are reluctant to prescribe disulfiram for fear of liver injury. From clinical experience, we hypothesized that aminotransferase levels would not rise in AD/HCV cases given disulfiram.
- Results: The test group showed no statistically or clinically significant changes from baseline at any of the time periods. The control group evidenced no statistically significant mean changes until 12 months when mean ALT rose slightly. In no case did ALT elevation reach above three times the limit of normal, indicating discontinuation.
- Conclusions: This preliminary study suggests that supervised disulfiram therapy may be safe in HCV-seropositive AD patients for periods up to one year so long as transaminase levels are monitored frequently.

References:

NR634 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Neural Correlates of Ethanol Effects Using PET Supported by the Glidden Family Foundation
Maria C. Santana, M.S., Department of Psychiatry, Emory University, 1639 Pierce Drive, Suite 4000, Atlanta, GA 30322; Robin Gross, B.A., Tim Ely, B.A., Sidney Vannes, B.S., Karen G. Drexler, M.D., Clinton D. Klitsch, Ph.D.

Educational Objectives:
- At the conclusion of this session, the participant should recognize the dose-dependent effects of alcohol in the brain and its implication on behavior, emotion, and cognition and to appreciate neuroimaging as a means of correlating the pharmacological actions of a drug with changes in neuronal activity and behavior.

Summary:
- Objective: Serotonin transporter (5-HTT) affects serotonergic neurotransmission and promoter region of 5-HTT gene has biallelic insertion/deletion polymorphism. The authors explored the hypothesis that serotonin promoter polymorphism (5-HTTLPR) was associated with alcohol dependence and violent behavior in alcoholic patients.
- Methods: One hundred and six patients with alcohol dependence by DSM-IV and 101 normal controls were participated in this study. The subjects were subdivided according to clinical variable such as presence of violent behavior, family history of alcohol dependence. Genotyping for 5-HTTLPR was performed by PCR method, which found short allele, the S type and long allele, the L type.
- Results: Frequencies of homozygous and heterozygous for L allele was higher in patient group than in normal controls, although frequencies of genotype and alleles were not significantly different between clinical subgroup (presence of violent behavior and family history of alcohol dependence).
- Conclusion: This result suggests that 5-HTTLPR may have putative role in the development of alcohol dependence, although
further studies with larger subjects from different anthropological origin would be warranted to confirm our finding.

References:

NR636 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Topiramate for the Treatment of Alcohol Dependence
National Institute of Mental Health, University of Texas Health Science Center at San Antonio, and Ortho-McNeil Pharmaceuticals
Bankole A. Johnson, M.D., Department of Psychiatry, University of Texas Health Science Center, 7703 Floyd Curl Drive, MS 7793, San Antonio, TX 78229-3900; Nassima Ait-Daoud, M.D., Charles L. Bowden, M.D., Jennie Ma, Ph.D., John Roache, Ph.D., Norman R. Rosenthal, M.D.

Educational Objectives:
At the conclusion of this session, the participant will gain new knowledge on the efficacy of an anticovulstive-type medication for treating alcoholism.

Summary:
Midbrain and cortical brain reward systems that modulate dopamine function are critical to establishing and maintaining alcohol-seeking behavior. Additionally, chronic alcoholics develop long-term GABA/glutamate neuronal changes that result in negative affect with abstinence. Alcohol-seeking behavior may, therefore, be maintained by alcohol’s rewarding effects and the desire to avoid abstinence-induced negative affect. Based upon this knowledge, we hypothesized that topiramate, a substituted fructo-pyranose derivative, would reduce alcohol-induced reward, and dampen neuronal hyperexcitability following abstinence. Briefly, these effects are probably due to topiramate-induced facilitation of central GABAergic function and the inhibition of chronic alcohol-mediated supersensitivity of AMPA/kainate glutamate receptors.

As a proof-of-concept test of this hypothesis, we showed, in a double-blind, randomized clinical trial (N = 150), that topiramate (up to 300 mg/day) was superior to placebo as an adjunct to medication compliance management at significantly reducing the amount and severity of drinking, and the objective measure of alcohol consumption, plasma GGT. Importantly, topiramate recipients also had significantly greater improvement in global well-being and psychosocial functioning. Average effect sizes for the therapeutic difference between topiramate and placebo were in the medium range. We propose that topiramate is a novel and promising medication for treating alcoholism.

References:

NR637 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
The Effect of Methamphetamine on Response Conflict Suppression
Ruth E. Salo, Ph.D., Department of Psychiatry, University of California, Davis, 1544 Newton Court, Davis, CA 95618; Thomas E. Noroahl, M.D., David R. Gibson, Ph.D., Martin H. Leaman, M.D., Gan-T P. Galloway, Pharm.D., Neil M. Flynn, M.D., Edith V. Sullivan, Ph.D.

Educational Objectives:
The goal of this poster is to present data related to cognitive and neural changes associated with methamphetamine use.

Summary:
Introduction: Methamphetamine dependence (MD) is associated with disruption of frontostriatal function. Clinically, MD individuals are highly distractible and have difficulty focussing. Here, we used a computerized task switching experiment (Rogers & Monsell, 1995) to examine selective attention and task switching.

Method: We tested 10 male MD subjects (35.3+8.3yr) and four female MD subjects (43 + 5.59yrs) who had used methamphet-amine for 13.5 + 8.02 yrs but were currently abstinent (range one month to four years).

Results: The MD group exhibited greater errors on response conflict trials compared to controls (p=.03, one-tailed) but not on switch trials (p = .25). In addition, increased errors were observed in those MD subjects who were abstinent a shorter period of time. A subset of the MD subjects underwent MRS scans with reduced levels of N-acetyl aspartate [NAA] noted in the anterior cingulate [ACC] (p < .05) but not in primary visual cortex.

Conclusions: The data suggest that the increased error rates in the MD subjects on response conflict trials may be modulated by drug abstinence and may be in part related to abnormal functioning of the ACC, which is a node within frontostriatal circuitry.

Support: DA14359-2 to TEN, AA10723 to EVS and DA10641 to GP6.

References:

NR638 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Temperamental Traits in Multiaddictive Behaviors
Alain Dervaux, M.D., Department of Psychiatry, Hopital Sainte Anne, Shu, 1 Rue Cabanis, Paris F-75014, France; Michel Lejouroux, M.D., Marie O. Krebs, Ph.D., Jean Aedes, M.D., Franck Bayle, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the influence of sensation seeking and impulsivity in multiaddictive behaviors.

Summary:
Objective: To examine the influence of sensation seeking and impulsivity on the number of chemical and behavioural addictions in psychiatric inpatients.

Method: Diagnoses of substance abuse or dependence were based on interviews using the Schedule for Affective Disorders and Schizophrenia (SADS). Assessments included the Zuckerman Sensation Seeking Scale (SSS), the Barratt Impulsivity Scale (BIS-10), the Hospital Anxiety and Depression Scale (HADS) and the Montgomery and Asberg Depression Scale (MADRS).

Results: The sample was divided in subgroups: no current or lifetime addiction (n=36), one addiction (n=53), two addictions (n=61), three addictions or more (n=35). Nicotine use and alcohol abuse or dependence were the most common addictive disorders.
The SSS, particularly the disinhibition subscale, and the BIS-10 non-planning scores were higher in multiaddicted patients with a significant group effect. There were no significant differences between the groups on HADS and MADS scores. When restricted to patients presenting only chemical addictions, the impact of temperamental traits was of lower importance.

Conclusions: Sensation seeking more than impulsivity is a major determinant to multiple addictions, independently of addiction subtype, anxiety and depression. Behavioral addictions and/or impulsive related disorders need to be carefully assessed when temperamental measures are used in patients with psychoactive abuse or dependence.

References:

NR639 Wednesday, May 21, 3:00 p.m.–5:00 p.m.
Results From a Long-Term Trial of Atomoxetine in the Prevention of Relapse in ADHD Supported by Eli Lilly and Company
David Michelson, M.D., Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, DC 0721, Indianapolis, IN 46285; Shuyu Zhang, M.S., Jan Bueltelaa, Ph.D., Marina Danckaert, Ph.D., Christopher Gillberg, M.D., Alessandro Zuddas, M.D., Thomas J. Spencer, M.D., Joseph Biederman, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate that long-term atomoxetine treatment is effective for maintaining ADHD symptom improvements and psychosocial functioning.

Summary:
Introduction: Atomoxetine is a selective norepinephrine reuptake inhibitor effective for the treatment of ADHD acutely, but no long-term, placebo-controlled results have been reported to date. We conducted a nine-month relapse prevention study to assess the efficacy of atomoxetine during chronic treatment.

Method: Patients aged 6–15 who met DSM-IV criteria for ADHD were treated for approximately 12 weeks with atomoxetine to an initial target dose of 1.2 mg/kg/day and a maximum dose of 1.8 mg/kg/day. Patients whose symptoms remitted were randomized to nine months of continuation therapy with atomoxetine or to placebo under double-blind conditions.

Results: 604 patients entered the study and received atomoxetine. Of these, 416 met response criteria and were randomized. After nine months, 52.6% of patients assigned to placebo compared with 29.7% of patients assigned to atomoxetine had a worsening > 50% in symptom severity post-randomization (p<.001). Psychosocial functioning was also superior in the atomoxetine group as assessed by the Child Health Questionnaire. Safety and tolerability were similar to those observed in acute treatment trials.

Conclusion: During nine months of continuation therapy, atomoxetine was superior to placebo in maintaining symptom improvements and psychosocial functioning.

References:

NR640 Wednesday, May 21, 3:00 p.m.–5:00 p.m.
Emotional Dysregulation in ADHD and Response to Atomoxetine
Frederick W. Reimherr, M.D., Department of Psychiatry, University of Utah, 30 North 1900 East, Room 5F218, Salt Lake City, UT 84132; Robert E. Strong, D.O., Dawson W. Hedges, M.D., Scott A. West, M.D., Lenard A. Adler, M.D., David Michelson, M.D., Barrie Marchant, M.A.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize ADHD in adults and response to treatment.

Summary:
Objective: We evaluated 500 ADHD adults using the Wender Reimherr Adult Attention Deficit Disorder Scale (WRAADDS) and Conner's Adult ADHD Rating Scale (CAARS) at baseline and following double-blind treatment with atomoxetine or placebo. Three WRAADDS items (temper, affective lability, and emotional over-reactivity) assess emotional dysregulation. The population was examined for the presence of these symptoms and their effect on medication response.

Method: Two identical studies were conducted at 31 sites. Patients met DSM-IV criteria for ADHD and no other Axis I disorders. Emotional dysregulation was defined as having moderate or worse symptoms on all three items at baseline.

Results: Thirty percent had symptoms of emotional dysregulation and showed significant improvement on the CAARS (p<.001) and WRAADDS (p<.001) on atomoxetine. There was a significant interaction effect between emotional dysregulation and treatment when using the WRAADDS (p=.031) and WRAADDS (p=.007) as dependent variables. The emotional factors displayed a treatment effect similar to the total CAARS and the total WRAADDS.

Conclusions: Adult ADHD patients with symptoms of emotional dysregulation had marked improvement in symptoms of ADHD on atomoxetine compared with placebo. Emotional symptoms showed statistically significant improvements, similar in size to that seen with traditional ADHD symptoms.

References:

NR641 Wednesday, May 21, 3:00 p.m.–5:00 p.m.
Using a Meta-Analysis to Draw Conclusions About ADHD Medication Effects
Supported by Shire Pharmaceutical Development, Inc.
Stephen V. Faraone, Ph.D., Department of Pediatric Psychopharmacology, Harvard Medical School, 4F South Main Street, #301, West Bridgewater, MA 02379; Joseph Biederman, M.D.
Educational Objectives:
After reviewing this poster, the participant should be able to distinguish between the effects and effect sizes of various medications used in the management of ADHD.

Summary:
Objective: To analyze published literature on the pharmacotherapy of ADHD, to describe the concept of effect size, and its strengths and limitations when used to compare drug-placebo effect sizes derived from different studies of ADHD medications.

Methods: A literature search was conducted to identify double-blind placebo controlled treatment studies of ADHD. We used meta-analysis to compute pooled effect sizes and assess the influence of medication type and study design parameters on medication effects.

Results: 37 trials met criteria and were included in this meta-analysis. These trials reported a total of 270 drug-placebo comparisons using 45 outcome measures. The most commonly identified treatments included both methylphenidate and amphetamine compounds. Meta-analysis regression showed significant effects of class of drug, type of outcome rating score and time of rating (all P values <.05). Statistical models of the effect size show how it can be influenced by study characteristics other than the medication tested.

Conclusion: There does not appear to be uniformity in how medication effectiveness is cited or assessed or in many study design parameters. Effect size, a measure of treatment effectiveness, varies greatly and is influenced by several study design variables. Comparing medication effect sizes from different studies will be biased if these influences are not accounted for.

References:
2. Schachter HM, Pham B, King J, Langford S, Moher D: How it can be influenced by study characteristics other than the medication tested. Schachter HM, Pham B, King J, Langford S, Moher D: How it can be influenced by study characteristics other than the medication tested. C Med Assoc J 2001; 165(11):1475–1486.

NR642 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
The Impact of Drug Holidays on OROS Methylphenidate Treatment for ADHD Supported by McNeil Consumer & Specialty Pharmaceuticals
Stephen V. Farane, Ph.D., Department of Pediatric Psychopharmacology, Harvard Medical School, 4F South Main Street, #301, West Bridgewater, MA 02379; Joseph Biederman, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the effect of drug holidays on children with ADHD.

Summary:
Objectives: To assess the impact of drug holidays on OROS® methylphenidate treatment for ADHD.

Methods: Children with ADHD (aged 6–13 years) enrolled in a multicenter, open-label, 12-month study received 18, 36, or 54 mg of once-daily OROS® MPH. Drug holidays were measured as number of days off medication. Baseline demographic variables (race, gender, age, height, weight), and baseline clinical variables ( tic history, school classroom type, OROS® MPH dose, ADHD subtype, SNAP-IV, IOWA Conners scores, oppositionality/defiance scores, parent/teacher global efficacy ratings, parent satisfaction) were assessed as predictors of drug holidays. Parent- and teacher-rated outcomes were used to assess impact of drug holidays on efficacy.

Results: A total of 207 children completed one year of treatment. Compliance was excellent: on average, children took 97% of doses. Drug holidays were substantial: children missed treatment 27% of the time. Drug holidays were predicted by the following baseline characteristics: older age (p=0.04); inattentive ADHD (p=0.06); fewer hyperactivity/impulsivity and oppositionality symptoms (p<0.05); history of tics (p=0.05); lower OROS® MPH starting dose (p=0.01); minority ethnic status (p=0.04). Parent/teacher efficacy ratings during initial treatment did not predict compliance (p>0.80). Drug holidays during follow-up were associated with poorer efficacy at home (p=0.03) but not school (p=0.49).

Conclusions: Drug holidays were common among ADHD children receiving OROS® MPH medication. Drug holidays were primarily observed for older, less impaired children, and ethnic minorities. Drug holidays may adversely impact ADHD children, particularly older children, and caution is recommended.

References:

NR643 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Efficacy of Atomoxetine Treatment for Adolescents With ADHD Supported by Eli Lilly and Company
Albert J. Allen, M.D., Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Denai R. Milton, M.S., David Michelson, M.D., Douglas K. Kelsey, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate that atomoxetine treatment is effective for treating core ADHD symptoms in adolescents and is associated with significant improvement in oppositionality.

Summary:
Objective: Assess the efficacy of atomoxetine in the treatment of adolescents with ADHD enrolled in two recently completed clinical trials.

Methods: Patients were randomized to acute (six to eight weeks), double-blind treatment with atomoxetine or placebo. ADHD symptom improvement was assessed by change from baseline to endpoint in ADHD RS total and subscales scores. Similarly, improvement in oppositionality was measured by change in the CPRS Oppositional subscale.

Results: Adolescents (12 to 18 years of age, 71 atomoxetine, 49 placebo) participated in the studies. Adolescents treated with atomoxetine had significant improvement in ADHD RS Total scores compared with placebo (p = .009). Similar improvement was observed in the ADHD RS inattentive (p = .018) and hyperactivity/impulsive (p = .051) subscales scores, and the CPRS Oppositional subscale score (p = .037).

Conclusions: Atomoxetine treatment is effective for treating core ADHD symptoms in adolescents and is associated with significant improvement in oppositionality. The results from these studies are consistent with outcomes observed in school-aged children treated with atomoxetine.
References:


NR644 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Comparison of Classroom Deportment in Six-Twelve Year-Old Children With ADHD After Administration of Two Once-Daily Extended Release Methylphenidate (MPH) Formulations
Supported by Celltech Americas, Inc. Rochester, NY
Laurence L. Greenhill, M.D., Department of Psychiatry, New York Psychiatric Institute, 1051 Riverside Drive, Box 78, New York, NY 10032

Educational Objectives:

At the conclusion of this session, the participants should be able to identify time-effect differences in deportment behavior and attention in children with attention-deficit/hyperactivity disorder (ADHD) from 2 AUC-equivalent doses of once-daily (qd) extended-release methylphenidate (MPH) formulations and to recognize the significance of these differences relative to the school classroom environment.

Summary:

Hypothesis: AUC-equivalent doses of two MPH extended-release formulations, OROS methylphenidate (MPH1) and beaded methylphenidate (MPH2), differ in their effects on classroom deportment.

Method: At 10 U.S. sites, based on their pre-study MPH dose, a total of 214 children with ADHD were randomly assigned to one week of once-daily doses of MPH1, MPH2, or placebo (PLA). Low, medium, and high doses of MPH1 versus MPH2 were, respectively, 18mg vs 20mg, 36mg vs 40mg, and 54mg vs 60mg. On the seventh day, at 1.5h intervals, double-blind ratings of deportment, attention, and math performance were assessed in a laboratory classroom.

Results: 171 children completed all three treatments. If averaged, deportment scores rated at 1.5h to 7.5h were significantly better on MPH2 than on MPH1 (p<0.0001) and for both treatments compared with PLA. MPH1 was statistically better (p<0.0001) than MPH2 at hour 12.

Discussion: Different MPH release patterns of MPH1 and MPH2, despite similar MPH plasma AUCs, lead to different ratings of deportment during the first few hours after ingestion.

References:


NR645 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Efficacy and Safety of Atomoxetine in Long-Term, Open-Label Treatment of Adults With ADHD Supported by Eli Lilly and Company
Lenard A. Adler, M.D., Department of Psychiatry, Faculty Practices, 530 First Avenue, Suite 5A, New York, NY 10016; Thomas J. Spencer, M.D., Frederick W. Reimherr, M.D., Denai R. Milton, M.S., David Michelson, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to demonstrate that long-term atomoxetine treatment is effective and safe in adults with ADHD.

Summary:

Objective: Understand long-term effects of atomoxetine in adults with ADHD.

Methods: Patients from two acute placebo-controlled studies could enter an open-label extension study. Data were analyzed for the 384 patients who entered it and received treatment (baseline acute studies versus last rating open-label study). The mean dose of atomoxetine in the 10-week acute studies was 94.3 mg/day. Patients stopped atomoxetine or placebo for up to four weeks and were then treated openly with atomoxetine 60-120 mg/day (mean dose of 96.5 mg/day for average ~34 weeks).

Results: Conners Adult ADHD Rating Scales: Investigator (CAARS:lnv) Total ADHD Symptom scores decreased from 34.5 ± 7.3 at baseline by 15.0 ± 11.3 (43.5%). Two-thirds of patients achieved ≥ 30% decrease in CAARS scores. CGI Severity decreased from 4.7 ± 0.7 at baseline to 1.4 ± 0.5 (29.8%); 80% achieved at least a one-point decrease and 47% achieved at least a two-point decrease in CGI-S scores. Atomoxetine was generally well tolerated; the discontinuation rate from adverse events was 8.5% in patients receiving atomoxetine in the acute studies and 7.8% in the open-label study.

Conclusions: The data from this ongoing open-label trial support the long-term efficacy and safety of atomoxetine in treating adults with ADHD.

References:


NR647 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Long-Term Safety and Efficacy of Once-Daily Adderall Extended Release in Adults With ADHD Supported by Shire Pharmaceutical Development, Inc.
Richard H. Weiser, M.D., Duke University, 700 Spring Forrest Road, Suite 125, Durham, NC 27609; Joseph Biederman, M.D., Allan K. Chrisman, M.D., Timothy P. Timothy, M.D., Neil Frazer, M.D., Simon J. Tulloch, M.D.

Educational Objectives:
After reviewing this poster, the participant should be able to discuss the long-term safety and efficacy of Adderal XR for the treatment of adults with ADHD.

Summary:
Objective: This 12-month, open-label extension study assessed the long-term safety, efficacy, and quality of life associated with use of Adderal XR (20, 40, or 60 mg once daily) in 223 adults (≥18 yrs) with attention-deficit/hyperactivity disorder (ADHD).

Methods: Patients met DSM-IV criteria for ADHD and had a history of ADHD before age 7; all patients rolled over from a four-week, randomized, double-blind, placebo-controlled, forced-dose titration study of once-daily Adderal XR, during which dose was titrated to optimum effect and minimum adverse effects. The intent-to-treat (ITT) population included 221 adults (mean age 39.8 yrs). Vital signs and AEs were collected monthly; ECGs and laboratory measures were collected at months 3, 6, and 12. Primary efficacy was assessed monthly using the 18-item ADHD Rating Scale (ADHD-RS) for adults.

Results: Patients who previously received placebo had the largest improvement in ADHD-RS scores (mean change = -11.9 from baseline to endpoint; P<0.001). Patients who received Adderal XR with interruption showed significant improvement from baseline to endpoint (mean change = -7.6; P=0.041), as did those with no interruption (mean change = -6.0; P<0.001). The most commonly reported adverse events were dry mouth (42% of patients), anorexia (30%), insomnia (25%), and headache (21%).

Conclusion: These preliminary data indicate that slow titration of rivastigmine improves tolerability while maintaining broad symptomatic efficacy.

References:
NR649  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Time Course of Vital Signs After Once-Daily Adderall Extended Release in ADHD Children
Supported by Shire Pharmaceutical Development Incorporated
Robert L. Findling, M.D., Department of Psychiatry, University Hospital, 11100 Euclid Avenue, Cleveland, OH 44106-5080; James T. McCracken, M.D., Neil Frazer, M.D., Simon J. Tulloch, M.D.

Educational Objectives:
After reviewing this poster, the participant should be able to discuss the cardiovascular safety profile of Adderall XR in the treatment of ADHD in children.

Summary:
Objective: To analyze the time course of vital signs (eg, blood pressure and pulse) throughout the day in children who received a single, morning dose of Adderall XR.

Methods: Children ages 6 to 12 yrs with a DSM-IV diagnosis of ADHD were enrolled in a randomized, double-blind, crossover, placebo- and active-controlled analog classroom study. Patients (N=51) were randomly assigned to receive each of the following daily morning doses for one week: Adderall XR 10, 20, or 30 mg, Adderall 10 mg, or placebo. On one day each of the five treatment weeks, resting sitting systolic and diastolic blood pressures and resting sitting pulse rate were measured predose and at 1.5, 4.5, and 7.5 hours postdose.

Results: Mean blood pressure and pulse measurements were similar across all treatments (including placebo) and all time points, from predose to 7.5 hours after a morning dose. Minimum and maximum vital signs measurements were similar across all treatments and time points. Unusually high or low blood pressure and pulse readings were sporadic and infrequent, and no trends were noted.

Conclusion: The time course of changes in blood pressure and pulse throughout the day after a single, morning dose of Adderall XR 10, 20, or 30 mg is similar to the time course observed in children receiving a placebo.

References:

NR650  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Long-Term Adderall Extended Release Treatment Improves Quality of Life in ADHD Children
Supported by Shire Pharmaceutical Development, Inc.
Frank A. Lopez, M.D., Department of Pediatrics, Childrens Development Center, 600 South Orlando Avenue, Suite 102, Maitland, FL 32751; Mark C. Chandler, M.D., Joseph Biederman, M.D., David A. Mays, Pharm.D., M. Alex Michals, M.D., Simon J. Tulloch, M.D.

Educational Objectives:
After reviewing this poster, the participant should be able to discuss the improvement in quality of life associated with long-term use of Adderall XR for the treatment of ADHD in children.

Summary:
Objective: This multicenter, open-label extension study was conducted to assess the long-term safety, efficacy, and quality of life associated with Adderall XR in the treatment of children with attention-deficit/hyperactivity disorder (ADHD). Safety and efficacy data will be reported separately.

Method: Children who previously participated in double-blind, placebo-controlled studies of Adderall XR were enrolled and received Adderall XR 10, 20, or 30 mg once-daily. Quality of life measures, including the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q), Social Adjustment Inventory for Children and Adolescents (SAICA), Family Environment Scale (FES), and a School Function Questionnaire (SFQ), were completed 12, 18, and 24 months after study enrollment.

Results: The intent-to-treat (ITT) population included 560 children 6 to 12 years of age. Mean Q-LES-Q Total Scores were significantly improved at 12, 18, and 24 months (mean ± SD; 56 ± 7; 57 ± 7; 56 ± 8) compared with a parent-rated historical assessment score (mean ± SD; 49 ± 9; P<0.00001 for each timepoint). Complete results for the SAICA, FES, and SFQ will also be presented.

Conclusion: Once-daily Adderall XR significantly improved the quality of life in children with ADHD, and these improvements persisted during long-term treatment (up to two years).

References:
2. McCracken JT, Biederman J, Greenhill LL, Swanson JM, McGough JJ, Spencer T, Posner K, Wigal S, Pataki C, Zhang Y, and Tulloch SJ: Analog classroom assessment score (mean ± SD, 49 ± 9; 56 ± 8) compared with a parent-rated historical assessment score (mean ± SD; 49 ± 9; P<0.00001 for each timepoint), complete results for the SAICA, FES, and SFQ will also be presented.

NR651  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Effects of Atomoxetine on the Quality of Life of Children With ADHD
Supported by Eli Lilly and Company
Douglas E. Faries, Ph.D., Department of Health Outcomes, Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46285; Amy R. Perwien, Ph.D., Douglas K. Kelsey, M.D., Calvin R. Sumner, M.D., David Michelson, M.D., Albert J. Allen, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should know which subgroups of ADHD patients have more significant psychosocial impairment and understand the magnitude of the effects of atomoxetine on a wide variety of quality-of-life domains.

Summary:
Introduction/Objectives: Recent work has documented the significant burden of ADHD on the quality of life (QOL) of both children and families. However, OOL data from controlled ADHD studies remain sparse and even less is known about effects of treatment in key patient subgroups. This research quantifies the effect of atomoxetine, a non-stimulant treatment for ADHD, on QOL measured by the Child Health Questionnaire (CHQ).

Methods: The CHQ is a quality of life measure including seven psychosocial (including both child and family functioning) and four physical domain scores. The CHQ was collected during three randomized, acute, double-blind, placebo-controlled clinical trials of atomoxetine and change scores were assessed using ANOVA.

Results: Atomoxetine had significantly greater improvement than placebo on all seven psychosocial domains. No differences were seen in physical domains. Atomoxetine also demonstrated consistent efficacy across subgroups of patients, including three
subgroups identified as being significantly impaired psychosocially at baseline: patients with severe ADHD symptoms, patients with comorbid oppositional defiant disorder, and patients with a family history of ADHD.

Discussion: Atomoxetine was associated with marked improvements in psychosocial functioning over a range of domains. In addition, atomoxetine was effective in subgroups of patients identified as having more severe psychosocial functioning impairment.

References:

NR652 Wednesday, May 21, 3:00 p.m.-5:00 p.m. Comorbidity in an ADHD Brazilian Adult Sample
Paulo E. Mattos, M.D., Department of Psychiatry, UFRJ, Rua Paulo Barreto 91, Rio De Janeiro, RJ 22280-010, Brazil; Eloisa Saboya, M.S.C., Vanessa Ayrao, M.D., Daniel Segenreich, M.D.

Summary:
Introduction: Psychiatric comorbidity is common in ADHD and modifies prognosis and also treatment strategies.
Objective: To evaluate comorbidity in a clinically referred adult sample of ADHD.
Methods: 83 adults were channeled through a non-profit advocacy group for ADHD. 53 (23 men and 30 women) fulfilled DSM-IV criteria for ADHD in a screening interview. Those ADHD patients (60% combined type, 30% inattentive type and 10% hyperactive type) were then interviewed using scid and mini as diagnostic tools.

Results: 26.4% (16) had a past depressive episode; 13.2% (7) had dysthymia, 13.2% (7) had social phobia and 11.3% (6) had GAD; 5.6% (3) had PTSD, showing a high prevalence of mood and anxiety disorders. Other diagnosis (less than 5%) were OCD, somatization disorder, panic and bipolar. Past (13.2%) and present (15%) alcohol abuse and also past (11.3%) and present (7.5%) dependence were diagnosed. Cannabis and cocaine abuse or dependency were seen in less than 5%. Binge eating was seen on 13.2% (2) patients.

Conclusion: A high prevalence rate of comorbidity is seen on an adult ADHD sample.

References:

NR653 Wednesday, May 21, 3:00 p.m.-5:00 p.m. Bioavailability of Two Long-Acting Formulations of Methylphenidate
Supported by Novartis Pharmaceuticals Corporation
John S. Markowitz, Pharm.D., Department of Pharmaceutics, Novartis, 67 President Street, Room 246N, Charleston, SC 29425; Art Straughn, Ph.D., Kennerly S. Patrick, Ph.D., C. Lindsay DeVane, Ph.D., Linda Pestreich, James S. Lee, Ph.D., Yanfeng Wang, Ph.D., Rafael Muniz, M.D.

Educational Objectives:
1. Identify distinguishing pharmacokinetic characteristics of two novel modified-release methylphenidate formulations. 2. Evaluate the relative bioavailability of two novel modified-release methylphenidate formulations. 3. Determine appropriate dosage strategies for two novel modified-release methylphenidate formulations.

Summary:
This study compared the rate and absorption of MPH in Ritalin®LA (20 mg) and Concerta® (18 mg) used to treat ADHD, and compared the AUC of MPH between formulations. Nineteen healthy subjects (10 male/9 female), aged 21–34 completed this two-way, crossover-study. On Day 1 subjects received Ritalin®LA 20 mg or Concerta® 18 mg (manufacturer recommended starting dose). On Day 8 subjects received the alternate treatment. Plasma samples were collected over 24 hours to determine MPH plasma concentrations, and the rates and extents of absorption. The mean Cmax and AUC0-4 of the treatments were compared using ANOVA for a 2x2 crossover design. The relative bioavailability in terms of AUC0-4 between the formulations was assessed using a 90% confidence interval. All AUC and Cmax variables were analyzed separately, with log-transformation. Ritalin®LA demonstrated a steeper initial absorption rate and reached substantially higher peak plasma concentrations over the absorption curve when compared to Concerta®. Ritalin®LA exhibited a distinctly bimodal plasma concentration-time profile, with peaks at 2.1 and 5.6 hours post-dosing (both peaks were statistically significantly different from Concerta® p<0.001). Plasma concentrations of Concerta® reached mean peak concentrations at 6 hours post-dosing. The 90% confidence interval of AUC0-t, mean ratio of Concerta® over Ritalin®LA was (0.80, 0.96).

References:

NR654 Wednesday, May 21, 3:00 p.m.-5:00 p.m. Medication Adherence and Depression Among Low-Income Children With Asthma
National Institute of Mental Health
Jennifer S. Brenneman, B.S., Department of Psychiatry, Emory University, 513 Carlyle Lake, Decatur, GA 30033; Marianne Celano, Ph.D., Shannon S. Croft, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize familial characteristics that may be associated with poor adherence to asthma treatment. The participant will also learn about state of the art methods for measuring medication adherence.

Summary:
Introduction: Poor adherence to asthma treatment increases the likelihood of mortality, hospitalizations, and emergency department visits. Caregiver and child mental health may play a critical role in promoting treatment adherence in children with asthma. This study explored the relationship between child and caregiver depression and asthma medication adherence in a low-income urban sample.

Method: Forty-two children ages 6–11 with persistent asthma were recruited from a pediatric asthma clinic or emergency center. Ninety-five percent of the families were African American. Adher-
ence to Flovent (delivered by MDI) and Singulair (an oral medica-
tion) was measured by electronic monitoring devices over a 14-
day period. Subsequently, caregivers and children rated the child’s
depressive symptoms and the caregiver rated her own depressive
symptoms.

Results: Mean daily adherence was 70% (20 – 100%, n = 36)
to Flovent and 83% (21 – 100%, n = 25) to Singulair. Caregiver-
rated child depressive symptoms were significantly and negatively
associated with Singulair adherence; children rated as more de-
pressed were less adherent to Singulair than children rated as
less depressed. Neither child-reported depressive symptoms nor
the caregivers’ self-reported depressive symptoms were signifi-
cantly associated with medication adherence.

Discussion: Implications for psychiatrists in consultation-liaison
and outpatient mental health services are discussed.

References:
1. Wright RJ, Rodriguez M, Cohen S: Review of psychosocial
stress and asthma: an integrated biopsychosocial approach.
Malveaux F, Wedner HJ: Characteristics of inner-city children
with asthma: the National Cooperative Inner-City Asthma

**NR655**  
**Switching to Divalproex Extended Release in Patients With Bipolar Disorder**  
**Supported by Abbott Laboratories**

Lori L. Davis, M.D., *Department of Research, VA Medical Center 116, 3701 Loop Road East (151C), Tuscaloosa, AL 35404; Sandira Ambrose, R.N., Brett English, Ph.D., Elizabeth Waldrop, R.N., L. Charles Ward, Ph.D., Tracy Allen, B.A.

**Educational Objectives:**

- At the conclusion of this session, the participant should be able
to interpret serum valproic acid levels across time according
to dose and formulation of divalproex, and understand how to switch
patients from divalproex to divalproex extended release.

**Summary:**

- **Objective:** Assess the pharmacokinetics, side effects, and effect-
eness when switching stable bipolar patients from divalproex
delayed-release to divalproex extended-release (ER).
- **Methods:** An eight-week study of divalproex switch to divalproex
  ER in stable bipolar patients. Serum valproic acid (VPA) levels
  were collected at +12hr, +16hr, +20hr, +24hr post-dose. Sym-
  ptoms were assessed with established rating scales.
- **Results:** Baseline mean ± SD dose (mg/d), a.m. and p.m. trough
  VPA level (μg/ml) for six males, were, respectively:
  - 1333 ± 516mg/d, 61 ±19.60, and 50.58 ±19.73 for divalproex
    split dose;
  - 1333 ± 516mg/d, 68.07±17.45, and 39.63 ±13.79 for divalproex
    total dose qhs;
  - 1333 ± 516 mg/d, 65.8±20.77, and 50.0±12.81 for divalproex
    ER (1:1);
  - 1833 ± 516 mg/d, 78.37±28.68, and 52.88±29.19 for divalproex
    ER (1:1+500mg).
- VPA levels of divalproex and divalproex ER (1:1) correlated highly
  at a.m. level (+12-hr post-dose). Divalproex ER yielded a sus-
  tained VPA trough level (+24-hr post-dose) compared to dival-
  proex, total dose qhs (p<0.001). There were no significant differ-
  ences in VPA levels for divalproex ER (1:1) versus divalproex ER
  (1:1+500mg). Clinical rating scales did not significantly change
  and divalproex ER was well tolerated.

**Conclusion:** The switch from divalproex to divalproex ER was
well tolerated, maintained symptom stability, and resulted in more
uniform VPA levels.

**References:**
1. Thibault M, Blume WT, Saint-Hilaire JM, Zakhari R, Sommer-
ville KW: Divalproex extended-release versus the original dival-
proex tablet: results of a randomized, crossover study of well-
controlled epileptic patients with primary generalized seizures.
2. Davis LL, Ryan W, Adinoff B, Petty F: A Comprehensive Re-
view of the Psychiatric Uses of Valproate. J Clin Psychophar-
macol 2000; 20:1:15–17S.

**NR656**  
**Wednesday, May 21, 3:00 p.m.-5:00 p.m.**

**A Placebo-Controlled Study of Nefazodone for the Treatment of PTSD**  
**Supported by Bristol-Myers Squibb Company**

Lori L. Davis, M.D., *Department of Research, VA Medical Center 116, 3701 Loop Road East (151C), Tuscaloosa, AL 35404; Michelle Jewell, M.A., Brett English, Ph.D., Sandra Ambrose, R.N., Al Bartolucci, Ph.D., Jason Farley, M.S.N., Frederick Petty, M.D.

**Educational Objectives:**

- At the conclusion of this session, the participant should be able
to treat patients with PTSD with nefazodone, and to understand
the effects of nefazodone vs. placebo in the treatment of patients
with PTSD.

**Summary:**

- **Objectives:** Test the efficacy of nefazodone in the treatment of
posttraumatic stress disorder (PTSD).
- **Methods:** Forty-one patients with PTSD were enrolled in a ran-
domized, double-blind, placebo-controlled 12-week trial of nefazo-
done. The Clinician Administered PTSD Scale (CAPS) was the
primary outcome measure. Fifteen patients were randomized to
placebo and 26 were randomized to nefazodone. Except for one
female civilian, all participants were male veterans.
- **Results:** In a repeated measures ANOVA with last observation
carried forward, patients on nefazodone showed a significant
improvement in the percent change of CAPS score from baseline
compared to those on placebo (p = 0.04; effect size of 0.6). Sample
size was not powered to test group differences in the CAPS crite-
ron B, C, or D. However, the criterion D subscale showed signifi-
cant improvement in patients treated with nefazodone compared
to those treated with placebo (p=0.006). In addition, the Hamilton
Rating Scale for Depression showed significant improvement
compared to placebo (p = 0.007). The nefazodone group also
showed a nearly significant improvement on the self-report PTSD
Checklist (p=0.08) and the Clinician Administered Dissociative
States Scale (p = 0.06).
- **Conclusions:** This study supports the efficacy of nefazodone
for the treatment of PTSD. Larger placebo-controlled studies are
warranted.

**References:**
1. Davis LL, English BA, Ambrose SM, Petty F: Pharmacotherapy
for Posttraumatic Stress Disorder: a Comprehensive Review.
treatment for chronic posttraumatic stress disorder: an open
Eating Disorders in Diabetes Mellitus and Obesity

Marcelo Papelbaum, M.D., Psychiatry Department, IPUB/UFRJ, Rua Barao de Jaguaripe 63/401, Rio De Janeiro, RJ 22421-000, Brazil; Jose C. Appollinario, M.D., O. Rodrigo Moraia, M.D., Leonardo F. Fontenelle, M.D., Vivian C. Ellenger, M.D., Walmir F. Coutinho, M.D., Leao Zagury, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the relationship between eating disorders and type 2 diabetes mellitus.

Summary:
Objective: To investigate whether obese patients with type 2 Diabetes Mellitus (T2DM) exhibit an increased prevalence of either eating disorders or disturbed eating behavior when compared with obese controls without T2DM.

Methods: Twenty-seven obese patients with T2DM (body mass index greater than 30) and 62 obese controls without T2DM were sequentially evaluated by means of the Structured Clinical Interview for DSM-IV (SCID-I/P), the Binge Eating Scale, and the Beck Depression Inventory; and had their levels of glycosylated hemoglobin (HbA1c) measured. Obese patients with T2DM were compared with their non-T2DM counterparts with the Student's T test for continuous variables and the Chi-square test for categorical ones.

Results: According to the SCID-I/P, an eating disorder was found in 25.9% of obese patients with T2DM (18.5% with BED and 7.4% with BN) and in 33.9% of their non-T2DM counterparts (21.0% with BED and 9.7% with BN) [χ²=4.45; df=1; p=0.04]. Among patients with T2DM, metabolic control measured by the levels of HbA1c were not different between patients with and those without an ED (Z=-0.63, p=0.52).

Conclusions: In our sample, rates of ED in patients with T2DM were similar to those found in obese controls and abnormalities in eating behavior was not associated with a disturbed metabolic control.

References:

Factors Related to Hedonic Responses in Eating Disorders

Renate Elber, M.D., Psychiatry I, General Hospital, 100 rue Leon Cladel BP 765, Montauban, France; van Berlin, M.D., Julien D. Gueffi, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate that hedonic responses could be influenced by numerous factors in eating disorder patients.

Summary:
Background: Hedonic responses to sucrose solutions are reduced in eating (ED) disorder patients.
Aims: Determining factors implicated in hedonic responses in ED patients.

Methods: Patients were evaluated by the Eating Attitude Test (EAT), Eating Disorder Inventory (EDI), MADRS, Scale for Social and Physical Anhedonia (Chapman) and body mass index (BMI).

Hedonic responses to sucrose in ED patients were studied in two different conditions: sucrose solution swallowed versus spit in a double blind, Latin square design of 0, 5, 10, 20, 40% of sucrose. Participants rated pleasantness on a nine-point category scale. The two conditions were randomly administered. A visual analogue scale assessed the fear of swallowing.

Results: Hedonic responses to sucrose were influenced by the test condition (p=0.019). When fear to swallow sucrose was included as covariate, there was no more difference between the conditions of "swallow split" (p=0.143) and there was a concentration by condition by fear to swallow interaction (p=0.03) and an almost significant main effect of fear to swallow (p=0.06). BMI influenced hedonic responses to sucrose whereas diagnostic category, vomiting, age and depression did not.

Discussion: Hedonic responses to sucrose in ED patients are decreased when solutions are swallowed. This may reflect excessive fear of gaining weight rather than decreased ability to experience pleasure.

References:
NR660  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Comparing ICD-10 Atypical Bulimia Nervosa and DSM-IV Binge Eating Disorder

Julia Fandino, M.D., Department of Psychiatry, IEDE and IPUB/UFFRJ, R. Lopes Trovao 88 1501A Icarai, Niteroi, RJ 24220-071, Brazil; Leonardo F. Fontenelle, M.D., Silvia R. Freitas, M.D., Mauro V. Mendlowicz, M.D., Marcelo Papelbaum, M.D., Jose C. Appolinario, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that the usefulness of concept of ICD-10 atypical bulimia nervosa may need to be reassessed.

Summary:
Objective: The ICD-10 atypical bulimia nervosa (ABN) encompasses syndromes that could be classified as the DSM-IV Binge Eating Disorder (BED). We investigated whether BED patients can be differentiated clinically from ABN patients who do not meet criteria for BED.

Methods: Fifty-three obese patients were examined using the Structured Clinical Interview for DSM-IV (SCID) and the ICD-10 criteria for eating disorders. All volunteers completed the Binge Eating Scale, the Beck Depression Inventory, and the Symptom Checklist-90 (SCL-90). Individuals fulfilling criteria for both ABN and BED (ABN=BED, N=18), ABN without BED (ABN=Bed, N=16), and obese controls without DSM-IV or ICD-10 eating disorders (OC, N=19) were compared using the MANOVA and chi-square tests.

Results: ABN=BED and ABN=BED did not differ from OC in any other aspect. When compared to ABN=BED, ABN=Bed showed increased lifetime rates of any anxiety disorder (p=.009) and increased scores in the somatization (p=.001), obsessive-compulsive (p=.01), anxiety (p=.02), anger (p=.005) and psychoticism (p=.01) SCL-90 dimensions.

Conclusions: ABN may be an heterogeneous diagnosis which may need to be reassessed.

References:

NR662  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Long-Term Weight Reduction With Topiramate Psychopharmacology and Pharmacopsychiatry Funds, MN Medical Foundation

Faruk S. Abuzzahab, Sr., M.D., Psychiatry, University of MN, F282/2A West, 2450 Riverside Avenue, Minneapolis, MN 55408-1052; Victoria L. Brown, B.A.

Educational Objectives:
At the conclusion of this session, the participant should recognize that the use of topiramate concomitantly with antidepressants and neuroleptics can help obese patients to lose weight.

Summary:
Introduction: Obesity in depressed and schizophrenic outpatients has been attributed to the use of selective serotonin reuptake inhibitors and the atypical neuroleptics. Topiramate, a novel anticonvulsant with a unique fructopyranose structure, has been reported to promote weight loss. It was added concomitantly to antidepressants and neuroleptics in outpatients to explore its long-term benefit in weight reduction.

Methods: Twenty-two outpatients, 17 females and five males, between the ages of 21 and 64 with an average age of 42.33 +/- 11.36 years received topiramate for over a year concomitantly with their current medications, which were kept constant. The average length of treatment in this study was between 12 and 25 months with an average of 15.41 +/- 4.19 months. Patients were started on a dose of 15-25 mg, which was gradually increased as tolerated.

Results: The weights of the 22 patients at pretreatment were between 52.27 kg and 129.55 kg with an average weight of 93.97 +/- 16.77 kg. The dosages that they reached were between 50
mg and 1200 mg with an average dose of 375 +/- 276.78 mg. After treatment the weights of the patients were between 51.36 kg and 120.91 kg with an average of 85.56 +/- 17.90 kg. With a 95% confidence level the weight loss that was attained was 18.52 +/- 23.22 kg.

Conclusion: There was no exacerbation of underlying psychiatric disorders when topiramate was used concomitantly with psychoactive medications in depressed and schizophrenic patients. Although the exact mechanism of topiramate's action is unknown, this preliminary report indicates that topiramate is effective in promoting weight reduction in outpatients when used concomitantly with antidepressants and neuroleptics.

References:

NR663 Wednesday, May 21, 3:00 p.m.-5:00 p.m. Anorexia and Bulimia Nervosa Among Female Medical Students in Brazil Universidade Federal do Ceara - Brazil Fabio G. Souza, M.D., Department of Medicina Clinica, Universidade Federal Do Ceara - UFC, RUA Manoel Jesuino, 974 Varjota, Fortaleza Ceara, CE 60175 270, Brazil; Maria C. Martins Educational Objectives: At the conclusion of this session, the participant should recognize the importance of screening behaviors suggestive of Anorexia and Bulimia Nervosa in medical students and their association with previous depressive episodes.

Summary:
Objective: This study estimated the prevalence of behaviors suggestive of Anorexia and Bulimia Nervosa in female medical students of the Federal University of Ceara, Brazil, and related body image perception of overweight and prior depressive episodes to the EAT-26 and BITE scores. This is the first study to our knowledge to report behaviors suggestive of Anorexia and Bulimia Nervosa among medical female students in a tropical area of Brazil.

Method: The sample consisted of 199 female medical students with mean age of 20.6 (+ 1.9) years. Self-reported questionnaires based on the EAT-26 and BITE and including questions about prior depressive episodes and body image perception were administered in the classrooms and collected in an urn in order to guarantee anonymity.

Results: According to the EAT-26 scores, 11 (5.5%) students showed high risk to develop Anorexia Nervosa and 53 (26.6%) showed low risk. According to the BITE scores, 7 (3.5%) students had compulsive eating behavior suggestive of Bulimia Nervosa and 46 (23.1%) had non-usual eating behavior. EAT-26 and BITE scores were statistically correlated to prior depressive episodes and body image perception of overweight.

Conclusion: There appears to be a significant number of students presenting behaviors suggestive of eating disorders in this sample.

References:

NR664 Wednesday, May 21, 3:00 p.m.-5:00 p.m. Eating Disorders in Alcohol and Drug-Dependent Women Fulya Maner, M.D., Department of Psychiatry and Neurology, Bakirkoy St. Edu Rsc Hospital, Incint Dikilitas Bakirkoy Ruh Sn, Istanbul Bakirkoy 34747, Turkey; Yuksel Hantas, M.D., Murat Erkiran, M.D.

Educational Objectives:
This study showed that the prevalence of eating disorders (ED) all of which are bulimia nervosa and atypical eating disorder type is significantly high (n=3, 16.1%) among Turkish female alcohol and drug dependent patients (n=72) compared to both controls and alcohol-drug abuse group.

Summary:
The comorbidity of eating disorders (ED) with other psychiatric disorders is of special interest in recent years. In this study we investigated in 72 females who met DSM IV (SCID-I) criteria of alcohol or drug use disorders. The ages of the subjects ranged from 15 to 51 years. We performed the study in Bakirkoy State of Education and Research Hospital for the Psychological and Neurological Diseases in Istanbul, between October 2001 and February 2002. The subjects are 56 (77.7%) alcohol- or drug-dependent and 16 (22.3%) alcohol or drug abuse females. The control group is 41 females within the same age range who have no history of drug use (use alcohol only as a social drinker) and no history of psychiatric admission. The social and familial backgrounds, clinical features of the two groups were assessed with the use of a semi-structured interview form developed for the study. We applied Eating Attitudes Test and DSM VI eating disorders question list. We performed chi-square tests, Fischer's Exact Test, and analysis of variance for statistical evaluations. Nine patients (16.1%) in the dependent group have eating disorders. It is significantly different from the control group (X^2=3.947, p:0.047). There is no ED in the abuse group. Among nine patients, 4 (44.4%) are alcohol, four (44.4%) are opioid, one (11.1%) is drug dependent. 3 (33.3%) of the dependent patients are bulimic, six (66.6%) are atypical ED, three of which are binge ED. In the control group, there is no bulimia and only one (2.4%) is atypical ED. There is no anorexia in dependent and control groups.

References:

NR665 Wednesday, May 21, 3:00 p.m.-5:00 p.m. Personality, Personality Disorders, and Eating Disorders Alexandra Pham-Scottetz, M.D., Department of Psychiatry, CMME, 100 Rue De La Sante, Paris 75674, France; Justine Perrotin, M.D., Christine Foulon, M.D., Julien D. Guelfi, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to assess personality dimensions and personality disorders in eating disordered patients.
Summary:

Introduction: All dominant models of eating disorders implicate personality variables in the development and maintenance of the symptoms. The aim of this study was to assess personality dimensions and disorders in eating disordered patients.

Method: 100 women (from 18 to 49 years old) meeting DSM-IV criteria for eating disorders and hospitalized for a cognitive-behavioral treatment program were interviewed using the SIDP-IV (Structured Interview for DSM-IV Personality Disorders) and were administered the NEO-PI-R (Neuroticism Extraversion Openness Personality Inventory-Revised).

Results: In terms of the NEO-PI-R five dimensions there were no significant differences between the three diagnostic groups (anorexia nervosa, restricting type: N=43, anorexia nervosa, binge-eating / purging type: N=25, bulimia nervosa: N=32).

47% of the patients of our sample had at least one DSM-IV Personality Disorder (PD), assessed with the SIDP-IV. The most frequent diagnoses were: obsessive-compulsive, borderline and dependent PDs. Patients in the PD subgroup, compared with the no PD subgroup:

- had higher Neuroticism scores (mean Neuroticism score 120 vs 93, p < 0.05)
- had more frequently attempted suicide in the past (45% of the PD subgroup vs 18%, p < 0.05)
- were more likely to drop out prematurely of hospital treatment (34% vs 13%, p < 0.05).

Conclusions: Personality disorder assessment is clinically meaningful in eating disorders. Proposals for the clinical management of the eating disordered patients with a personality disorder will be discussed.

References:


NR666 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Some Features of Mothers of Patients With Eating Disorders
Ana M. Garcia de Amusquibar, M.D., Department of Psychiatry, Hospital Italiano, Pje. M Padilla 4065, Buenos Aires 1430, Argentina; Cecilia De Simone, M.D., Carlos A. Finkelsstein, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize some characteristics that are present in mothers of patients with eating disorders at the beginning of consultations.

Summary:

Objective: To compare some features of mothers of patients with eating disorders (E.D.) with a control group of non-consulting adolescents' mothers.

Method: Fifty mothers of patients with E.D. (anorexia nervosa, bulimia nervosa, and non-specified ED), group I, and 30 mothers of non-consulting adolescents, group II, were interviewed. The Eating Attitudes TEST-26 (EAT-26) was administered to both groups and the following aspects were explored: body mass index, breastfeeding or bottle-feeding, mother's history of child abuse, family violence, psychotherapy, psychiatric drugs, abortions (spontaneous and provoked), dieting, binge-eating, eating disorder symptoms, mother-grandmother relationship, maternal grandmother-granddaughter cohabitation.

Results: Patients' mothers scored higher in the bulimic factor of the EAT-26, showed higher binge frequency, more symptoms of eating disorder, depression episodes, bottle-feeding, provoked abortions, and poor mother-daughter relationship with their own mothers versus the control group.

Conclusions: Our data suggest the convenience of holding one-on-one encounters with mothers of patients with E.D. during the diagnostic phase. Data collected in the interviews are discussed and processed with a view to designing a therapeutical strategy which, if necessary, will include the individual approach of the mother, or a mother and daughter session with the therapist.

References:

of spatial ($r=0.56$, $p<0.03$), figural ($r=-0.57$, $p<0.03$) and verbal working memory ($r=-0.64$, $p=0.01$).

**Conclusion:** These data confirm the value of measuring the shape, as well as volume, of cognitively relevant brain regions of interest (ROIs) in neuropsychiatric conditions and offer further support for the association of intrinsic pathology in the caudate nucleus, unrelated to medication, with cognitive abnormalities in the schizophrenia spectrum.

**References:**

### NR669 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
**Stability of Personality Disorder Across the Transition to Young Adulthood**
**Supported by the Victorian Health Promotion Foundation**
Andrew Chanen, M.B.B.S., Department of Psychiatry, University of Melbourne, 35 Poplar Road Road Parkville, Melbourne Victoria 3052, Australia; Henry Jackson, Ph.D., Patrick D. McGorry, M.D.

**Educational Objectives:**
- At the conclusion of this session, the participant should (1) recognize the caveats upon diagnosis of personality disorder prior to age 18 in DSM-IV and ICD-10 do not accord with empirical data, (2) demonstrate a reason for early intervention in personality disorders.

**Summary:**
- **Background:** The literature on 'normal' personality suggests no sudden increase in trait stability at the transition into the third decade of life. Moreover, studies suggest similar patterns of temporal stability and diagnostic efficiency for some personality disorders (PDs), across a range of settings, in teenagers compared to young adults. However, no study has examined teenage outpatients and no clinical study has encompassed the transition into adulthood.
- **Objective:** To examine the two-year temporal stability of categorical and dimensional measures of PD in an outpatient sample of 15–19 year-olds.
- **Method:** 101 outpatients were assessed using the Structured Clinical Interview for DSM II Disorders (SCID-II) at baseline and 37 were re-interviewed, face-to-face, at two years.
- **Results:** Stability of categorical PD was low for all except Antisocial. At the dimensional level, rank order and mean level stability ranged from high (antisocial, schizoid) to moderate (borderline, histrionic, schizotypal) to low (other PDs).
- **Conclusion:** The stability of dimensionally rated PD traits in late adolescent outpatients appears to be similar to that found in young adults in a variety of settings. Early intervention, especially for some Cluster A and B PDs in this age group, appears as justified as intervention in young adults.

**References:**

### NR670 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
**The Impact of Maternal Emotional Well-Being on Infants**
Kimberly A. Ragan, M.S.W., Department of Psychiatry, Emory University, 13658 Clifton Road, Suite 6100, Atlanta, GA 30322; Zachary N. Stowe, M.D., Patricia Brennan, Ph.D., D. Jeffrey Newport, M.D.
Educational Objectives:

At the conclusion of this session, the participant should 1) be familiar with the literature on the impact of maternal depression on infant well-being. 2) The potential confounds and limitations of the literature will provide a basis for a more critical analysis. 3) Appreciate the multi-dimensional impact of maternal mental illness.

Summary:

A broad literature has investigated the impact of maternal emotional status on early mother-infant interactions and infant well-being. A MEDLINE search using keywords “maternal anxiety”, “maternal depression”, “maternal stress”, cross referenced with “infant outcomes” was conducted. Studies that included children over the age of 5 years and/or did not include a systematic assessment of both mother and infant were excluded from further analysis. A total of 70 studies with 35,501 mother-fetal/infant pairs were included for further scrutiny. Outcome measures were categorized as (1) obstetrical outcome (n=18: 21,360 infants); (2) infant physiology/neurobiology (n=23: 2192 infants); (3) behavioral (n=26: 11,077 fetus/infants); and (4) mother-infant interactions (n=22: 2634 infants). Seventeen studies (n=3533) employed measures spanning different categories. Meta-analysis is pending, as the potential confounds were alarming. Five studies documented or excluded based on medication use during pregnancy, no study noted medication use in breast-feeding, and the duration of maternal symptoms. Despite the potential association of maternal depression with pre-term delivery and low birth weight, 32 of the infant studies made no mention of obstetrical data such as birth weight, pre-term delivery, etc. The contribution of these confounds in the final meta-analysis will be discussed in light of treatment planning for women during pregnancy and the postpartum period.

References:


NR671  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Quality of Life in Outpatients With Personality Disorders

Kjersti Narud, M.D., Department of Psychiatry, University of Oslo, Soesvannsveien 27, Oslo 0320, Norway; Alv A. Dahl, M.D., Arnstein Mykletun, M.A.

Summary:

Objective: Quality of life (QoL) in patients with personality disorders (PD) has not been well studied, and was compared to QoL in Axis I disorders and a representative sample of the general population.

Method: Patients (N=130) were recruited from an outpatient department in Oslo, Norway. The material consisted of 72 patients with PD and 36 patients with Axis I disorders. QoL was measured by the eight dimensions of Short Form 36 (SF-36). Age- and gender adjusted means of SF-36 from a representative sample of Norwegians was used as norms. The means of the dimensional scores were compared.

Results: The PD and Axis I groups scored significantly lower than the adjusted norms on all SF-36 dimensions. The PD group had significantly lower scores than the Axis I group on almost all dimensions. No significant differences were found between the PD clusters. Pure PD and comorbid PD differed significantly on social functioning and mental health.

Conclusions: Patients with PD have significantly lower QoL on all dimensions compared to normal subjects, and on most dimensions compared to Axis I patients. Belonging to various PD clusters, having pure or comorbid PD hardly influenced QoL, neither did the number of PD present in the patients.

References:


NR672  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
An International Survey of Pharmacotherapy in BPD Supported by Janssen Pharmaceutica Products, L.P.

Mark Taylor, M.D., Spring Park Centre, 101 Denmark Street, Glasgow G22 5EV, United Kingdom; Harriet Devlin, B.S.C., Michael Schwiers, B.S.C., Kenneth R. Silk, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize symptom profiles in borderline personality disorder (BPD) identified in the survey as being amenable to medication, and compare their own prescribing practice in BPD with the survey consensus.

Summary:

Introduction: Most individuals with borderline personality disorder receive psychotropic medication, but the evidence base guiding good clinical practice is limited. We decided to compare real-life practice on two continents by surveying experienced psychiatrists’ views.

Method: A structured standardized questionnaire regarding prescribing in borderline personality disorder was sent to psychiatrists at the department of psychiatry at the University of Michigan, and to a random sample of psychiatrists in Victoria State, Australia. A total of 177 completed questionnaires (85/115 American, 92/150 Australian) were analyzed. Respondents were asked their views on which symptoms they hoped to treat, and what were their first- and second-choice medications.

Results: In both countries, the majority of psychiatrists felt that depression and other mood disturbance was the key area for pharmacotherapy, with impulsivity rated second. SSRI antidepressants were the most commonly prescribed class of medication. Antipsychotics were preferred to mood stabilizers as augmenting agents, particularly where aggression and paranoia existed. Mood stabilizers were preferred for those with impulsivity and labile affect. There were differences between locations, with American psychiatrists more commonly using non-SSRI antidepressants and valproate in first- and second-line therapy.

Conclusion: The vast majority of psychiatrists surveyed wish to prescribe in borderline personality disorder, and mostly use SSRI antidepressants. Medication choice is guided by symptom profile, and minor international differences in practice exist.

References:

NR673 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Quetiapine Treatment of BPD
Supported by AstraZeneca Pharmaceuticals
Evens Villeneuve, M.D., Department of Psychiatry, CH-Robert Giffard, 2601 Canardiere, Quebec, PQ G1S 4V5, Canada; Sophie Lemelin

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate which domain of borderline pathology could be treated with medication, and estimate how important it is to treat impulsivity on borderline patients.

Summary:
Among Axis-II disorders, borderline personality disorder (BPD) is the more critical to treat. BPD includes four main domains of symptoms (affective, psychotic symptoms, impulsive behaviors, interpersonal problems) of which, the first three can be addressed by pharmacotherapy. From studies in patients with schizophrenia, it may be expected that quetiapine will improve these three domains, and the functional铜 ownership of BPD patients.

Objective: To evaluate the impact of quetiapine on BPD symptomatology.

Method: Eleven BPD outpatients (DSM-IV criteria; DIB-R > 7) completed a 12-week open-label study with quetiapine. The clinical impact of quetiapine was evaluated using the following measures: Hamilton Depression and Anxiety Rating Scales, Brief Psychiatric Rating Scale, Impulsivity Scale, Buss-Durkey Hostility Inventory, Temperament and Character Inventory, Global Assessment Functioning, Social Adjustment Scale. Attentional functioning was examined using a computerized battery evaluating different attention components (selective attention, divided attention, working memory, executive functions).

Results: Mean daily dose of quetiapine was 250 mg/day. Depressive, anxiety, social functioning, impulsivity, hostility, and character dimensions were significantly (p<0.05) reduced, but not psychotic symptoms on the BPRS. There was significant amelioration on selective attention (Stroop test) and divided attention (Dual task).

Conclusion: Quetiapine is effective in reducing many clinical and attentional deficits in BPD patients.

References:

NR674 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Childhood-Onset Neuropsychiatric Disorders and Personality Disorders
Henrik Soderstrom, M.D., Department of Forensic Psychiatry, Göteborg University, RPA Box 4024, Hisingen Backa 42204, Sweden; Maria Rastam, M.D., Elisabet Wenn, M.D., Stefan Westergren, M.D., Christopher Gillberg, M.D., Anders Forsman, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to consider the possibility of personality disorder being broader phenotypes of childhood onset neuropsychiatric disorders such as AD/HD or autism spectrum disorders.

Summary:
The DSM-IV personality disorders refer to stable maladaptive patterns of cognitions, affects, interpersonal functioning, and impulse control since adolescence. Dimensional models distinguish between basic temperaments (reaction patterns), assumed to be relatively stable throughout life, and character (conceptual maturity). Childhood-onset neuropsychiatric disorders (e.g., AD/HD and autism spectrum disorders) are diagnosed according to behavioural criteria that overlap with the definitions of personality and may express the same underlying factors. To describe common and discriminating aspects, we analysed the outcome of SCID-II, KSP, and TCI in three samples of adult subjects with neuropsychiatric disorders. Most subjects fulfilled the SCID-II criteria for several personality disorders, often for at least one from each Cluster. Autism spectrum disorders were most closely associated with the Cluster A or C disorders, while AD/HD was most strongly related to the Cluster B disorders, and the DSM-IV personality disorder diagnoses rarely added valuable clinical information to the neuropsychiatric diagnostic work-up. In Cloninger’s biosympathetic model, however, temperament was influenced by the neuropsychiatric disorders but varied widely also in groups with common neuropsychiatric diagnoses, whereas the character dimensions “Self-Directedness” and “Cooperativeness” revealed severe immaturity in all groups, indicating that a neuropsychiatric disorder may hamper character development in the same way as “difficult temperaments.”

References:
no-PTSD showed less activation to fearful faces than normal-controls, and did not differ significantly from each other.

Conclusions: Among frontal cortical structures implicated in emotion regulation, opposite patterns of activation during viewing of fearful faces were found in the ACC and OFC for BPD patients depending on the presence of PTSD, while a similar pattern was found in BA10, suggesting distinct and shared neural correlates for these frequently comorbid conditions.

References:

NR676 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Long-Term Treatment of PMDD Supported by GlaxoSmithKline
Kevin M. Bellew, M.S., Department of Psychiatry, GlaxoSmithKline, P.O. Box 61540, King of Prussia, PA 19406; Lee S. Cohen, M.D., Jane St. Lambert, Ph.D., Ian M. Bridges, M.Sc., James P. McCafferty

Educational Objectives:
At the conclusion of this presentation, the participant will be able to critically evaluate the long-term efficacy of paroxetine CR in the treatment of PMDD.

Summary:
Objective: To evaluate the long-term efficacy and safety of paroxetine CR in the treatment of PMDD.
Methods: A multicenter, double-blind, placebo-controlled, three-arm, fixed-dose extension study comparing treatment with paroxetine CR 25 mg (n=348) and 12.5 mg (n=333) with placebo (n=349). Following completion of a three-month, double-blind clinical trial, patients with a CGI improvement score of 1, 2, or 3 (very much improved, much improved, or minimally improved) were given the opportunity to continue on double-blind treatment for an additional three menstrual cycles. Patients with ongoing clinically significant adverse events were excluded from the three-month extension. Patients rated daily mood symptoms (irritability, tension, affective lability, and depressed mood) using visual analog scales (VAS). The primary measure of efficacy was the change in baseline in mean luteal phase VAS-Mood score at treatment cycle 6 LOCF. VAS-Mood score was calculated using a composite of the four mood symptoms. Secondary measures included a physical symptoms VAS and the Sheehan Disability Scale.
Results: A statistically significant difference was demonstrated in favor of paroxetine CR 25 mg and 12.5 mg versus placebo for the treatment cycle 6 LOCF endpoint (p<0.001 for both doses). A statistically significant difference was also demonstrated in favor of paroxetine CR 25 mg and 12.5 mg versus placebo for the physical symptoms VAS (p<0.01 for both doses) and for the social, work, and family life domains of the SDS (p<0.01 for both doses). Conclusion: Paroxetine CR is effective in treating PMDD for up to six months. The nature of adverse events in this 6-month study was comparable to the profile of paroxetine CR studied in other psychiatric disorders.

References:

NR677 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Pooled Analysis of Three Large Clinical Trials in the Treatment of PMDD Supported by GlaxoSmithKline
Kimberly A. Yonkers, M.D., Department of Psychiatry, Yale University School of Medicine, 142 Temple Street, Suite 301, New Haven, CT 06510; Kevin M. Bellew, M.S., Timothy E. Rolfe, M.Sc., Philip Perera, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant will be able to critically evaluate the results of a large clinical development program in PMDD.

Summary:
Objective: To increase the generalizability of results obtained from the paroxetine CR PMDD clinical development program to a worldwide population.
Methods: Data from three independent, multicenter, double-blind, placebo-controlled, fixed-dose studies were pooled to evaluate the effect of paroxetine CR in treating PMDD. The primary analysis of all three studies involved assessing the effect of paroxetine CR at doses of 12.5 mg and 25 mg on a composite of visual analog scales (VAS) measuring irritability, tension, affective lability, and depressed mood, for up to three cycles. Secondary analyses included the evaluation of paroxetine CR on physical symptoms (e.g., breast tenderness/ swelling, headache, and sensations of bloating) and on occupational and social functioning.
Results: Data from 933 PMDD patients obtained at 126 sites across the U.S., Europe, and South Africa were available for this analysis. At study endpoint, paroxetine CR was statistically superior to placebo in treating symptoms of PMDD as measured by patient-rated visual analog scales (p-value less than 0.01 for both doses vs. placebo). Paroxetine CR was also statistically superior compared with placebo in treating associated physical symptoms of the disorder (p-value less than 0.01 for both doses). The Sheehan Disability Scale (SDS) total score, which is a composite measure of impairment in work, social, and family life, showed significant improvements for paroxetine CR-treated patients compared with placebo-treated patients (p-value less than 0.05 for both doses vs. placebo). Approximately 9% of paroxetine CR patients withdrew from the study due to an adverse event. The most common adverse events leading to withdrawal in paroxetine CR patients were asthma (4%) and nausea (3%).
Conclusion: Paroxetine CR is effective in treating the core psychiatric symptoms of PMDD along with associated physical symptoms and impairment in social functioning.

References:
Educational Objectives:
At the conclusion of this session, the participants should be able to examine the efficacy and tolerability of intermittent dosing of venlafaxine for the treatment of PMDD.

Summary:
Objective: To examine the efficacy and tolerability of intermittent dosing of venlafaxine for the treatment of PMDD.
Methods: An open study, with one cycle as a diagnostic confirmation phase; one cycle as a single-blind, placebo phase; and two cycles as a treatment phase. Women aged 18–45 years, with regular cycles, who did not meet criteria for any major Axis I psychiatric disorder were recruited for the diagnostic phase. Daily Rating of Severity of Problems (DRSP) forms and the Discontinuation-Emic Signs and Symptoms Self-Rated (DESS-SR) checklist were administered throughout the study. Treatment efficacy was measured based on changes in luteal DRSP total scores and sub-scores (depression, physical symptoms, anger, overall functioning). Remission was defined as CGI-severity ≤ 2 at the end of treatment.

Results: One hundred and four subjects entered the diagnostic confirmation phase. Twenty-four subjects had their diagnosis of PMDD confirmed by evaluation with DRSP forms. Six out of 17 subjects who completed the placebo phase were considered placebo responders. Eleven subjects entered the treatment phase. Study completers (N=9) had a significant decrease in luteal DRSP total scores and sub-scores, and overall improvement in functioning (p<0.05 for all comparisons, Wilcoxon signed ranks tests). Six of nine women (67%) had CGI scores ≤ 2 at the end of study treatment. No significant discontinuation symptoms were observed.

Conclusion: Intermittent use of venlafaxine is an efficacious and well-tolerated treatment for women who suffer from PMDD.

References:

NR679 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Multicenter Study of Bupropion in Female Hypoactive Sexual Desire Disorder Supported by GlaxoSmithKline
Robert T. Segraves, M.D., Department of Psychiatry, Case Western Reserve University, 2500 Metro Health Drive, Cleveland, OH 44109-1996; Anita L.H. Clayton, M.D., Harry A. Croft, M.D., Abraham Wolf, Ph.D.

Educational Objectives:
At the conclusion of this presentation, the participant should understand current investigation of bupropion for the treatment of female hypoactive sexual desire disorder.

Summary:
Objective: Single-blind research suggests the efficacy of bupropion for the treatment of idiopathic global hypoactive sexual desire disorder (HSDD) in premenstrual women. This study assessed this hypothesis using a more rigorous research design.
Methods: A total of 72 women (ages 23.7 to 46.2) who met operational criteria for hypoactive sexual desire disorder (HSDD) were studied for four months in a randomized, placebo-controlled, double-blind, titrated dose, multi-site study. Entry criteria included duration of HSDD between six months and 10 years, Hamilton Depression and Hamilton Anxiety scores both below ten, stable sexual partner, absence of interpersonal conflict, serum free testosterone equal to or above 1.1 pg/ml at days 20–24 of the menstrual cycle, and absence of other active psychiatric disorder. Response was measured at screening, baseline, day 28, 56, 84, and 112 by Changes in Sexual Functioning Questionnaire (CSFQ), a 14-item self-report standardized test.

Results: Women receiving bupropion had significantly higher total CSFQ scores at day 28 (45.1 ± 1.1 SEM vs. 41.1 ± 1.3 SEM, t=2.3, p=0.03); scores continued to increase at each time point for women receiving the drug.

Conclusions: Bupropion may be effective in a subgroup of premenopausal women with HSDD.

References:

NR680 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
An Open-label Trial of Sildenafil Addition in Risperidone-Treated Male Schizophrenia Patients With Erectile Dysfunction
Alex Aviv, M.D., Aabrabel Mental HC 8b, 10 Tolkowsky Street, Tel-Aviv 69-358, Israel; Assaf Shelef, M.D., Abraham Weizman, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to recognize the importance of identifying erectile dysfunction in schizophrenia patients who are treated with antipsychotic medications, and to treat those patients with sildenafil.

Summary:
Objective: Sexual dysfunctions frequently occur in schizophrenia patients. Sildenafil is used for treatment of erectile dysfunction caused by diverse factors. The aim of our study was to evaluate its efficacy, safety and effect on compliance with antipsychotic medications in risperidone treated schizophrenia patients suffering from erectile dysfunction.

Methods: In a six-week, open-label trial, sildenafil was administered to 12 patients, treated with risperidone and reporting erectile dysfunction. Starting dose was 25 mg with possibility to increase the dose to 75 mg. Three patients who did not respond stopped sildenafil after three weeks. Efficacy was assessed by the International Index for Erectile Function and Valevski-Weizman Male Sexual Function scales.

Results: Nine out of 12 patients completed the six weeks trial and three patients stopped taking sildenafil after three weeks due to lack of response. We observed statistically significant improvements in all sexual function domains (desire, erectile function, orgasmic function, intercourse satisfaction and overall satisfaction) in the nine patients who completed the trial, and in most of the domains for the whole 12 participants. 57% of the patients exhibited partial or much improvement.

Conclusions: Sildenafil is an effective agent for the treatment of erectile dysfunction in risperidone treated schizophrenia patients.

References:
Quetiapine for Antipsychotic-induced Sexual Dysfunction: An Open-Label Trial
Supported by AstraZeneca Pharmaceuticals, L.P.

Matthew J. Byerly, M.D., University of Texas Southwestern Psychiatry, 5959 Harry Hines Blvd Suite 600, Dallas, TX 75235; E. Lescomflair, M.D., M.T. Weber, Ph.D., Rhiannon Holland, B.A., Robert Fisher, B.S., Thomas J. Carmody, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should recognize that persons with schizophrenia and antipsychotic-induced sexual dysfunction experienced improved sexual functioning when switched to quetiapine.

Summary:

Background: Sexual dysfunction is common with antipsychotic treatment. This study's primary objective was to evaluate the effect of switching outpatients with schizophrenia and antipsychotic-induced sexual dysfunction to open-label quetiapine treatment. Secondary aims were to compare the prolactin-related and antipsychothtic effects of quetiapine vs. pre-study antipsychotic treatment.

Method: Eight patients with at least moderately severe antipsychothctic-induced sexual dysfunction (n=7 taking risperidone, dosage 4-6 mg/day; n=1 taking haloperidol, dosage = 10 mg/day) were evaluated prospectively after switching to six weeks of quetiapine treatment. Sexual functioning was assessed with the five-item, Arizona Sexual Experience Scale (ASEX); psychopathology with the Positive and Negative Syndrome Scale (PANSS).

Results: Switching to quetiapine was associated with consistent and statistically significant improvement in ASEX total scores (P = 0.008). In addition, PANSS total scores decreased significantly (P=0.03). Improvements in PANSS General Psychopathology subscale scores were larger than those on Positive and Negative Symptom subscales, suggesting that changes in PANSS total scores may have resulted from improvements in sexual functioning. Plasma prolactin levels tended to decrease after the switch to quetiapine (P = 0.09).

Conclusion: Switching patients with antipsychotic-induced sexual dysfunction to open-label quetiapine treatment resulted in consistent and marked improvements in sexual functioning of outpatients with schizophrenia.

References:
Results of recent studies suggest that Lofexidine is less hypoten-
sive than Clonidine at equally effective doses. It makes eminently
good sense therefore, to assess Lofexidine in a controlled double
blind trial.

Method: Seventy subjects were recruited via newspaper and
word of mouth. Sixty five of the subjects randomly assigned to
either Lofexidine plus supportive treatment or Placebo plus sup-
portive treatment, were completers/evaluable. The study took
place on inpatient units at three sites across the United States.
It was divided into three phases, (1) opioid agonist stabilization
phase (Days 1–3 100mg of sc morphine daily), (2) Detoxification/
Medication or Placebo Phase (Days 4–8, Lofexidine/Placebo), and
(3) Postdetoxification/Medication phase (days 9–11, all subjects
receive placebo).

Results: Data analysis using ANCOVA suggest that lofexidine
plus supportive treatment was significantly (P < 0.0035) superior
to placebo plus supportive treatment.

Conclusion: Lofexidine is a promising non opioid medication for
heroin detoxification.

References:
Phase II/II study of Lofexidine (Alpha-2 Adrenergic Agonist) for
opiate detoxification. Drug and Alcohol Dependence. 68/supp. 1, s200.

NR684 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Anxiety and Smoking Cessation: Results From an
Open Trial
National Institute on Drug Abuse
Rene P. LaJe, Ph.D., Clinical Psych Department, NYS
Psychiatric Institute, 1051 Riverside Drive, Unit 116, New York,
NY 10032; Lirio S. Covey, Ph.D., Fay Stetner, M.A., Roger
Vaughan, D.P.H., Alexander H. Glassman, M.D., Jenny R.
Masmela, B.A., Catherine Loduca, B.S.

Educational Objectives:
At the conclusion of this session, the participant should be able
to recognize anxiety symptoms that may contribute to a patient's
inability to quit smoking during smoking cessation treatment.

Summary:
Introduction: We examined the relationship between failure to
quit smoking and increases in state anxiety during a smoking cessation
study with bupropion sustained-release (SR) and nicotine
transdermal patches.

Methods: Two-hundred and seventeen patients (55% male,
mean age = 43) participated in the open trial of 300 mg of bupro-
propion SR and 21 mg of nicotine patches for smoking cessation.
At baseline, they smoked at least 15 cigarettes a day, did not
experience a major depressive episode in six months prior to
entry assessed with the SCID, and had no unstable medical or
psychiatric conditions. We administered the Spielberger State
Anxiety Inventory (SAI) (scores ranging from 20–60), before and
after four weeks of treatment.

Results: One hundred and forty-one patients (65%) completed
four weeks of treatment. Forty-three patients dropped out prior to
week 4 (adverse events (n=17), lost to follow-up (n=12), withdrew
consent (n=13), protocol violation (n=11) and 33 patients did not
take the dosage of medication as per protocol. Increased change
in state anxiety was significantly associated with failure to quit
smoking (OR=1.07, CI: 1.02–1.12, p=0.004).

Conclusions: The results suggest that increases in state anxiety
may be associated with inability to quit smoking during smoking
cessation treatment.

References:
1. Jorenby DE, et al. A controlled trial of sustained-release bu-
propropion, nicotine patch, or both for smoking cessation. The
2. West R, Hajck P. What happens to anxiety levels on giving up

NR685 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Differences in Regional Gray Matter Between
Smokers and Nonsmokers
National Institute on Drug Abuse
Arthur L. Brody, M.D., Department of Psychiatry, UCLA, 300
UCLA Medical Plaza, #2200, Los Angeles, CA 90025; Mark A.
Mandelkern, M.D., George Bartzokis, M.D., Murray E. Jarvik,
M.D., Grace Lee, B.S., Joe Huang, B.S., Eedythe D. Lonon,
Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should under-
stand brain volume differences between smokers and nonsmok-
ers, along with their functional significance.

Summary:
Objective: Magnetic resonance imaging (MRI) studies have
demonstrated associations between cigarette smoking and large-
scale brain abnormalities, such as ventricular enlargement and
atrophy. Prior research indicates that smokers and non-smokers
have functional differences in more localized brain regions, such
as the lateral prefrontal cortex (PFC), anterior cingulate cortex
(ACC), ventral caudate, and thalamus. Using MRI, we examined
differences in regional gray matter between smokers and non-
smokers.

Method: Thirty-six otherwise healthy adults (19 smokers and
17 non-smoking controls) underwent spoiled-gradient-recalled ac-
quision MRI of the brain. Both hand-drawn regions of interest
(ROIs) and voxel based morphometry (VBM) were used to assess
overall group differences and group differences with age in re-
regional gray matter volumes and density, respectively.

Results: The ROI and VBM analyses revealed that smokers
had smaller gray matter volume and lower gray matter density in
the lateral PFC. Smokers also had smaller gray matter volumes
in the dorsal anterior cingulate cortex (ROI analysis) than non-
smokers.

Conclusions: Smokers and non-smokers differed in regional
gray matter in brain areas previously linked with nicotine depen-
dence. Lower gray matter volume and density in the PFCs of
smokers may help explain functional differences between smokers
and nonsmokers in working memory tasks.

References:
history and nicotine effects on cognitive performance. Neuropsy-
2. Brody AL, Mandelkern MA, London ED, Childress AR, Bota
RG, Ho ML, Lee GS, Saxena S, Baxter LR, Madsen D, Jarvik
ME: Brain metabolic changes during cigarette craving. Arch
Gen Psychiatry 2002; 59:1162–1172.

NR686 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Early Diagnosis of Dual Disorders During Detox
Using Mood and Behavior Dimension Assessment:
High Obsessivity in Stimulant Abuse Patients
Robert O. Morton, M.D., Department of Psychiatry, Tulsa
Center Behav, 2323 South Harvard, Tulsa, OK 74114; Marilyn
Davis, B.S., William Yarborough, M.D., William R. Yates, M.D.
Educational Objectives:
At the conclusion of this session, the participant should be able to distinguish dual disordered patients early in detox using the described mood and behavior self assessments.

Summary:
Objective: Their has been a need to identify dual patients early in detox in order to stabilize the underlying comorbid psychiatric condition, thus allowing the patient to take full cognitive and emotional advantage of the treatment options offered. Utilizing self-assessments of mood and behavior, we were able to identify dual patients within five days of detoxification, and initiate aggressive psychopharmacological intervention.

Method: 275 patients in various stages of detoxification (0 to >30 days) were assessed utilizing the Zung depression and anxiety indices and the Marin apathy, Barratt impulsivity, and Maudsley obsessivity self-assessment scales. A single index of psychopathology was derived from these scores. 186 non-chemically dependent patients with a psychiatric disorder were similarly assessed. 92 patients were assessed pre and post 60-day inpatient treatment. Diagnosis of the dual disorder was made by a DSM-IV-based interview blind to the results of the assessments.

Results: Dual patients had significant and persisting pre-treatment elevations of the index when compared with a similar detoxified, non-dual diagnosis CD population at 0-5 days (p<.05), 6-10 days (p<.01), 11-30 days (p<.01) and >30 days (p<.01). Non-dual patients had mild elevations at 0-5 days but were normal at 6-10, 11-30 and >30 days. In dual patients completing an inpatient program, their was a significant reduction in the pretreatment index compared with post treatment (p<.01). There were no significant differences in specific assessment scores within the dual diagnosis group when patients were separated based on diagnosis or drug of choice categories with the exception of obsessivity. Elevated scores were found on the Maudsley scale in cocaine (16.7, CI=2.41) and methamphetamine (16.43, CI=2.89) dependent patients compared with alcohol (10.26, CI=2.28), polysubstance (8.54, CI=3.77) cannabis (8.75, CI=4.39), opioid (7.30, CI=5.11) and anxiolytic (4.25, CI=6.79) dependent patients. These elevated pre-treatment values were reduced in all categories after the 60-day treatment period with the exception of the stimulant-dependent groups.

Conclusion: These preliminary data suggest that there is significant global alteration in mood and behavior dimensions in dual diagnosis patients unaffected by type of substance use or length of time since detoxification. Using an index of psychopathology, these patients can be distinguished from non-dual CD patients as early as five days post detox. Aggressive psychosocial and pharmacological intervention markedly reduces these dysfunctional symptom states. The unexpected high levels of obsessivity unrelated to drug seeking found in stimulant abuse suggests a disruption in obsessivity-compulsivity neural circuitry that in stimulant users may not be immediately reversible. Further studies are underway to clarify this phenomenon.

References:
2. Caton C, Samet S, Harin D: When Acute-Stage Psychosis and Substance use co-occur: Differentiating Substance-Induced and Primary Psychotic Disorders.

NR687 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Dopaminergic Receptor D1 Is Associated With Psychostimulant Methamphetamine Abuse
Hsiing-Cheng Liu, M.D., Department of Psychiatry, Taipei City Psychiatric Center, 309 Sung-Te Road, Taipei 110, Taiwan.

Chih-Ken Chen, Su-Lien Chen, Sy-Jye C. Leu, Ph.D., Shih-Ku Lin, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that DRD1-48A polymorphism is associated methamphetamine abuse.

Summary:
Objective: Alterations in the serotonin transporter (5-HTT) have been implicated in a variety of psychiatric disorders including cocaine dependence. A polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) appears to influence the expression of 5-HTT in human cell lines. We investigated whether 5-HTTLPR variants were related to differences in measures of platelet serotonin sites in cocaine dependent controls and healthy volunteers.

Methods: Polymerase chain reaction based genotyping of of 44-base pair (bp) insertion/deletion polymorphism in 5-HTTLPR was performed in 138 cocaine-dependent African-American subjects and 60 African-American controls. This yielded a short (S) and a long (L) allele. Platelet 5-HTT sites were measured using

NR688 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Relationship Between 5HT Transporter Gene Polymorphism and Platelet 5HT Transporter Sites Among African-American Cocaine-Dependent Individuals and Healthy Volunteers
National Institute on Drug Abuse
Louai A. Bilal, M.D., Department of Psychiatry, Thomas Jefferson University, 833 Chestnut East, Suite 210D, Philadelphia, PA 19107; Ashwin A. Patkar, M.D., Wade H. Berrettini, M.D., Raman N. Gopalakrishnan, M.D., Paolo Mannelli, M.D., Michael J. Vergare, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate that genotypic variations in the serotonin transporter do not influence levels of platelet 5-HTT in cocaine abuser or healthy subjects.

Summary:
Objective: Alterations in the serotonin transporter (5-HTT) have been implicated in a variety of psychiatric disorders including cocaine dependence. A polymorphism in the promoter region of the serotonin transporter gene (5-HTTLPR) appears to influence the expression of 5-HTT in human cell lines. We investigated whether 5-HTTLPR variants were related to differences in measures of platelet serotonin sites in cocaine dependent controls and healthy volunteers.

Methods: Polymerase chain reaction based genotyping of of 44-base pair (bp) insertion/deletion polymorphism in 5-HTTLPR was performed in 138 cocaine-dependent African-American subjects and 60 African-American controls. This yielded a short (S) and a long (L) allele. Platelet 5-HTT sites were measured using
the tritiated paroxetine binding assay. Relationship of 5-HTTLPR genotypes with Bmax (density of serotonin transporter) and Kd (affinity constant) were examined.

Results: Consistent with our previous findings, Bmax values were significantly lower in cocaine patients (640 ± 233) than controls (906 ± 225) (p<.001), however 5-HTTLPR genotype distribution or allele frequencies did not differ between the two groups. There were no significant differences in Bmax between the three patients showing comparable reductions in Bmax than the corresponding genotypes in controls. Demographic variables, severity of substance use or depression were unrelated to Bmax or 5-HTTLPR genotype.

Conclusions: Although platelet 5-HTT densities are reduced in cocaine patients compared to healthy volunteers, genotypic variations in the serotonin transporter do not seem to influence levels of platelet 5-HTT in cocaine abuser or healthy subjects.

References:

NR690 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Levetiracetam Prevents Signs of Alcohol Withdrawal in Mice

Barbara Bennett, Ph.D., Clinical Development, UCB Pharma Inc., 150 Lake Park Drive, Smyrna, GA 30080; Yves Lamberty, Ph.D., Jean C. Bizot, Ph.D., Fabrice Trovero, Ph.D., Henrik Klitgaard, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss a new potential treatment to prevent certain symptoms of alcohol withdrawal using a new anticonvulsant with a novel mechanism of action.

Summary:
Objective: A need exists for new treatment opportunities of alcohol withdrawal that offer advantages in terms of abuse potential and interactions with alcohol compared to benzodiazepines (Malcolm et al., 2002). Levetiracetam (LEV) is a novel antiepileptic drug that has been shown recently to prevent signs of anxiety in mice submitted to a benzodiazepine withdrawal (Lamberty et al., 2002). We further investigated the potential of LEV to prevent certain behaviours observed after alcohol withdrawal in mice.

Methods: Male DBA/2 mice were subjected to a forced ethanol drinking procedure during eight weeks. During the last week of forced ethanol consumption, animals received a daily intraperitoneal (i.p.) administration of saline, or levetiracetam 17, 54 and 170 mg/kg (n = 10–11/group). Then, ethanol was withdrawn and spontaneous tremors and handling-induced convulsions were observed (day 70).

Results: The results indicated that LEV did not increase ethanol consumption during the treatment period. Ethanol withdrawal resulted in a significant appearance of spontaneous tremors and handling-induced convulsions. LEV dose-dependently prevented these behaviours with a statistically significant effect appearing at a dose of 170 mg/kg.

Conclusions: These experimental results suggest that LEV might be an effective treatment of alcohol withdrawal in humans.

References:

NR691 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
A Neuronal Correlate of Alcohol Urges: A PET Study

Andreas Heinz, M.D., Department of Psychiatry, Charite, Stralauaplatz 2, University of Berlin, Germany; Mattias Reimold, M.D., Janu Wraa, Dieter F. Braus, M.D., Goetz Mundle, M.D., Hans-Jurgen Machulla, M.D., Karl Mann, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that, the availability of |x-opiate receptors is increased in alcoholics in the nucleus accumbens, amygdalae, frontal cortices, and thalamus and correlated positively in the nucleus accumbens with alcohol craving. Alcoholics with elevated |x-opiate receptor in the brain reward system may profit from anti-craving medication.

Summary:
Introduction: The pleasant effects of alcohol are partially mediated by central |x-opiate receptors stimulated by alcohol-associated endorphine release. Conversely, blockade of |x-opiate receptors with naltrexone reduces the relapse risk among alcoholics. We tested the hypothesis that alcohol craving is pronounced among alcoholics with a high availability of |x-opiate receptors in the brain reward system.

Methods: We measured |x-opiate receptors in vivo with positron emission tomography (PET) and the radioligand [111]O-carfentanil in 22 male alcoholics and in 12 age-matched healthy males. The Obsessive Compulsive Drinking Scale (OCDS) was used to assess the severity of alcohol craving.

Results: The availability of |x-opiate receptors in the bilateral ventral striatum/nucleus accumbens, amygdalae, frontal cortices, and thalamus was significantly elevated in alcoholics compared with healthy subjects. Higher availability of |x-opiate receptors in the ventral striatum was associated with craving for alcohol.

Conclusion: For the first time we showed that the availability of |x-opiate receptors was increased in the ventral striatum/nucleus accumbens, a core area of the brain reward system, and in brain areas implicated in executive behavior control and associative learning. These findings reveal a neuronal network of alcohol urges. Alcoholics with elevated |x-opiate receptors in the brain reward system may profit from anti-craving medication.

References:
Educational Objectives:

At the conclusion of this session, the participant should understand the childhood and adolescent psychosocial factors that predict SUDs in young adulthood, as assessed by a longitudinal study using a representative sample of the community. This study controls for parental SUDs and for earlier diagnoses of SUDs.

Summary:

Introduction: The purpose of this longitudinal study is to extend previous research in the assessment of childhood and adolescent psychosocial factors that predict substance use disorders (SUDs) in adulthood.

Methods: Subjects consisted of a random, community-based sample of 736 young adults living in upstate New York, who were interviewed at five points in time over a 27-year period. The average age of the subjects at the most recent interview was 27. Trained interviewers administered a structured questionnaire, which consisted of a number of widely used scales assessing aspects of development from childhood through early adulthood. Substance use disorders (SUDs) were assessed using a version of the UM-CIDI, but SUDs were considered present only if they met modified DSM-IV criteria. The results were analyzed using hierarchical logistic regression analyses, as well as separate multivariate logistic regression analyses.

Results: The findings indicated that reduced family bonding was associated with drug-conducive personality traits, which in turn, were related to self-drug use and ultimately to substance use disorders. The results also indicated that earlier self-drug use, family drug use, and an early diagnosis of SUDs were directly related to SUDs in adulthood.

References:

NR693 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Relative Glucose Metabolism and Post-Acute Opiate Withdrawal
William H. Gottdiener, Ph.D., Psychiatry Department, Beth Israel Medical Center, First Avenue at 16th Street, Room 6K40, New York, NY 10003; John A. Matochik, Ph.D., Lisa J. Cohen, Ph.D., Edythe London, Ph.D., Alane S. Kimes, Ph.D., Carlo Contoreggi, M.D., Varughese Kurian, M.H.S.C., Enid C. Gertmenian-King, B.A., Igor I. Galynker, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand that post-acute withdrawal from opiates can create changes in brain glucose metabolism.

Summary:
Objectives: To assess regional cerebral glucose metabolism (rCMRglc) in opiate abusers at different times (six to 24 months) after completion of methadone detoxification in relation to symptoms of a putative post-acute opiate withdrawal syndrome (PAW) (Kleber, 1999).

Method: PET FDG was used to evaluate rCMRglc in two groups of participants with histories of opiate dependence and methadone maintenance therapy (MMT), but who were drug-free at the time of testing. One group had been detoxified for <12 months (MW6–12, n = 4), the other group for >12 months (MW12–24, n = 7).

Results: Whole brain SPM99 analysis showed that compared with the MW12–24 group, MW6-12 subjects had higher rCMRglc in the cingulate gyrus. Peak voxels that were in clusters that showed significant differences had MNI coordinates 2/52/12 (right anterior cingulate gyrus, ACG), 4/52/12 (right perigenual ACG), 2/54/10 (left perigenual ACG), 2/8/40 (left middle cingulate), and 6/18/40 (right midcingulate). They had lower relative rCMRglc in the left temporal cortex (−60–18−24), right superior frontal cortex (22/−8/68), and left pulvinar (−20−28/2).

Conclusion: Although differences in relative rCMRglc were seen in drug-free opiate abusers at different times (6–12 months vs. 12–24 months) after methadone detoxification, further research is needed to determine whether these differences are related to PAW syndrome.
NR694  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Smoking Behavior and Hormonal Change After Naltrexone in Nicotine Dependence
Chul Na, M.D., Department of Psychiatry, Chung-Ang University Hospital, 65-207 Hangang-Ro 3 Yong-San Ku, Seoul 140-757, Korea; Young-Sik Lee, M.D.

Educational Objectives:
At the conclusion of this session, the Naltrexone effects on smoking cessation are confirmed in this study, but its treatment mechanism has not been elucidated.

Summary:
Objective: The authors have investigated the effect of naltrexone on smoking cessation and the action mechanism of naltrexone.
Methods: The experimental method was a double-blind, placebo controlled design. 25 healthy male smokers voluntarily participated. 13 subjects were assigned to naltrexone and 12 subjects were assigned to placebo. Naltrexone group ingested naltrexone, 23.4 mg/day in first week and 37.1 mg/day in second week. Total cigarette consumptions, Brief Questionnaire for smoking urge, expiratory CO level was checked. Tragerstrom Tolerance Questionnaire was also checked at baseline and 4 weeks later. Plasma β-endorphine and dynorphin A and plasma ACTH were checked together.
Results: In Naltrexone group, total cigarette consumption (p<0.05), the expiratory CO level (p<0.05); B-QSU score (p<0.05). TITQ score (p<0.05) were significantly different than placebo. Dynorphin A and ACTH level were not significantly change but plasma β-endorphine levels has a tendency to decrease.
Conclusions: Naltrexone can be a possible tool to treat the Nicotine Dependence.

References:

NR695  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
High-Dose Naltrexone and Its Safety: Hepatic Transaminase Profiles
Suck Won Kim, M.D., Department of Psychiatry, University of Minnesota MC, F256/2A West 2450 Riverside Dr, Minneapolis, MN 55454; Jon E. Grant, M.D., Kyle A. Williams, B.A., Rorry P. Remmel, Ph.D., Rebecca L. Grosz, B.A.

Educational Objectives:
At the conclusion of this presentation, the participant should understand the safe use of high-dose naltrexone.

Summary:
Objective: Published evidence suggests that naltrexone causes hepatotoxicity dose dependently. However, concurrent use of over-the-counter analgesics was not accounted for in any of the previously published treatment studies in which doses of naltrexone greater than 50 mg/day were associated with significant increases in hepatic transaminases. The purpose of the present study was to assess the effect of naltrexone on hepatic transaminases in outpatients treated with high-dose naltrexone.
Methods: Forty-two outpatients diagnosed with various impulse control disorders were assessed by chart review. All subjects were treated with naltrexone at doses greater than or equal to 100 mg/day. Patients were instructed to avoid analgesics.
Results: The mean period of treatment was 328.24 (±410.77) days. The mean dose naltrexone was 142.07 (±38.50) mg/day. The mean number of liver tests per patient was 4.24 (±2.58). The mean ALT and AST at the most recent visit was, respectively, 21.49 (±10.70) and 22.54 (±6.00).
Discussion: The present study shows that 150 mg/day of naltrexone for up to one year (average) in physically health subjects who have impulse control disorders causes little or no hepatic toxic risk.

References:
with three patients in 2000 that were found to have medical conditions necessitating emergency care that was related or possibly related to the medical clearance process.

The test protocol for medical clearance of psychiatric patients was found valid as compared with the usual medical clearance evaluation performed in the ED.

References:

NR697 Wednesday, May 21, 3:00 p.m.–5:00 p.m.
Brief Intervention for Adolescents With Amphetamine Misuse

Manit Srisurapanont, Psychiatry, Chiang Mai University, PO Box 102 Chiang Mai University, Muang Chiang Mai 50202, Thailand; Sangworn Sombatmai, M.S.W., Theerarat Boripuntakul, M.S.C.

Educational Objectives:
At the conclusion of this session, the participant should recognize the benefits of brief intervention for the treatment of adolescents with amphetamine misuse.

Summary:
Objective: To estimate the short-term benefits of brief intervention in adolescents with amphetamine (AMPH) misuse.

Methods: The study was carried out at Chiang Mai University Hospital. The participants were randomly assigned to receive two 20-minute sessions of brief intervention (Bl) or one 15-minute session of psychoeducation (PE). Primary outcomes of interest were the decrease of amphetamine (AMPH) use in the units of use days (per week) and AMPH tablets used (per use day). Secondary outcomes included the participants with positive urine tests, the participants who returned to AMPH use, and duration of abstinence. All outcomes were assessed at baseline (week 0), week 4 and week 8 (endpoint).

Results: A total of 48 participants were enrolled in the study (24 on Bl and 24 on PE treatment), and 36 were included in the intention-to-treat and last-observation-carried-forward analysis (17 on Bl and 19 on PE treatment). The frequency and amount of AMPH use decreased significantly in both groups. At week 8, the decrease of AMPH use days in Bl group was significantly larger than that in PE group (t = 2, df = 34, p = 0.04).

Conclusions: Bl appears to have some minimal short-term benefits for adolescents with AMPH use disorders.

References:

NR698 Wednesday, May 21, 3:00 p.m.–5:00 p.m.
Barriers to Care of Persons With Dual Diagnoses in a Region in Alberta, Canada

Alberta Health and Wellness and Alberta Medical Association

Charl Els, Department of Addiction Medicine, CAMH, ARF Site, 33 Russell Street, Toronto, ON M5S 251, Canada;

Educational Objectives:
At the conclusion of this session, the participant should learn if genetic polymorphisms of dopamine receptors (DAT-1, DBH, and DRD4) correlate with clinical treatment outcomes in children with attention deficit hyperactivity disorder.

References:
Objective: Genetic polymorphisms of the dopamine neurotransmitter system have been identified in ADHD. Since stimulant medications act through this system, a pharmacogenetic relationship may exist. We previously have shown that ADHD children with dopamine receptor-4 (DRD4) 7-repeat polymorphism require higher doses of methylphenidate (MPH) to achieve 10-point improvement on Conners Global Index Parent (CGI-P) (30mg vs 20mg; p=0.0002) and to achieve CGI-P T-score normalization (47mg vs 3.1mg; p<0.0002). We now examine other dopamine polymorphisms.

Methods: A total of 45 ADHD children ages 7–15, confirmed by NIMH DISC-IV-P, were enrolled in this prospective double-blind pharmacogenetic study. Subjects received increasing MPH doses based on serial CGI-P. Dopamine polymorphisms were correlated with treatment outcomes.

Results: ADHD children with dopamine transporter (DAT-1) homozygous 10 repeat (n=15) required similar stimulant dosing compared with children with one or no 10 repeats (n=30) for normalization T-score <60 (39mg vs 38mg; p=0.62; power to detect 10mg difference >95%). Dopamine beta-hydroxylase (DBH)2 allele had no effect on treatment outcomes (DBH2 allele present n=39: 39mg vs absent DBH2 allele n=6: 39mg; p=0.97; power >95%).

Conclusions: Although ADHD children with DRD4-7R allele require 1.5-times more MPH to normalize ADHD symptoms, we found no influence on methylphenidate responsiveness based on DAT-1 10 repeat or DBH2 allelic status.

References:

NR700 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Comparison of Olanzapine and Risperidone in Children and Adolescents
Texas Department of Health and Mental Retardation
Anthony de Leon, Pharm.D., Pharmacy Department, University of Texas, 11350 Four Points Drive #1215, Austin, TX 78726; Daniel Lane, Pharm.D., Nick C. Patel, Pharm.D., Molly Lopez, Ph.D., M. Lynn Crismon, Pharm.D.

Educational Objectives:
The purpose of this naturalistic study is to evaluate and compare the effectiveness of olanzapine and risperidone in children and adolescents with schizophrenia, schizoaffective disorder, or schizophreniform disorder.

Summary:
Objective: The purpose of this naturalistic study is to evaluate and compare the effectiveness of olanzapine and risperidone in children and adolescents with schizophrenia, schizoaffective disorder, or schizophreniform disorder.

Methods: Children and adolescents, who were between the ages of 4 and 18 years and started olanzapine or risperidone on an outpatient basis, were considered eligible for the study. Treatment, internalizing, and externalizing Child Behavior Checklist (CBCL) scores were analyzed at baseline, 90-day, one-year, and four-year periods utilizing repeated measures analysis of variance. Two-year hospitalization rates and time to hospitalization were analyzed by the Kaplan-Meier formula.

Results: Both groups had significant improvements in internalizing and total CBCL scores at 90 days, one year, and two years post baseline (p<0.05). There were significant differences between groups for total CBCL scores at one year (p=0.034), and for internalizing CBCL scores at one and two years post baseline (p<0.05). There was a significant difference in time to hospitalization between groups (p=0.015), but no differences in two-year hospitalization rates.

Conclusions: Olanzapine and risperidone were effective in reducing total and internalizing CBCL scores, but there was no improvement for either group in externalizing CBCL scores. Patients receiving risperidone had an increase in time to hospitalization.

References:


**NR702**

**Wednesday, May 21, 3:00 p.m.-5:00 p.m.**

**SSRI Therapy for Pediatric Patients With Social Anxiety Disorder or OCD**

**Supported by GlaxoSmithKline**

Karen D. Wagner, M.D., Department of Psychiatry, University of Texas Medical Branch, Room 3.258, 301 University Boulevard, Galveston, TX 77555-0188; Ray Berald, M.D., David J. Carpenter, Ph.D., Christel Gardiner, Ph.D., Andrea Macnin, Ph.D.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to recognize that paroxetine is an effective and well-tolerated treatment for social anxiety disorder and obsessive-compulsive disorder in children and adolescents.

**Summary:**

**Objective:** To evaluate the efficacy of paroxetine treatment for pediatric patients (7–17 years) with an anxiety disorder.

**Method:** Randomized, double-blind, placebo-controlled studies were conducted in social anxiety disorder (SAnD; 16-weeks) and obsessive-compulsive disorder (OCD; 10-weeks).

**Results:** Significantly more patients with SAnD were responders (CfI global improvement scale score of 1 or 2) with paroxetine (77.6%; 125/161) than with placebo (38.3% 59/154) at endpoint (adjusted odds ratio 7.2; 95% CI: 4.07, 12.11; p<0.001). The adjusted mean difference in LSAS-CA total score between paroxetine and placebo at endpoint was 23.7 points in favor of paroxetine (95% Cl: -29.77, -17.74; p<0.001). More than three times as many paroxetine-treated patients (47.5%; 77/162) were “very much improved” (Cfi-I = 1) compared with placebo (14.9%; 23/154). After 10-weeks of treatment for OCD, paroxetine resulted in significantly greater improvements than placebo: based on adjusted mean change in CY-BOCS total score of -8.78 versus -5.34, respectively (adjusted mean difference -3.45; 95% Cl: -5.60, -1.29; p<0.002). Neither study reported any serious unexpected adverse events.

**Conclusions:** These studies demonstrate the efficacy of paroxetine treatment for pediatric patients with SAnD or OCD.

**NR703**

**Wednesday, May 21, 3:00 p.m.-5:00 p.m.**

**Trauma Exposure and PTSD in an Inner-City Child and Adolescent Psychiatric Clinic**

Illyan S. Ivanov, M.D., Department of Psychiatry, Mount Sinai Medical Center, 306 E 96th Street #16J, New York, NY 10128; Jeffrey Newcorn, M.D., Edward Greenblatt, Ph.D., Rachel Yehuda, Ph.D., Claude Chemtob, Ph.D., Dana Charatan, B.A., Tara Brennan, B.A.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to recognize high prevalence of trauma exposure and self/other reported rates of PTSD in an Inner-City population sample.

**Summary:**

**Objective:** This study examines child/parental reports of traumatic exposure and PTSD over one year in an inner-city outpatient clinic.

**Methods:** 162 youth ages 4 to 17 were assessed using the parent and/or child Posttraumatic Stress Reaction Index.

**Results:** Fifty-five percent of parents (76/138) reported the occurrence of a stressor to the child. Twenty-three cases (17%) had full PTSD and 20 (14%) had partial PTSD. Seventy-four children (71%) reported a stressor, 21 (20%) had full PTSD, and 25 (24%) partial PTSD. Eighty-one cases (50%) had both the PTSD-R&C and/or child reported trauma. Twenty-one (31%) children reported full/partial PTSD not confirmed by parent, and 11 parents (16%) described PTDS but the child did not. Despite high self/other-reported rates of PTSD, clinicians diagnosed PTSD in only five cases, with one other case in remission, and nine “rule-outs.”

**Conclusions:** Trauma exposure and PTSD were highly prevalent in this clinic, which does not specialize in treatment of PTSD. There was substantial discordance among parents and youth, as child reports of trauma exposure/PTSD being higher than parent reports. Clinician diagnosis of PTSD was much less frequent, suggesting either (1) the impact of trauma in children is under-appreciated by clinicians, (2) clinicians diagnose disorders other than PTSD preferentially, or (3) the instrument over-estimates PTSD.

**References:**


**NR704**

**Wednesday, May 21, 3:00 p.m.-5:00 p.m.**

**Atomoxetine Versus Placebo for Treating Pediatric Nocturnal Enuresis**

**Supported by Eli Lilly and Company**

Calvin R. Sumner, M.D., Neuroscience, Eli Lilly and Comp, Lilly Corporate Center DC4135, Indianapolis, IN 46285; Douglas K. Kelsey, M.D., Virginia Sutton, Ph.D., Jill Gonzales, B.S., Kory Schuh, Ph.D.

**Educational Objectives:**

At the conclusion of this session, participant should be able to acknowledge the benefit of atomoxetine for childhood nocturnal enuresis.

**Summary:**

**Objective:** Nocturnal enuresis is a condition in children older than five years of age who are incontinent of urine at night. Atomoxetine, a potent inhibitor of the presynaptic noradrenergine transporter, is used to treat ADHD. This study tested the hypothesis that a specific noradrenergine agonist, such as atomoxetine, will provide significant therapeutic benefit for nocturnal enuresis.

**Methods:** The effects of atomoxetine for improving nocturnal enuresis were studied in 87 pediatric subjects using an outpatient, multicenter, randomized, double-blind, parallel, placebo-controlled study. Efficacy was determined by measuring the number of dry nights per week using an intent-to-treat analysis of the primary outcome measure, the Dry Night Log-Parent Report (DNL-PR), a daily parent diary.
Results: Baseline and endpoint DNL-PR data were available from 42 atomoxetine-treated and 41 placebo-treated subjects. Atomoxetine increased the average number of dry nights per week by 1.47 compared with .60 for placebo (p=.01). Fifteen of the atomoxetine-treated subjects had an increase of at least two dry nights per week compared with only six of the placebo-treated subjects (p=.042). There were no significant differences in adverse events between the groups.

Conclusion: Atomoxetine produced a significant increase in dry nights in children with nocturnal enuresis.

References:

NR705 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Milnacipran in Adolescents Suffering From Major Depression and/or Dysthymia
Sittra Tauscher-Wisniewski, M.D., Department of Neuropsychiatry, University Hospital, Wahringer Gurtel 18–20, Vienna A-1090, Austria; Max H. Friedrich, M.D., Johannes Tauscher, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that obsessive-symptoms symptoms had similar characteristic in non-referred adolescents with or without tics, in opposite to previous studies on clinical series.

Summary:
Objective: Despite clinical trials in adults and adolescents with serotonin reuptake inhibitors or serotonin-norepinephrine reuptake inhibitors (SNRI), both of which have proven to be safer and at least equally effective as tricyclic antidepressants, the latter are still largely used in depressed children and adolescents. We assessed safety and efficacy of the SNRI milnacipran in depressed adolescents, which is approved for the treatment of depression from age 15 in Austria.

Methods: We conduct an ongoing, open, naturalistic 12-week trial with the SNRI milnacipran in 20 adolescents aged 15 to 18 years suffering from major depression (DSM-IV: 296.2) or dysthymia (DSM-IV: 300.4), who receive milnacipran 50 to 100 mg b.i.d. Clinical symptoms and side effects were rated according to the Global Impressions Scale (CGI), Montgomery-Asberg and Hamilton Depression Scale.

Results: A preliminary analysis of the first 10 patients enrolled revealed, that 80% of adolescent patients (mean age 16 years) showed a CGI-R score of >2 (much improved). Their average daily dose was 131 mg. Side effects were generally mild and transient, the most common being nausea seen in approximately 25%.

Conclusions: Preliminary data from a 12-week, open trial with the SNRI milnacipran suggest a favorable safety profile, comparable to SSRI, with good clinical efficacy in depressed adolescents.

References:

NR706 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Phenomenology of Obsessive-Compulsive Symptoms in Nonreferred Young Adolescents With OCD and Tic Disorders
Anita Brynska, Ph.D., Department of Child Psychiatry, Medical University of Warsaw, Marszałkowska 24, Warszawa PL00-576, Poland; Pawel Stefanoff, M.D., Tomasz Wolanczyk, M.D., Malgorzata Turek, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that obsessive-symptoms symptoms had similar characteristic in non-referred adolescents with or without tics, in opposite to previous studies on clinical series.

Summary:
Objective: To compare the phenomenology of obsessive-compulsive symptoms in two groups of non-referred adolescents: with "pure" obsessive-compulsive disorder (OCD) and with OCD with concurrent tic disorders.

Method: Two-stage ascertainment procedure (school screening and diagnostic evaluation) was used to identify two groups of affected individuals in two parallel epidemiological studies assessing the frequency of OCD or tic disorders in non-referred Polish adolescents. The first "pure" OCD group was selected from 3,110 pupils and the second group of OCD patients with concurrent tic disorders was selected from 2,927 pupils. At the diagnostic stage of these studies, the presence of obsessions and compulsions was assessed with the authors' structured interview questionnaire based on DSM-IV and ICD-10 diagnostic criteria for OCD and the Children's Yale-Brown Obsessive-Compulsive Scale (CY-BOCS).

Results: Among 11 subjects with "pure" OCD the most frequent symptoms were aggressive (fear harm will come to others), contamination or hoarding obsessions and washing, checking, ordering rituals. Among nine subjects with OCD and tic disorders, the most frequent obsessions were aggressive (fear harm will come to self), sexual, contamination obsessions and washing, checking, repeating, ordering compulsions.

Conclusions: The identified obsessive-compulsive symptoms had similar characteristic in both groups and also when compared with those previously described for clinical and non-referred samples with "pure" OCD.

References:
NR707  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
ADHD in Girls: Response to Once-Daily OROS Methylphenidate (MPH)
Supported by McNeil Consumer & Specialty Pharmaceuticals
Jeffrey Newcorn, M.D., Psychiatry, Mount Sinai School of Medicine, 1 Gustave L. Levy Place, New York, NY 10029;

Educational Objectives:
At the conclusion of this session, the participant should understand the clinical presentation of treatment response in ADHD girls, and recognize that, compared with placebo, once-daily OROS® MPH produces statistically significant symptom improvement in girls with ADHD (an underdiagnosed and undertreated population), via multiple efficacy measures.

Summary:
Objective: ADHD is an important cause of psychiatric disability in girls that is currently under-recognized and undertreated. This study evaluates the efficacy of once-daily OROS® MPH in managing ADHD symptoms in girls.

Methods: Results were pooled from three clinical studies that included 397 subjects, of which 65 were girls (ages 6–12). More girls than boys had inattentive subtype ADHD (35% vs. 16%); the majority of other subjects were diagnosed with combined type ADHD (girls 66%; boys 77%). Studies included two double-blind, randomized, placebo-controlled, seven-day, crossover studies, and one 28-day, multicenter, double-blind study. Subjects received OROS® MPH (18.36, or 54 mg) once-daily, MPH tid (5, 10, or 15 mg), and/or matched placebo as appropriate. Efficacy was measured in multiple settings by parents and teachers using established attention and behavior measures (e.g., IOWA Conners and SNAP-IV). Treatment response by ADHD subtype was also examined.

Results: Girls taking either of the active MPH treatments had statistically significant symptom improvement compared with placebo on multiple efficacy measures. In girls, after seven days of treatment, teacher IOWA Conners inattention/overactivity scores were: placebo 7.29, OROS® MPH 2.86; p < 0.05. After 28 days of treatment, parent SNAP-IV inattention subset scores were: placebo 2.11, OROS® MPH 1.25; p < 0.05.

Conclusion: OROS® MPH is effective and superior to placebo in managing the symptoms of ADHD (combined and predominately inattentive subtype) in school-aged girls, and offers another treatment option for this underdiagnosed and undertreated patient population.

References:

NR709  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
A Long-Term Trial of Methylphenidate in the Treatment of ADHD in Adults
Paul H. Wender, M.D., Department of Psychiatry, University of Utah, PMB 341, 9 Bartlet Street, Andover, MA 01810-3884; Frederick W. Reimherr, M.D., Barrie Marchant, M.A., Eve Sanford, Ph.D., Laura Czajkowski, Ph.D.

Educational Objectives:
At the end of this presentation, the audience should be better able to diagnose and treat Attention Deficit Hyperactivity Disorder in adults, and to recognize the changes that occur with effective treatment.

Summary:
Objective: To determine the effects of long-term methylphenidate treatment of adults with attention deficit hyperactivity disorder (ADHD) on symptom severity and social adjustment.

Methods: 120 adults meeting the Utah Criteria for adult ADHD were entered into a double-blind placebo-controlled trial of methylphenidate. Following this phase all subjects received an open trial of methylphenidate for four weeks and those manifesting moderate or marked improvement were entered into the long-term trial and evaluated at six and 12 months. Severity of symptoms was measured by a structured interview, Profile of Mood States, Global Assessment of Functioning. Social adjustment was evaluated by the Weissman Social Adjustment Scale.

Results: In the double-blind trial, 68% of the patients on methylphenidate showed a more than 50% decrease in score on the structured interview, compared with 19% during the placebo phase. 90 patients were evaluated at six months and 64 at 12 months. Both cohorts showed an 80% decrease in ADHD symptom severity and an improvement in the WSAS from “moderate impairment” to “good functioning.”

Conclusions: A long-term treatment of adults with ADHD results in a marked decrease in ADHD symptoms, and a very large improvement in social adjustment.

References:
and an improvement on the WSAS from “moderate impairment” to “good” functioning.

**Conclusions:** A long-term treatment of adults with ADHD results in a marked decrease in ADHD symptoms—and a very large improvement in social adjustment.

**References:**


**NR710** Wednesday, May 21, 3:00 p.m.–5:00 p.m.

Learning Disabilities in Children With Psychiatric Disorders

Susan D. Mayes, Ph.D., Department of Psychiatry, Penn State Medical College, P.O. Box 850, Hershey, PA 17033; Susan L. Calhoun, M.S., Susan L. Lane, Ph.D.

**Educational Objectives:**

At the conclusion of this session, the participant should know the prevalence of learning disabilities in reading, math, and written expression in children with psychiatric disorders (ADHD, bipolar disorder, autism, oppositional defiant disorder, adjustment disorder, anxiety, and depression) and the clinical and educational implications of these findings.

**Summary:**

**Objective:** Learning disabilities (LDs) are common in children with psychiatric disorders, but no study to date has compared the relative prevalence in children with different clinical diagnoses.

**Method:** Only children with DSM-IV diagnoses agreed upon by a child psychiatrist and psychologist were included in the study. The sample comprised 905 children (6 to 16 years) with attention deficit hyperactivity disorder (ADHD), oppositional defiant disorder, anxiety, depression, autism, bipolar disorder, adjustment disorder, spina bifida, and traumatic brain injury. LD was defined as a WIAT reading, math, or written expression score significantly lower than the child’s WISC-III IQ.

**Results:** LD percentages were highest for bipolar disorder (86%), spina bifida (80%), ADHD (76%), and autism (62%). Children with oppositional defiant disorder, adjustment disorder, anxiety, and depression had relatively low LD rates (26–55%). LD in written expression was twice as common as reading or math.

**Conclusion:** Learning disabilities (ADHD, autism, and bipolar disorder) should be assessed for possible learning disabilities because of the high potential yield and the need to intervene educationally if learning problems exist. An evaluation of written expression is especially critical because this is the most common type of LD and the easiest to address using remedial and compensatory strategies.

**References:**


**NR711** Wednesday, May 21, 3:00 p.m.–5:00 p.m.

Clinical Characteristics of Children Diagnosed With Bipolar Disorder

Susan D. Mayes, Ph.D., Department of Psychiatry, Penn State Medical College, P.O. Box 850, Hershey, PA 17033; Susan L. Calhoun, M.S.

**Educational Objectives:**

At the conclusion of this session, the participant should know the controversy surrounding bipolar disorder (BPD) in children and the clinical differences between children diagnosed with BPD (acute and episodic mania) and BPD-NOS (chronic and nonepisodic).

**Summary:**

**Objective:** Childhood bipolar disorder (BPD) is controversial, especially whether or not children with chronic mania are diagnosed clinically and clinically distinct from children who have acute manic episodes.

**Method:** The sample comprised 64 children (6 to 14 years) diagnosed with BPD by both a child psychiatrist and licensed psychologist. Children were divided into those with BPD (acute and episodic mania) and BPD-NOS (chronic and nonepisodic). Frequencies for each of the 31 symptoms on the Checklist for Bipolar Disorder in Children were compared for the two groups.

**Results:** Most children (86%) had nonepisodic symptoms (BPD-NOS). These children were indistinguishable from children with discrete episodes of mania on the clinical variables. All children had mood and behavior problems dating back to the preschool years, a positive family history for psychiatric disorders, and (for those who were not newly diagnosed) extensive treatment histories including behavior therapy (92%), educational intervention (87%), psychiatric admissions (76%), and multiple medications (100%). The majority of children had most checklist symptoms including emotional lability (100%), opposition and aggression (97%), ADHD symptoms (97%), grandiosity (83%), thought disorder (77%), morbid or gory preoccupation (58%), delusions (58%), and hallucinations (52%).

**Conclusion:** Children diagnosed with BPD and BPD-NOS are similar on clinical variables and have significant impairments.

**References:**


**NR712** Wednesday, May 21, 3:00 p.m.–5:00 p.m.

Association Between CBF Change Measured by Brain SPECT and Cognitive Characteristics in Children With ADHD: Quantitative Analysis Using SPM and ADHD Diagnostic System (TOVA)

Eun-Young Oh, M.D., Department of Psychiatry, Ajou University, San5 Wonchon-Dong, Paldal-Gu, Suwon, Kyunggi-Do 442-749, South Korea; Isaac Hwang, M.D., Chan-Hee Park, M.D., Seok-Nam Yoon, M.D., Jaejin Yang, M.D., Young-Moon Lee, M.D., Sunmi Cho, Ph.D.

**Educational Objectives:**

Participants should be able to recognize that rCBF of left temporal and frontal area is significantly decreased in children with ADHD and their impulsivity or disinhibition is associated with decreased rCBF in these areas.
NR713 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Atopic Disorders in Youth With Internalizing Disorders
Marcia Jean Slattery, M.D., Mayo Clinic, 200 First Street SW, Rochester, MN 55905; Mauricio Infante, M.D.

Educational Objectives:
At the conclusion of this session, participants will be knowledgeable of research investigating association between internalizing and atopic disorders in youth.

Summary:
Objective: Studies suggest an association between atopic disorders (asthma, allergic rhinitis, atopic dermatitis, and urticaria) and internalizing disorders in youth. This study examines rates of atopic disorders in a clinical sample of youth with anxiety and depressive disorders.

Methods: Subjects were 200 consecutive youth (aged 4 to 20 years; mean = 13.2 years) evaluated in a child and adolescent outpatient psychiatry clinic. Current DSM-IV child and adolescent psychiatric disorders were determined by clinical interview with a child and adolescent psychiatrist. Lifetime history of atopic disorders was assessed by parental report of a medical history of one or more atopic disorders in the child. Rates of atopic disorders were compared among youth (latency-age and adolescents) with internalizing disorders and among youth without internalizing disorders.

Results: Results suggested a statistical trend toward increased rates of atopic disorders among youth age 10 or younger with internalizing disorders compared to rates among same-age youth with non-internalizing disorders (OR=2.8; p=0.09).

Conclusion: These results suggest that the pathophysiology of impulsivity or disinhibition in ADHD children is associated with hypofrontality in attention deficit hyperactivity disorder during higher-order motor control: a study with functional MRI, Am J Psychiatry 1999.

References:

NR714 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
EEG Abnormalities Are Not Associated With Symptom Severity in Childhood Autism Supported by Janssen Research Autism
Michal Hrdlicka, M.D., Department of Child Psychiatry, Charles University, V Uvalu 84, Prague 5 15006, Czechoslovakia; Vladimir Komarek, M.D., Faladova Ludvika, M.D., Alena Zumrova, M.D., Robert Kulisek, M.D., Marek Blatny, Ph.D., Tomas Urbanek, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to better understand the relationship of EEG abnormalities to psychopathological symptoms and their severity in childhood autism.

Summary:
Objective: The aim of our study was to evaluate the importance of EEG abnormalities in the relationship to the severity of childhood autism.

Method: We examined a group of 77 autistic children (61 boys, 16 girls) with an average age 9.1 ± 5.3 years. The rating scale CARS, structured interview ADI-R, IQ testing, and 21 channel EEG (including sleep EEG recording) were performed EEG records were divided into three groups: normal EEGs, EEGs with non-epileptiform abnormality of background activity, and abnormal EEGs with epileptiform discharges.

Results: Approximately 80% of the children were mentally retarded. It was possible to obtain evaluable EEG records in 63 patients. There were 28 normal EEGs (44.4%), 11 non-epileptiform abnormal EEGs (17.5%), and 24 abnormal EEGs with epileptiform discharges (38.1%). Using the median test, we compared the psychopathology in these three groups. No significant differences among the groups in the total CARS score, or ADI-R subscores were found. In the analysis of CARS items, there was only one significant difference among the groups in the 10th item-Fear or Nervousness (χ²=7.963; df=2; p=0.019).

Conclusions: In our study EEG abnormalities were not associated with symptom severity in childhood autism.

References:
NR715  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Treatment for ADHD With OROS Methylphenidate:
Long-Term Effect on Growth
Supported by McNeil Pharmaceuticals
Thomas J. Spencer, M.D., Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, Boston, MA 02114

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that OROS® MPH produces no clinically meaningful changes in height, and minimal, transient, impact on weight. These findings are consistent with the lack of long-term height/weight issues related to MPH reported in the recent literature.

Summary:
Objective: To assess the long-term effect on growth of once-daily OROS® methylphenidate (MPH) in ADHD children.
Methods: 407 ADHD children, aged 6–13 years, were enrolled in this open-label, multicenter study, and received once-daily OROS® MPH for up to 24 months. Height and weight were recorded at baseline, every month for the first 12 months, and every three months until Month 24. Children’s growth was compared with that of the general population, adjusted for age and sex, using z-score transformations.

Results: Mean absolute weight increased by 2.2 kg at Month 12, and 7.0 kg at Month 24 (baseline, 34.2 kg; Month 12, 36.4 kg; Month 24, 41.2 kg). Mean absolute height increased by 4.8 cm at Month twelve and 11.5 cm at Month 24 (baseline, 137.1 cm; Month 12, 141.9 cm; Month 24, 148.6 cm). Children were heavier (0.67) than historical controls. Body mass index (BMI) decreased over the first three months but stabilized over the remainder of the study (mean BMI 24 months, 18.2). Height z-scores decreased slightly from baseline (mean height z-scores 24 months, 0.16).

Conclusion: OROS® MPH produces no clinically meaningful changes in height, and has minimal impact on weight in this sample of ADHD children.

References:

NR716  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Once-Daily Atomoxetine in Childhood ADHD:
Continuous Symptom Relief
Supported by Eli Lilly and Company
Douglas K. Kelsey, M.D., Dept. of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285; Calvin R. Sumner, M.D., Virginia Sutton, Ph.D., Jill Gonzales, B.S., Sandra Malcolm, B.S., Kory Schuh, Ph.D., David Michelson, M.D.

Educational Objectives:
At the conclusion of this session, participant should realize that a new once-daily treatment of childhood ADHD is available, which is safe and effective throughout the day and into the evening and early morning.

Summary:
Objective: We assessed the efficacy throughout the day, including evening and early morning, of atomoxetine administered once daily in children with attention-deficit/hyperactivity disorder (ADHD).
Methods: Children (n=197) with ADHD, aged 6–12 years, were randomized in a 2:1 ratio to eight weeks of once-daily atomoxetine placebo treatment. ADHD symptoms were assessed using parent and investigator rating scales. Parent assessments of children’s home behaviors in the evening and early morning were collected using the Daily Parent Rating of Evening and Morning Behavior-Revised (DPREMB-R) and the Conners’ Global Index: Parent Evening Scale (CGI-PE).

Results: Once-daily atomoxetine (final mean daily dose of 1.3 mg/kg) was significantly more effective than placebo in treating core symptoms of ADHD. Efficacy outcomes into the evening hours in atomoxetine-treated patients were superior to those of placebo-treated patients as assessed by the DPREMB-R and CGI-PE. The DPREMB-R showed significant reduction of symptoms in the morning and onset of effect significantly different than placebo after the first day on medication. Discontinuations due to adverse events were <5% for both groups.

Conclusion: Once-daily administration of atomoxetine provided safe, rapid and continuous ADHD symptom relief that lasted into the evening and early morning.

References:

NR717  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Distinguishing Bipolar Affective Disorder and ADHD in Aggressive Adolescents
Mark J. Smith, M.D., CNS Department, George Washington University, 4460 MacArthur Boulevard NW, Washington, DC 20007; Paula Gaudio, M.A., Daniel Matthews, M.D., Sidney Binks, Ph.D.

Educational Objectives:
At the conclusion of this session, participants should be aware of the value of non-symptomatic diagnostic aids in distinguishing Bipolar Disorder from ADHD.

Summary:
Objective: bipolar affective disorder (BAD) is an increasingly prevalent diagnosis in aggressive adolescents, but its clinical criteria are imprecise and subjective. Patients with attention deficit hyperactive disorder (ADHD) can resemble BAD patients, and structured interviews often diagnose the two as comorbid.

Method: We compared 12 adolescents hospitalized for aggressive behavior meeting K-SADS diagnostic criteria for bipolar disorder with 12 not meeting BAD diagnostic criteria on: sex, age, K-SADS diagnoses, Continuous Performance Test (CPT) scores, presence of cognitive disorders based on the Woodcock-Johnson III: Tests of Cognitive Ability and Achievement, and presence or absence of P300 evoked potentials to frequent stimuli. We hypothesized that K-SADS diagnoses of ADHD, CPT anomalies, and absence of P300 responses to frequent stimuli would be significantly more prevalent in the BAD group.

Results: There were no significant differences in sex, age, CPT results or K-SADS diagnoses, but ADHD was found in 100% of
the BAD patients. BAD patients had significantly more diagnoses of intermittent explosive disorder than non-BAD patients, fewer diagnoses of cognitive disorder, NOS, and more cases of absent P300 evoked potentials to frequent stimuli.

Conclusions: We believe that aggressive behavior in ADHD patients may be erroneously diagnosed clinically as BAD. Symptomatology alone may not distinguish these two disorders.

References:

NR718 Wednesday, May 21, 3:00 p.m.-5:00 p.m. Clinical Evaluation of Children With Inattention and Hyperactivity Catholic University of Korea Yong-Sil Kweon, M.D., Psychiatry, Wujongbu St. Mary’s Hospital, 65-1 Kumoh-dong, Uijongbu Kyunggi-d 480-130, South Korea; Ji-Hyun Lee, M.D., Jung-Tae Lee, M.D., Haekook Lee

Educational Objectives:
At the conclusion of this session, the participant should that clinicians should carefully screen for comorbid condition of ADHD as part of comprehensive assessment of inattention and hyperactivity.

Summary:
Objective: The aim of this study is to examine diagnostic profiles and related clinical variables of children with inattention and hyperactivity in outpatient clinic.
Methods: Seventy-one children ages of 5 to 14 were evaluated by an assessment battery including KEDI-WISC(Korean Educational Development Institute-Wechler Intelligence Scale for Children), KPI-C(Korean Personality Inventory for Children), CPT(Continuous Performance Test). The subjects were divided into three diagnostic groups: ADHD only(n=17), ADHD comorbid(n=27), Other diagnosis(n=27).
Results: In ADHD comorbid group, tic disorder, developmental language disorder, borderline intellectual function, and oppositional defiant/conduct disorder were combined in descending order. Other diagnosis groups consisted of tic disorder, borderline intellectual function, depression/anxiety, and oppositional defiant/ conduct disorder. There were significant differences in IQ, PIQ, and VIQ among the three groups, and ADHD-only group showed higher scores of IQ and VIQ than ADHD comorbid group. On the CPT, omission error and sensitivity showed significant differences among the three groups, and ADHD comorbid group represented higher omission error and lower sensitivity than other diagnostic group.
Conclusion: The inattentive and hyperactive children could be diagnosed into diverse psychiatric disorders, and ADHD with comorbidity will represent more difficulties in school performance than other diagnostic groups. Clinicians should carefully screen for comorbid conditions of ADHD as part of comprehensive assessment of inattention and hyperactivity.

References:

NR719 Wednesday, May 21, 3:00 p.m.-5:00 p.m. A DSM-IV-Based Rating Scale Correctly Identifies Patients in Community Eyup S. Ercan, M.D., Department of Psychiatry, EGE University, TIP Fakultesi Psikiyatri Bolumu, Bornova-Izmir, Turkey; Sonia Amado, M.D., Oya Soner, M.D., Sibel Cikoglu, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the use of a practical rating scale to successfully identify the cases with ADHD.

Summary:
Objective: To review the diagnostic sensitivity of Turgay ADHD and Disruptive Behavior Disorders Screening and Rating Scale (TDBDSRS) in a community school sample and a clinical sample of children with ADHD.
Method: The clinical sample consisted of 109 children (94 male, 15 female; age: 8–14). Twenty-seven children had ADHD alone, 53 had ADHD+Oppositional Defiant Disorder (ODD), and 29 had ADHD+Conduct Disorder (CD). The community comparison sample consisted of 120 students (101 male, 19 female) matched with the clinical sample in age and gender. Two child psychiatrists interviewed the subjects and their parents independently. Structured interviews and commonly used rating scales (Conners) aided the diagnosis. TDBDSRS(1995) consists of 18 ADHD, eight oppositional defiant disorder, and 15 conduct disorder DSM-IV criteria items translated into parent and teacher friendly descriptive statements with rating options from 0 to 3.
Results: TDBDSRS analysis alone correctly diagnosed 90% of the patients in the clinical sample and denied DBD diagnosis for 89.4% of the students from the school sample for ADHD. The correct identification rates of the DBDs by rating scale analysis alone were 93% for ADHD, 95.5% for ODD and 96% for CD.
Conclusion: This study provided support for the use of DSM-IV-based rating scales for community screening for the early identification and treatment of children with DBDs and established high diagnostic sensitivity for the scale tested.

References:

NR720 Wednesday, May 21, 3:00 p.m.-5:00 p.m. High-Lethality Suicidal Attempts in Adolescents and Risk Factors Carlos A. Finkelsztein, M.D., Department of Psychiatry, Hospital Italiano, Gascon 450, Buenos Aires, Argentina; Martin Ruiz, M.D., Maria C. Vairo, M.D., Maria F. Blanco, M.D., Daniel Matusevich, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify risk factors for suicidal attempt in adolescents in order to create prevention strategies for this high risk population.

Summary:
Objective: To estimate the frequency of risk factors for suicidal behavior in a sample of adolescents admitted after a suicidal attempt and to correlate them with high lethality suicidal attempt.
Method: It is a retrospective study; based on information from 115 medical records. Risk factors such as age, sex, suicidal
method, suicidal ideation, major depressive disorder, hopelessness, disruptive disorders or Axis II disorders, previous suicidal attempts, substance abuse or dependence, home runaway, homosexuality, school dropping, academic difficulties, social holding perception, recently first sexual relationship, acute stressors, one parent families, adoption, physical abuse, sexual abuse, family psychiatric disorders, and suicide or suicidal attempt in siblings, were processed by bivariated analysis; relative risk was obtained considering high lethality suicidal attempt as a dependent variable.

Results: Our sample shows similar epidemiological characteristics found elsewhere. Correlation was found between high lethality suicidal attempt and no Axis II diagnosis [p<0.05; $R^2=65.03$; RR=14.17 (5.96<RR<33.66)] and with the appearance of hopelessness [p<0.05; $R^2=69.45$; RR=14.73 (6.22<RR<34.88)].

Discussion: Suicidal attempts in adolescents with an Axis II diagnosis may be more related to self-injuring than to a wish to die. Hopelessness may be considered an independent variable that determines the lethality of the suicidal attempt.

References:

**NR722 Wednesday, May 21, 3:00 p.m.-5:00 p.m.**
**Comorbidities in Child and Adolescent Major Depression**
**Scarborough Hospital**
Atilla Turgay, M.D.; Department of Psychiatry, Scarborough Hospital, 3030 Birchmount Road, Toronto, ON M5G 2C4, Canada; JoAnna Blanchard, M.A., David Ng, M.D., Nadeem A. Chaudhry, M.D., Sushil K. Sharma, M.D., Amer M. Jilani, M.D., Khalid M. Jat, M.D., Mahpara S. Khan, M.D., Aruz Mesci, Benjamin Wood, M.P.H.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to identify the frequency, age and gender distribution of various comorbid disorders with major depression.

**Summary:**
Objective: To review the frequency of various comorbidities in child and adolescent major depression given that there has been no large sample studies in this area.
Method: All children and adolescents (age 18 and under) with major depression whose diagnostic work up were completed during the last seven years were included in the study. The sample consisted of 188 (51.5%) males and 177 (48.5%) females. An experienced child and adolescent psychiatrist made the diagnosis by interviewing the patients and parents and reviewing the ratings scales (Gadow-Sprafkin, Offord and Boyle, Turgay) completed by patients, parents, and teachers.
Results: Only 104 patients (28.4%) had major depression alone, while the remaining had comorbid disorders. ADHD was an important comorbidity; 125 patients (34.24%) were diagnosed with ADHD as well (65% were combined type). Out of 91 patients with oppositional defiant disorder, 57 were males (62.63%). Conduct disorder was diagnosed in 45 patients (12.32% of all patients); 62.32% were males. A total of 112 patients (30.68% of the total) had generalized anxiety disorder, half of whom were male.

Conclusion: Major depression is a common psychiatric disorder in children and adolescents, with frequent comorbidities. Third-fourths of the patients with major depression have significant comorbidities. Physicians should use structured interview and/or general rating scales reviewing all disorders to identify associated comorbidity disorders since the presence of other comorbid disorders often require additional medications and specific psychosocial interventions.

References:
Comorbidity in Oppositional Defiant Disorder in Children and Adolescents
Scarborough Hospital

Atilla Turgay, M.D., Department of Psychiatry, Scarborough Hospital, 3030 Birchmount Road, Toronto, ON M1S 2C4, Canada; Llewelyn W. Joseph, M.D., Penny Duncan, R.N., David Ng, M.D., Rubaba Ansari, M.A., Khalid M. Jat, M.D., Mahpara S. Khan, M.D., Amer M. Jilani, M.D., Nadeem A. Chaudhry, M.D., Sushil K. Sharma, M.D., Aruz Mesci, Ruthanne Playford, M.A.

Educational Objectives:
At the conclusion of this presentation, the participants should be able to understand the importance of ODD and its association with major psychiatric disorders like ADHD, conduct disorder, and mood disorders.

Summary:
Objective: To study the comorbid disorders of ODD.
Method: An experienced child and adolescent psychiatrist used DSM-IV criteria, patient and parent interviews and Gadow-Sprafkin, Offord-Boyle symptom checklists to aid the diagnosis. A total of 1,717 patients (356 females and 1361 males), ranging from two to 19 years of age, were selected from a total of 4,013 patients fully screened for the last seven years. The patients were seen at a university-teaching hospital in Canada.

Results: 97% of ODD patients had more than one disorder. The most common comorbidity was ADHD (92.99% of all cases), mostly combined type (87% of ADHD cases), and 33% had conduct disorder. Since the study was conducted at an ADHD clinic, the rate of ADHD in ODD may be much higher than in the general population. Out of 4,013 patients, 624 were diagnosed with CD. 92.31% of the CD patients had ODD. Patients with ODD had other comorbidities (10.72% generalized anxiety disorder, 5.91% dysthymic disorder and 5.33% major depression).

Conclusion: ODD occurring alone is the exception rather than the rule. Physicians should be able to identify ODD and associated comorbidities as their treatments may influence the course of the ODD and may prevent its possible development into conduct disorder.

References:


ADHD in Children and Adolescents With Pervasive Developmental Disorders
Scarborough Hospital Canada

Atilla Turgay, M.D., Department of Psychiatry, Scarborough Hospital, 3030 Birchmount Road, Toronto, ON M1S 2C4, Canada; Maria Fe Astorga, M.D., Michael Schwartz, Ph.D., Jody Markow, M.A., Sushil K. Sharma, M.D., Khalid M. Jat, M.D., Mahpara S. Khan, M.D., Amer M. Jilani, M.D., Nadeem A. Chaudhry, M.D., Aruz Mesci, Benjamin Wood, M.P.H.

Educational Objectives:
At the end of this session, participants will be able to identify the frequency, age, and gender distribution of ADHD in children and adolescents with pervasive developmental disorders.

Summary:
Objective: This clinical study reviewed the frequency of ADHD and its subtypes in children and adolescents with pervasive developmental disorders (PDDs), if DSM system allowed the use of ADHD diagnosis in the patient population.
Method: The diagnosis was made by an experienced child psychiatrist in PDD and was supported by Gadow and Sprafkin Child Symptom Inventory IV, DuPaul ADHD Rating Scale (Teacher and Parent versions), Offord and Boyle Ontario Child Health Study Rating Scales, and Krug et al. Autism Screening Instrument.

Results: 177 (85.92%) males and 39 (18.93%) females with pervasive developmental disorders formed the study group. The subtypes of PDD were: autistic disorder 79 (38.35%), PDD NOS 119 (57.77%) and Asperger disorder 8 (3.88%). Age distribution was, 110 (53.39%) in 2–5 yrs, 80 (38.83%) in 6–12 yrs, and 12 (5.82%) in 13–15 yrs. 147 (71.35%) would meet the criteria of diagnosis of ADHD. The subtypes were: combined type 137 (93.19%), ADHD predominantly inattentive type 8 (5.4%). One male patient would be diagnosed as ADHD hyperactive impulsive type and one male patient would have ADHD NOS diagnosis.

Conclusion: ADHD combined type is very common in pervasive development disorders. Future DSM should allow the diagnosis of ADHD in PDD so that these disorders may be identified and treated in PDD patients.

References:

NR726  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Major Depression Among Minority Patients With Osteoarthritis: Prevalence and Response to Pain Treatment
Supported by Pfizer Inc.
Henry Chung, M.D., LNS, Pfizer, 235 East 42nd Street 235-10-24, New York, NY 10017; Tricia Quinn, B.S., Pritha Bhadra, M.D., Kenneth Baht, M.D.

Educational Objectives:
At the conclusion of this session, the participant should (1) recognize the high prevalence of depression in minority patients with osteoarthritis. (2) understand the importance of screening and monitoring depressive symptoms in such patients.

Summary:
Background: Previous studies of depression in patients with osteoarthritis have been limited by small samples and the lack of diagnostically valid measures. The goal of this analysis was to evaluate the prevalence of major depression among ethnic minority patients with osteoarthritis before they were enrolled in a pain treatment trial.

Methods: African American, Hispanic, and Asian patients with osteoarthritis of the knee were enrolled in three separate and identically designed six-week, multicenter, randomized, double-blind, parallel-controlled studies with flexible dosing of celecoxib, naproxen, or placebo. The targeted enrollment for each study was 300 patients. The PHQ-9, a nine-item validated measure for depression assessed in primary care settings was used at screening evaluation. Scores ≥10 have an 88% sensitivity and specificity for DSM-IV major depression. Preliminary analyses with over 85% of the target enrollment are cited below.

Results: A total of 294 African Americans, 288 Hispanics, and 255 Asians were available for analysis. The mean PHQ-9 by group ranged from 3.1 (sd 4.3) to 6.2 (sd 5.5), with Hispanics having the highest mean score. Using a PHQ-9 cut off score of >20, 23.8% of African Americans, 22.9% of Hispanics, and 10.2% of Asians had major depression. Among patients that reported any depressive symptoms, 50.7% of African Americans, 45.8% of Hispanics, and 32.5% of Asians reported that the symptoms made it difficult to carry out normal daily functions.

Conclusion: Major depression is highly prevalent among minority patients with osteoarthritis and is associated with functional burden. Clinicians are advised to screen for depression among these patients and monitor their symptoms during pain treatment.

References:

NR727  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Medication Adherence in Latinos
National Institute of Mental Health
Esperanza Diaz, M.D., Department of Psychiatry, Yale University, 34 Park Street, Room 510, New Haven, CT 06519-2103; Scott W. Woods, M.D., Robert A. Rosenheck, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize predictors of medication adherence relevant to Latinos.

Summary:
Relapse as a consequence of medication non-adherence is costly. Considering that Latinos underutilize mental health services, it is possible that ethnicity might influence adherence but this has not been explored empirically. We hypothesized that medication adherence in Latinos was different from non-Latinos.

Methods: We compared medication adherence rates in three groups of patients seen at a community mental health center (CMHC) monolingual Hispanics at a cultural specialty clinic, bilingual Hispanics at the regular CMHC, and all other patients at CMHC. Adherence was measured via an electronic monitor for a month.

Results: We recruited 49 monolingual Hispanics, 26 bilingual Hispanics, and 54 other non-Hispanics. Medication adherence rates were rather high 76 to 82%. There were no differences in medication adherence between the three groups. Within the non-Hispanic control group, African Americans had the lowest adherence. Multivariable regression analyses showed associations with higher adherence: older age, less family instability, less depression, and less conduct disorder.

Conclusion: In this sample medication adherence did not differ between the Hispanic and Non-Hispanic groups. Possible differences should be sought among populations with lower overall adherence. Older age, family instability, depression, and conduct disorder were predictors of adherence. Non-adherence in African Americans needs to be further understood.

References:

NR728  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
The Treatment of American Hispanics With Antipsychotics: What Do we Know?
Humberto Marin, M.D., Psychiatry Department, 671 Hoes Lane, Room D-321, Piscataway, NJ 08855-1392

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the existing knowledge regarding treatment of American Hispanics with antipsychotics and the main gaps, as well as some options to correct them.

Summary:
Justification: American Hispanics, 35.3 million and 12.5% of the U.S. population, grew 60% in the last decade. However, they are underrepresented in drug clinical trials, neither do these trials analyze treatment efficacy within the group.
Objective: Review the information available on the treatment of American Hispanics with antipsychotics, draw some conclusions, discuss them, and make some proposals for the pharmacogenomic era of psychiatry.

Method: A review of all publications regarding treatment of Hispanic Americans with antipsychotics, using Medline and the references from available publications. A review of existing information on pharmacokinetics of antipsychotics in Hispanics was also done in the discussion.

Conclusions: 13 studies were found, they are retrospective and have other limitations. However, some trends are perceived in spite of no differences in response rates or side effects, Hispanics tend to receive lower doses of antipsychotics, less atypical antipsychotics and more depot antipsychotics.

The role of socioeconomic vs cultural/ethnic factors in the genesis of these differences needs to be ascertained. The dose differences are not accounted for by our current knowledge of pharmacokinetics in Hispanics.

Some suggestions are made if Hispanics as a group are to benefit from the current pharmacogenomic progress in psychiatry.

References:

NR729 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Deficits of Object Relations in Schizophrenia: A Transcultural Comparison Between Brazil and the U.S.
Wilte L. Bruscato, D.R., Psychology, Santa Casa, Borges Lagoa 1231 Conj 82, Sao Paulo, SP 04036020, Brazil; Sergio L. Bley, D.R.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the hypothesis of cutting the deficits of object relations in schizophrenia.

Summary:
Introduction: The person with schizophrenia has a long-lasting incapacity to have a relationship, even when the symptoms are controlled by medication. Object relation is the capacity of the individuals for the human relationships.

Objective: To verify if the deficits of object relations are an ordinary characteristic of schizophrenia in different cultural samples.

Method: The BORRTI Form—O (Bell Object Relations Inventory) was translated to Portuguese, determining its validity and reliability index, and it was applied to 61 Brazilian patients with schizophrenia. Scores were compared with an American patient sample matched by their age, gender, and diagnosis subtypes. It also applied the PANSS as part of the study.

Results: There were no significant differences in age, gender, and scholarship. The groups also didn’t differ between paranoid and nonparanoid, marital-status, race and these groups had a starting-age, age of the first treatment, and years of illness similar. The American sample was clearly more years in scholarship and the PANSS scores were uniformly higher for the positive scale. The pathologic elevation frequencies in the BORRTI scales for Brazilians and Americans were not significantly different. (Attachment = 57.45% and 45.9%, X^2(1)=1.16, p=ns; Insecure Attachment = 26.2% and 16.4%, X^2(1)=1.77, p=ns; Egocentrism = 67.2% and 41.0%, X^2(1)=8.5, p<0.004; Social Incompetence = 37.7% and 29.5%, X^2(1)=0.92, p=ns). The frequency of the patients who presented a certain type of deficit in object relations was 85.6% for Brazilians and 68.2% for Americans. (X^2(1)= 3.66, p=ns).

Conclusion: The findings give support to the ubiquity hypothesis of the deficits of object relations in schizophrenia.

References:

NR730 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Psychometric Properties of the Beck Disruptive Behavior Inventory
Brian H. Gordon, M.S., Psychology, Mississippi College, Box 4013, 105 Lowrey Hall, Clinton, MS 39058; John B. Jolly, Psy.D., Krishan K. Gupta, M.D., Julie E. Leech, B.A., Janet M. Jolly, B.S.N., Sandra Halabi, M.S.

Educational Objectives:
At the conclusion of this session, the participant should recognize the value of the BDBY for assessing conduct-problem adolescents.

Summary:
Introduction: This study examines the psychometric properties of the new, 20-item self-report measure, the Beck Disruptive Behavior Inventory (BDBY) for Youth (Beck, Beck, & Jolly, 2001), in court-referred outpatient adolescents from a county youth offender program.

Method: Thirty-nine adolescents (71.8% male; 94.9% African Americans; 59% legal histories) with limited intellectual/academic capabilities (WISCIII Full Scale IQ =70.1; WRAT-3 Reading Standard Scores Mean=81.9) were administered the BDBY with the 155-item, Jesness Personality Inventory (JPI).

Results: Cronbach alpha estimates of reliability were .84 and .91 in the BDBY and JPI, respectively. BDBY concurrent validity was demonstrated by significant correlations among BDBY scores and six of 11 JPI Personality Scale scores and six of nine JPI Subtype Scale scores.

Discussion: The BDBY appears to be a valid and reliable self-report scale for the measurement of delinquent thoughts, attitudes, and self-reported behaviors. Given its brevity, first-grade reading level, and correspondence with DSM-IV criteria for conduct disorder and oppositional defiant disorder, it may have greater clinical utility than other such measures of acting out behaviors and attitudes.

References:

NR731 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Psychometric Properties of the Beck Self-Concept Inventory for Youth
John B. Jolly, Psy.D., Psychology, Mississippi College, Box 4013, 105 Lowrey Hall, Clinton, MS 39058; Health B. Gordon, Krishan K. Gupta, M.D., Julie E. Leech, B.A., Janet M. Jolly, B.S.N., Sandra Halabi, M.S.
Educational Objectives:
At the conclusion of this session, the participant should recognize the value of the BSCY for assessing self-concept in outpatient adolescents.

Summary:

Introduction: This study examines the psychometric properties of the new 20-item self-report measure, the Beck Self-Concept Inventory (BSCY) for Youth (Beck, Beck, & Jolly, 2001), in court-referred outpatient adolescents from a county youth offender program.

Method: Thirty-nine adolescents (71.8% male; 94.9% African Americans; 59% legal histories) with limited intellectual/academic capabilities (WISCIII Full Scale IQ M=70.1; WRAT-3 Reading Standard Scores M=81.9) were administered the BSCY with the 82-item Tennessee Self-Concept Scale, Second Edition (TSCS-2).

Results: Cronbach alpha estimates of reliability were .78 and .87 in the BSCY and TSCS-2, respectively. Concurrent validity was established by demonstrating that BDBY scores correlated significantly with nine of 11 TSCS-2 clinical scale scores, including the TSCS-2 total score, and physical, moral-ethical, personal, family, social, identity, behavior, and self-satisfaction subscales.

Discussion: The BSCY appears to be a valid and reliable self-report scale for the measurement of self-concept in conduct-problem youth. Given its brevity and first grade reading level, it may have greater clinical utility than other such clinical measures of self-concept.

References:

NR732 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Psychometric Evaluation of a New Method for Measuring Denial in Sex Offenders: The Cognitive Distortion Interview for Sex Offenders (CODIS) Supported by The Health Research Board of Ireland
Patrick J. Gibbons, M.B., Department of Psychiatry, Lakeview University, NAAS Hospital, Kildare, Ireland; Jeanine Devolder, Patricia R. Casey, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the theory and psychometric properties of the first quantitative method for measuring denial in sex offenders.

Summary:

Introduction: Sex offenders are known to display wide range of cognitive distortions which help them to justify their behavior or protect them from associated shame. While the cognitive theory of the sexual offending cycle has become the primary paradigm on which current psychological treatments are based, there is a death of psychometrically robust methods for measuring relevant cognitive variables.

Objective: The principal aim of the study was to assess the validity and reliability of a new interview based method of measuring different denial variables.

Method: A semi-structured interview method was used to assess a mixed group of 188 convicted sex offenders in relation to 49 denial variables. These data were factor analyzed to identify the constructs underlying denial, with a 6-factor solution being chosen. These factors were validated against existing measures of related constructs, including the Blame Attribution Inventory and Victim Empathy Scale.

Results: Six factors were identified, accounting for 53% of the variance of the 30 variables included in the analysis. These addressed victim empathy, attribution of blame to the victim, attribution to current life problems, denial of sexual motivation, denial of needs for legal sanction, and the item content reveals considerable face validity. Some important aspects of denial, such as attribution of blame to intoxication and minimization of the extent of the abuse, did not load onto any of these factors. Both victim empathy and attribution to victim factors were strongly correlated to the Victim Empathy Scale scores as well as the BAI External Attribution Scales. The Denial of Guilt factor showed a moderate negative correlation to the BAI Guilt Element Scale. The Attribution to Current Life problems was weakly correlated to the BAI Mental Element Scale. The Denial of Sexual Motivation factor was not correlated with any of these alternative measures. Reliability scores for the internal, test retest and inter-rater ratings were largely satisfactory.

Conclusions: The CODIS provides a valid and reliable interview based measure of several important aspects of denial in sex offenders. Attribution of blame to intoxication or to mood states such as anger or a wish to dominate, particularly prevalent in at least some rapists, are not adequately addressed by the current measure.

References:

NR733 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Metabolic Syndrome Comparison Between Olanzapine, Aripiprazole, and Placebo Supported by Bristol-Myers Squibb Company and Otsuka Pharmaceutical Co, Ltd.
Daniel E. Casey, M.D., P3 MireCC, Portland VA Medical Center, 3710 SW, U.S. Veterans Hospital Road, Portland, OR 97239; Gilbert L’Italien, Ph.D., Reg Waldeck, Ph.D., Paul Cislo, Ph.D., William H. Carson, Jr., M.D.

Educational Objectives:
At the end of this session, the audience should be able to understand the in risk of metabolic syndrome with aripiprazole, olanzapine, or placebo therapy.

Summary:

Objective: Metabolic syndrome constitutes a set of risk factors for diabetes and heart disease. We compared its incidence in two schizophrenia treatment trials after 26 weeks.

Methods: Criteria for metabolic syndrome was based on clinically relevant changes in and levels of constituent risk factors, consistent with national guidelines. Survival analysis was performed on individual and pooled studies (N = 314 and N = 306 for trials 1 and 2, respectively).

Results: The cumulative metabolic syndrome incidence for the pooled analysis (= SE) was 19.2% ± 4.0% (olanzapine), 12.8% ± 4.5% (placebo), and 7.6% ± 2.3% (aripiprazole) (log-rank p = 0.007 in trial 1 and p = 0.23 for aripiprazole vs placebo in trial 2. The hazard ratio (95%CI) for aripiprazole vs placebo was 0.53
(0.18; 1.54) and 0.31 (0.12; 0.77) for aripiprazole vs olanzapine (69% relative risk reduction).

Conclusion: The findings suggest increased risk for metabolic syndrome among olanzapine patients, and comparable risk among aripiprazole patients versus placebo. The cardiovascular consequences of antipsychotic therapy warrant consideration by physicians.

References:

NR734 Wednesday, May 21, 3:00 p.m.-5:00 p.m. Anxiety and Depression in Relation to Physical Activity
Erlend Bergesen, M.D., 5643 Strandvik, Norway; Ann-Christin Rivenes, M.D., Arntzen Myklethun, M.A., Alv A. Dahl, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the relation between physical activity and anxiety/depression. This is especially useful and important to psychiatrists who deal with public health.

Summary:
Objective: To investigate the level of physical activity in persons with symptoms of anxiety and depression.

Material and methods: All inhabitants aged 20 to 89 years (N=92, 100) were invited to take part in The Health Study of Nord-Trindelag County, Norway. (HUNT) 65,648 subjects participated. Anxiety and depression were assessed by the self-rating scale HAD (Hospital Anxiety and Depression). Both intensity and duration of physical activity were measured by self-rating in a structured questionnaire, and both physical activity related to leisure time and occupation were registered.

Results: People who are physically inactive in their leisure-time are more often suffering from anxiety and depression than physically active people, and the association holds up when adjusted for age, gender and occupation-related physical activity. The intensity or duration of the activity seems to be off less importance.

Conclusion: In this study (HUNT), physically active people have less anxiety and depression than physically inactive.

References:

NR735 Wednesday, May 21, 3:00 p.m.-5:00 p.m. Hepatitis-B and -C Amongst Veterans on a Psychiatric Ward
Donna A. Wirshing, M.D., Department of Psychiatry, Greater Los Angeles Healthcare, 11301 Wilshire Boulevard, Building 210, B151, Los Angeles, CA 90073; Michael D. Kisicki, B.A., Shirley J. Mena, B.S., Ann Faerden, Joseph M. Pierre, M.D., Stephen R. Marder, M.D., William C. Wirshing, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the alarming prevalence of hepatitis B and C amongst psychiatric patients and to be aware of this populations particular risk factors.

Summary:
Objective: Hepatitis B and C are of epidemic proportion in the general community. Psychiatric patients may be at greater risk of contracting hepatitis B and C due to their lifestyle and comparative lack of access to health care. The goal of this work is to determine the prevalence of hepatitis B and C as well as associated risk factors in consecutively hospitalized veterans with psychiatric disorders.

Method: Voluntary patients acutely hospitalized at the West LA VA were approached to participate in this study. Those consenting were screened for hepatitis risk factors, hepatitis B antibody and antigen and hepatitis C antibodies.

Results: Two weeks into the three-month study, 20 of 30 hospitalized patients agreed to participate. 50% and 28% of these tested positive for hepatitis C and B respectively. Prevalence of seropositivity in the general population ranges from 5% to 20% for hepatitis B and 1–2% for hepatitis C. Those with positive serology endorse an average of eight risk factors, but even those with negative serology averaged 3.

These preliminary findings suggest an alarming rate of hepatitis B and C infection within a psychiatric inpatient population. Attention to the risk factors and preventative measures for this vulnerable population is necessary.

References:
prevalence of antidepressant and hypnotic use according to gender or according to age for antidepressants and anxiolytics. However, when corrected for alcoholism treatment, the female prevalence was significantly higher for antidepressants. One half of the youngest age group used antidepressants for less than three months. Estimated use of antidepressants and hypnotics was 54% and 61%, respectively, of sales figures. Odds ratios were higher for smokers. Limited education and low income predicted higher prevalence of antidepressants and anxiolytics.

Conclusions: Use of these drugs was extensive, but less than sales figures suggested. Prevalence of use, especially long-term, increased with age. As expected the use was most prevalent among the socio-economically disadvantaged.

References:

NR737 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
The Relationship of Comorbidity to Disability in Routine Psychiatric Practice
Joshua E. Wilk, Ph.D., APIRE, American Psychiatric Association, 1000 Wilson Boulevard, Arlington, VA 22209; Joyce C. West, Ph.D., William E. Narrow, M.D., Darrel A. Regier, M.D., Steven C. Marcus, Ph.D., Maritza Rubio-Stipec, Sc.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the projected risk of diabetes with long-term aripiprazole or placebo therapy.

Summary:
Objective: Previous studies suggest an association between some of the newer antipsychotics and diabetes. We compared the projected risk of diabetes for patients on aripiprazole and placebo using randomized trial data (N = 306).

Methods: The risk from baseline for diabetes at 7.5 years of maintenance treatment was estimated using a logistic regression model with risk factors for each individual patient, at baseline and 26 weeks. Risk between treatment arms was compared using ANCOVA.

Results: Observed changes from baseline (± SE) for placebo at 26 weeks were: fasting plasma glucose (FPG = 4.89±2.96 mg/dL) high density lipoprotein (HDL = -2.41±1.71 mg/dL), blood pressure (SBP = 10.83±2.15 mm Hg), and body mass index (BMI = 0.49±0.30 kg/m²). The changes for aripiprazole were: FPG = 0.61±2.33 mg/dL; HDL = -3.51±1.35 mg/dL; SBP = -5.31±1.70 mm Hg, and BMI = -0.54±0.23 kg/m². The change between treatment arms was not statistically significant (MANOVA, p=0.75).

Estimated changes in diabetes risk at 7.5 years increased by 6.42%±3.15% for placebo, and decreased by 0.33%±2.48% for aripiprazole (p=0.10).

Conclusions: Patients with schizophrenia are at higher risk for diabetes than the general population; hence, it is reassuring to have antipsychotic therapy that would not elevate this risk in these vulnerable patients.

References:

NR739 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
The Prevalence of Metabolic Disturbances in Schizophrenic and Bipolar I Patients Prior to Antipsychotic Use
Terrance J. Bellnier, M.P.A., Pharmacy Department, State University of New York at Buffalo, 36 Forest Meadow Trail, Rochester, NY 14624; Adam Decatur, Ph.D., Kashinath B. Patil, M.D., Tulio R. Ortega, M.D., Gerald Ginsberg, M.D.
Educational Objectives:

At the conclusion of this session, the participant should realize the importance of routine screening of psychiatric patients for diabetes, hypertension and obesity.

Summary:

**Objective:** Metabolic disturbances associated with atypical antipsychotics have been suggested. The study goal was to evaluate the prevalence of risk factors for metabolic syndrome in psychiatric patients prior to the use of all antipsychotics.

**Method:** Included a retrospective chart review of 1000 randomly selected patients, admitted to a state psychiatric hospital between the years 1940–1950. Records were blinded/reviewed independently by two psychiatrists using DSM-IV criteria. 592 patients met criteria for schizophrenia or bipolar I disorder and became the study group (SG). Annual physical exams and laboratory results were reviewed. Diabetes, hypertension and overweight rates were determined and compared to the expected rates from national norms (GP).

**Results:**

**Subject Characteristics:** 37 ± 13 years; 262 males, 429 schizoaffectives

**Prevalence:**

<table>
<thead>
<tr>
<th>Condition</th>
<th>SG%</th>
<th>GP%</th>
<th>Analysis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diabetes (glucosuria)</td>
<td>20.9</td>
<td>2</td>
<td>$X^2 = 658.5, df=1, P&lt;.00001$</td>
</tr>
<tr>
<td>Hypertension</td>
<td>29.1</td>
<td>16.5</td>
<td>$X^2 = 55.7, df=1, P&lt;.00001$</td>
</tr>
<tr>
<td>Overweight</td>
<td>28.2</td>
<td>21.8</td>
<td>$X^2 = 11.2, df=1, P&lt;.00001$</td>
</tr>
</tbody>
</table>

**Conclusion:** Metabolic disturbances found were significantly greater than the general population. The sample size limits our ability to make population inferences yet an association between schizophrenia and bipolar I disorder and metabolic disturbances seems to exist independent of antipsychotic use. Findings suggest that improvements in comprehensive psychiatric care should include routine screening for diabetes, hypertension and overweight.

**References:**


**NR741** Wednesday, May 21, 3:00 p.m.-5:00 p.m.

**Quetiapine-Associated Diabetes Mellitus**

Elizabeth A. Koller, M.D., Endocrinology, University of Nebraska, 983020 Nebraska Medical Center, Omaha, NE 68198; P. Murali Doraiswamy, M.D., James T. Cross, M.S., Bruce S. Schneider, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should understand the potential for hyperglycemia with the use of the atypical antipsychotic quetiapine and how spontaneously reported adverse events can provide a signal for further investigation.

**Summary:**

**Objective:** Diabetes has been observed with older atypical antipsychotic agents, but the risks and clinical characteristics of hyperglycemia in patients treated with quetiapine remain unclear.

**Design:** An epidemiologic survey of spontaneously reported adverse events in quetiapine-treated patients was conducted using reports from the Food and Drug Administration MedWatch surveillance program (1/1/97–6/15/02) and published cases.

**Results:** We identified 46 reports of quetiapine-associated hyperglycemia and nine additional reports of acidosis that occurred in the absence of hyperglycemia. Of the reports of quetiapine-associated hyperglycemia, 34 patients had newly diagnosed hyperglycemia, eight had exacerbation of pre-existing disease, and 4 could not be classified. The mean (±SD) age was 35.3±16.2 years (range 5 to 76). New-onset patients (31.2±14.8 years) tended to be younger than those with pre-existing diabetes (43.5±16.4 years; p=0.08). The overall male:female ratio was 1:9. Most cases appeared within six months of quetiapine initiation. The severity of cases ranged from mild glucose intolerance to diabetic ketoacidosis or hyperosmolar coma. There were 21 cases of ketoacidosis or ketosis. Eleven patients died.

**Conclusions:** Atypical antipsychotic use may unmask or precipitate hyperglycemia. The onset may be rapid and severe. Although most cases occur soon after treatment initiation, risk is not eliminated with extended therapy.

**References:**


**NR740** Wednesday, May 21, 3:00 p.m.-5:00 p.m.

**Effect of Olanzapine Versus Haloperidol on Brain Pathomorphology In First-Episode Psychosis Supported by Eli Lilly and Company**

Jeffrey A. Lieberman, M.D., Department of Psychiatry, Univ. of North Carolina School of Medicine, Room 7025, Neurosciences Hospital, CB7160, Chapel Hill, NC 27599; Cecil Charles, Ph.D., Tonmoy Sharma, M.D., Robert B. Zipursky, M.D., Robert M. Hamer, Ph.D., Gary D. Tollefsen, M.D.

**Educational Objectives:**

At the conclusion of the study, the participant will be able to delineate differences in the effects of olanzapine and haloperidol on brain pathomorphology, measured by quantitative MRI over a 2 year period.

**Summary:**

Longitudinal neuroimaging studies of first-episode schizophrenic patients have demonstrated morphological changes in cortical gray matter and ventricular volumes. The current study examined the effects of haloperidol and olanzapine on psychopathology, cognition, and brain morphology in patients with schizophrenia or schizoaffective disorder in a multicenter, randomized, double-blind trial. Patients were assessed with sMRI at baseline and after 12, 24, 52, and 104 weeks of treatment.

A total of 167 (of 263) patients (mean age 24 years, 70% male) had baseline and >=1 follow-up sMRI. We assessed group differences at the end of the acute phase (week 12) and at 24, 52, and 104 weeks. For acute phase data analysis, we used the end-of-acute-phase week 12 volume as the response, with baseline volume as a covariate, adjusting for investigator, age, and gender. For total cerebral gray matter, the 12-week changes to least squares means ± SE for haloperidol was −10.60±2.39, while olanzapine was −0.26±2.15 (P<0.001). For lateral ventricular volume, the changes to least squares means for haloperidol was 0.54±0.44, while olanzapine was −0.38±0.41 (P=0.06).

These results replicate prior studies that found progressive changes in brain morphology consistent with the hypothesized effect of illness progression that can be selectively attenuated by treatment with olanzapine.

**References:**


NR742 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Risperidone-Associated Diabetes Mellitus
Elizabeth A. Koller, M.D., Endocrinology, University of Nebraska, 983020 Nebraska Medical Center, Omaha, NE 68192; P. Murali Doraiswamy, M.D., James T. Cross, M.S., Bruce S. Schneider, M.D.

Educational Objectives:
At the conclusion of this session, the participant should understand the potential for hyperglycemia with the use of the atypical antipsychotic risperidone compared to haloperidol and how spontaneously reported adverse events can provide signals for future investigation.

Summary:
Objective: To explore the clinical characteristics of hyperglycemia in risperidone-treated patients.
Design: The Food and Drug Administration MedWatch surveillance program was queried (1/93 to 2/02) for spontaneously reported events and results pooled with published cases. Reports of haloperidol-associated hyperglycemia served as a control.
Results: We identified 131 reports of risperidone-associated hyperglycemia, seven additional cases with combined risperidone-haloperidol therapy, and six additional reports of acidosis occurring in the absence of hyperglycemia. There were 13 reports of haloperidol-associated hyperglycemia and 11 reports of acidosis without hyperglycemia. Of the reports of risperidone-associated hyperglycemia (monotherapy), 78 patients had newly-diagnosed hyperglycemia, 46 had exacerbation of pre-existing diabetes, and seven could not be classified. Mean (±SD) age was 39.8±17.4 years (range 8 to 96). New-onset patients (34.8±15.7 years) were younger than those with pre-existing diabetes (48.2±17.5 years). The overall male/female ratio was 1.5. Most cases appeared within three months. Severity ranged from mild glucose intolerance to diabetic ketoacidosis or hyperosmolar coma. There were 26 cases of acidosis or ketosis. Four patients died.
Conclusions: Atypical antipsychotics may unmask or precipitate hyperglycemia. While the numbers attributed to clozapine or olanzapine are greater than those associated with risperidone, the latter number is relatively higher than that observed with haloperidol.

References:

NR743 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Pancreatitis Associated With Atypical Antipsychotic Use
Elizabeth A. Koller, M.D., Endocrinology, University of Nebraska, 983020 Nebraska Medical Center, Omaha, NE 68192; P. Murali Doraiswamy, M.D., Saum N. Malozowski, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the potential for pancreatic inflammation in patients using clozapapine, olanzapine, and risperidone compared to those using haloperidol and to understand how reporting rates can suggest relative risk.

Summary:
Objective: To investigate the relative numbers and clinical characteristics of pancreatitis in patients treated with atypical antipsychotic agents (clozapapine, olanzapine, and risperidone) versus the conventional neuroleptic haloperidol.
Design: An epidemiologic survey was conducted using spontaneously reported adverse events from FDA’s MedWatch surveillance program and MEDLINE through February 2002.
Results: We identified 192 patients who developed pancreatitis during treatment with one or more of these agents. Most cases occurred within six months. 40%, 33%, 16%, and 12% of events occurred in patients using clozapine, olanzapine, risperidone, and haloperidol, respectively. In 50% of the haloperidol cases, an atypical antipsychotic was listed as a concomitant drug. Valproate was used concomitantly in 23% of cases. Concomitant hyperglycemia and acidosis in the setting of pancreatitis, although uncommon, occurred for all drugs except haloperidol. There were 22 deaths. In contrast to those using atypical antipsychotics, patients who developed pancreatitis on haloperidol tended to be female and older.
Conclusions: The number of reports for the atypical antipsychotic agents and the relative paucity of reports for haloperidol, despite its more extensive patient-exposure, suggest that atypical antipsychotics may precipitate pancreatitis—although the risk may not be equal for all agents. The temporal relationship to drug initiation further supports an association.

References:
with none (3.60), moderate (5.62), and severe (9.39) pain (p<0.009). Long-term U.S. total costs differed across depressed patients with varying degrees of pain: none ($1,234.12), moderate ($1,497.17), and severe ($2,725.45) pain (p<0.003).

Conclusion: Depressed patients with greater pain had higher costs and lower QoL. This relationship persisted over time. Country-specific data were too few to conclusively state relationship between pain and economic outcomes: Better recognition and treatment of complete depression symptomatology may improve outcomes.

References:
2. Simon GE, Chisholm D, Treglia M, Dbushnell D: Course of depression, health services costs, and work productivity in an international primary care study. General Hospital Psychiatry 2002; 328–335.

NR745 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Degree of Involvement in Risk Behaviors and Belief in Near-Future Death

Adela Valadez-Meltzer, M.D., University of Maryland, 701 West Pratt Street, Room 474, Baltimore, MD 21201; Tomas J. Silber, M.D., Lawrence N. D’Angelo, M.D., Arthur A. Meltzer, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize the association between an adolescent's degree of involvement in particular risk behaviors and the corresponding link with a belief in their (possibly) premature death.

Summary:

Introduction: We investigated whether a belief in near future death varied with the nature of an adolescent's involvement in a particular risk behavior.

Methods: We examined the association between a belief in one's mortality within the next two years and various risk-taking behaviors or situations (i.e., alcohol use, drinking and driving, drug use, drug selling, carrying a gun, or being injured by a weapon) among urban adolescents. Level of participation in the particular risk behavior was defined as self only (active), friends only (passive), both self and friends (active and passive), or neither self nor friends (referent). Cross-sectional data obtained from April 1994 to March 1997 were analyzed for a total of 2,694 adolescents (1,817 females and 877 males). The odds of belief in one's future mortality were calculated through a series of logistic regression models adjusted for age, sex, education, and living arrangements.

Results: A belief in near future death was reported by 7.1% of males and 5.4% of females. Among those risk behaviors with two or more statistically significant levels of participation associated with death belief, meaningful differences were noted for active and passive drug selling relative to passive drug selling only (OR=4.58 [95% CI=2.84 – 7.39] versus OR=1.76 [1.18 – 2.64], respectively); and active and passive weapon injury compared with passive-only weapon injury (OR=5.23 [3.07 – 8.93] versus OR=1.63 [1.11 – 2.40]). Additionally, respondents who reported suicidal ideation or acts had a statistically significant three-fold increase in future death belief; adolescents residing in a foster home environment showed a borderline significant increase in death belief across all risk behaviors.

Discussion: Assessment of degree of involvement in a particular risk behavior is useful in defining the likelihood of an adolescent's, possibly inappropriate, belief in his future demise and in directing such an individual to treatment.

References:

NR746 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
A Demographic and Psychiatric Study of 116 Applicants for Sex Reassignment in a Spanish General Hospital

Esther Gomez-Gil, M.D., Department of Psychiatry, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain; Josep-Maria Perl, M.D., Angela Vidal, M.D., Joan De Pablo, M.D., Manuel Valdes-Miyar, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should recognize however demographic and psychiatric characteristics of transsexuals in Spain are in line with findings in other countries, there are certain differential characteristics.

Summary:

Introduction: Little is known about transsexualism in Spain. The aim of this study was to examine the socio-demographic features and psychiatric comorbidity of applicants for sex reassignment in a Spanish general hospital.

Method: 116 consecutive patients requesting for sex reassignment were evaluated at the psychiatric unit of the hospital clinic, Barcelona. Diagnosis of transsexualism (ICD-10), demographic and clinical data, and psychiatric comorbidities were analyzed.

Results: 107 patients (92.2%) did meet criteria for transsexualism. The male-to-female/female-to-male ratio was 3:1 (80/27). The average age at the time of the consultation was 28.78 years (S.D.: 7.76; range 15 to 53). Only twelve (11%) had studied post high school. About 15% were unemployed and 26% were sex-workers or sex-show-workers. 46.7% lived with their family, 29.5% with their partner and 16.2% alone. Four had been previously married. Family history of transsexualism was present in four. Congenital and/or hypogonadism was diagnosed in four patients. Sexual interest were mainly toward subjects of their own sex (93.5%). 53% were taking hormonal therapy, 80% by self-therapy. The most common psychiatric diagnoses were alcohol and substance use disorders, personality disorders and social phobia.

Conclusions: The results of our population were in line with the findings of similar studies in other countries. We highlight certain differential characteristics in the Spanish population as regards age when applying for sex-reassignment, living situation, and percentage of sex workers.

References:
A Study of the Potential Association of Polycystic Ovarian Syndrome (PCOS) With Chronic Administration of Valproate in Nonhuman Primates

Michel Ferin, M.D., Department of Obstetrics and Gynecology, Columbia University, 630 W. 68th Street, New York, NY 10019; Martha J. Morrell, M.D., Ennian Xiao, M.D., Qian Fang, M.D., Thomas Wright, M.D., Lisa Kochan, Ph.D., Mark Sauer, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize that long-term valproate treatment is not associated with endocrine or reproductive disturbances, in a healthy primate model.

Summary:

Objective: To determine the potential association of chronic valproate treatment with PCOS, in the absence of bipolar disorder or epilepsy, in non-human primates.

Methods: Divalproex sodium 120mg/kg/day was administered to seven healthy rhesus monkeys for greater than one year (range: 12.7–15.7 months). Menstrual cycles and reproductive function were monitored monthly by obtaining estradiol, progesterone, and androgen levels, follicular and luteal phase lengths, LH:FSH. Body weight, lipid profiles, GnRH agonist stimulation and glucose tolerance tests (GTT) were determined. Plasma valproate levels were measured biweekly. All 14 ovaries were removed and analyzed for gross and microscopic examination.

Results: Overall mean valproate levels at two hours post AM dose were 88.7±4.0 μg/ml. No significant differences were observed during the treatment period for menstrual cycle length, follicular and luteal phases, estradiol, progesterone, LH:FSH, testosterone, androstenedione and lipids, compared with controls. No significant differences were observed following GnRH agonist stimulation and glucose tolerance tests, compared to controls. Weight gain was significant in six of seven primates, after nine months of treatment. All ovaries demonstrated normal gross and histological features.

Conclusions: This study demonstrated that prolonged treatment with valproate in healthy primates does not induce PCOS or endocrine abnormalities.

References:

SSRI Treatment of Hot Flashes in Menopausal Women Supported by GlaxoSmithKline

Katherine L. Beebe, Ph.D., GlaxoSmithKline, 5 Moore Drive, PO Box 13388, Research Triangle Pk, NC 27709-3388; Vered Stearns, M.D., Malini Iyengar, Ph.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to recognize the therapeutic utility of SSRI therapy for menopausal women seeking treatment for vasomotor symptoms.

Summary:

Long-term treatment with hormone replacement therapy (HRT) is associated with excess for breast cancer, cardiovascular disease, and other disorders (1). Although HRT is first-line therapy, SSRIs can also reduce not flash symptoms (2). A double-blind, placebo-controlled, parallel group study of paroxetine CR was conducted, which is the first study of an SSRI in a general cross-section of menopausal women, rather than a breast cancer survivor population. A total of 165 women were randomized to receive paroxetine CR 125 mg/day, 25 mg/day or placebo for 6 weeks. At study endpoint, paroxetine CR significantly improved hot flash (HF) composite score (product of daily frequency and severity ratings). The mean placebo-adjusted reductions for paroxetine CR were -4.7 (p<0.007 vs placebo, 95% CI -8.1 to -1.3) and -3.6 (p=0.029 vs placebo, 95% CI 6.8 to -0.4) for 12.5 and 25mg/day, respectively. This equated to 62.2% and 64.4% reductions in HF score for the paroxetine CR 12.5 and 25mg/day groups, compared with a 37% reduction for placebo. Adverse events were mild and consistent with the tolerability profile of paroxetine. The results of this study indicate that paroxetine is an effective and well-tolerated alternative to HRT in treating hot flash symptoms.

References:
References:

NR750 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Does Sleep Lead to Postpartum Psychosis?
Verinder Sharma, M.D., Regional Mental Health Care London, 850 Highbury Avenue, PO Box 5532, London, ON N6A 4H1, Canada; Angela R. Smith, B.S.C., Mustaq Khan, Ph.D.

Educational Objectives:
At the conclusion of this session, the participants will learn about the prevention, early identification and treatment of postpartum psychosis.

Summary:
Background: The pathophysiological basis of postpartum psychosis remains poorly understood, but factors such as difficult labor, primiparity, genetic predisposition, and hormonal changes have been implicated. Sleep loss is an early and prominent symptom in postpartum psychosis. We hypothesized that women who develop postpartum psychosis are more likely to have a longer duration of labor and nighttime deliveries, and hence more sleep disturbance.

Methods: The charts of women delivering at three general hospitals, who developed psychosis within four weeks of delivery, were reviewed. Twenty-six were found to have suffered from postpartum psychosis. These women were age and parity matched with a control group of 26 women who delivered at the same hospitals. Detailed clinical and obstetrical information including duration of labor and time of delivery were obtained. Women who had caesarian sections were excluded from the study.

Results: Compared to the controls, women in the psychosis group had a significantly longer duration of labor and more nighttime deliveries. The most frequently occurring symptom in the psychosis group was insomnia. The majority of patients met the criteria for bipolar disorder-mixed.

Conclusions: These results are consistent with the evidence that sleep disruption is linked to mood instability. Treatment implications of these findings are discussed.

References:

NR751 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Ziprasidone for Elderly Dementia: Case Series Supported by Pfizer Inc.
Alan Lee Berkowitz, M.D., Behavioral Medical Center, 15725 Pomerado Road #206, Poway, CA 92064-2059.

Educational Objectives:
At the end of this presentation, the participant should be able to discuss the reported results on the clinical efficacy and safety of ziprasidone in elderly patients with dementia-related behavioral disturbances or depression-related psychosis, and describe methods developed for managing treatment-associated sedation by dosage adjustment.

Summary:
Introduction: We evaluated use of ziprasidone in fragile, elderly patients with dementia-related behavioral problems (irritability, agitation, combativeness, depression, mood lability).

Methods: We conducted a chart review of 14 patients admitted to an inpatient psychiatric facility with Axis I diagnoses of mood and behavior disturbances secondary to multi-infarct dementia, Alzheimer's disease, schizoaffective disorder, bipolar disorder, and major depression. All patients had ≥1 major medical illness, including in some cases atrial fibrillation or congestive heart failure.

Results: Most patients had received antipsychotic therapy before hospital admission. Treatment with various psychotropic agents (haloperidol, olanzapine, risperidone, paroxetine, fluoxetine, lamotrigine, oxcarbazepine, divalproex sodium, topiramate), often given concomitantly, failed to resolve symptoms or caused intolerable side effects. Ziprasidone, usually in combination with other psychotropics, minimized behavioral symptoms, agitation, depression, and cognitive decline sufficiently to enable discharge. Most common side effect was sedation, which generally responded to 20-mg dose reductions and tended not to recur with reintroduction of ziprasidone. There were no significant QTc findings or recorded postural hypotension or syncope.

Conclusions: In summary, ziprasidone proved safe and effective in 14 elderly patients with dementia-related behavioral disturbances and depression-related psychosis when other atypical antipsychotics failed to relieve symptoms or caused intolerable side effects.

References:

NR752 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Defining Fetal Exposure to Atypical Antipsychotic Medications
Ada M. Loughhead, B.S., Department of Psychiatry, Emory University, 1365 Clifton Road, Suite 6100, Atlanta, GA 30322; D. Jeffrey Newport, M.D., Sandra L. Graybeal, B.A., Amy L. Hostetter, B.A., James C. Ritchie, Ph.D., Zachary N. Stowe, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to be aware of the preliminary data on the extent of fetal and neonatal exposure to olanzapine and quetiapine when used during pregnancy and lactation.

Summary:
The management of mental illness during pregnancy and lactation has received considerable attention over the past decade. Introduction and use of atypical antipsychotics underscore the need to expand the data regarding fetal and neonatal exposure to these compounds. Women who chose to continue atypical antipsychotic medications during pregnancy and/or lactation were recruited to participate in a study. Maternal serum, amniotic fluid, umbilical cord blood, and nursing infant sera were collected for determination of medication concentration by HPLC-electro-chemistry detection, using the ESA Coularray. A total of seven patients submitted paired maternal and umbilical cord blood samples (olan-
zapine n=4; quetiapine n=3). Breast milk samples (n=4) and nursing infant sera (n=2) were obtained from four women taking olanzapine while nursing. Olanzapine was <1 ng/ml in a single amniotic fluid sample with paired maternal serum concentration of 3 ng/ml. The placental passage of olanzapine is 0.8±0.28 (n=3), implying that the fetus achieves a serum concentration similar to maternal serum. Olanzapine was below the limit of detection (<0.25 ng/ml) in a single nursing infant serum. Quetiapine assays are pending at time of submission. These preliminary data will be discussed in defining the extent of fetal exposure to atypical antipsychotic medications.

References:

NR753  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Locally Advanced Breast Cancer: Magical Thinking or Caretaking?
Marijo B. Tamburrino, M.D., Department of Psychiatry, Medical College Ohio, RHC 3120 Glendale Avenue, Toledo, OH 43614; Kristi S. Williams, M.D., Imran E. Mohamed, M.D., John M. Wryobeck, M.A., Susan E. Carter, M.Ed.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify factors associated with delay in early diagnosis and treatment of breast cancer in women; be aware of compelling reasons and unique life circumstances that prevent women from presenting for early treatment of breast cancer; and recognize the influence of spouses’ health beliefs on early diagnosis and treatment.

Summary:
Objective: Identifying factors that contribute to delay in seeking treatment by women with locally advanced breast cancer (LABC) is important due to increased risk of death from postponing treatment.
Methods: Women with LABC (n=11) and matched controls (MC), (n=11) with stage I or II breast cancer were recruited from a large midwestern medical school. The majority of both groups had college education/degrees. Participants completed a semi-structured interview and HADS, Life Orientation Test, Multidimensional Health Locus of Control, Body Image, Monitor-Blunter Style, and Religious Coping scales. Spouses, if accessible, were similarly evaluated.
Results: Group differences on self-report measures were analyzed using independent sample t-tests. No significant differences were found between the patient groups; however, LABC spouses (n=5) reported significantly greater active religious surrender (t=2.37, p=0.037) and depression (t=3.54, p=0.047) than the MC spouses (n=8). Semi-structured interviews yielded richer information including significant caretaking roles by LABC patients and high endorsement of magical and nontradicional treatments by LABC patients and spouses.
Conclusion: Patients who delay treatment have compelling reasons, e.g. caretaking roles, magical beliefs, and trust issues. Elicitation of these behaviors and beliefs will take extra clinician time, but is essential for treatment optimization.
References:

NR754  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Prevalence of Psychiatric Diagnoses in HIV-Positive Incarcerated Women
Catherine F. Lewis, M.D., Department of Psychiatry, University of Connecticut, 263 Farmington Avenue, Farmington, CT 06030-2103;

Educational Objectives:
At the conclusion of this session, the participant should develop an understanding of psychopathology likely to be seen in HIV+incarcerated women and understand treatment implications specific for the female incarcerated HIV+ population.

Summary:
Objective: To examine demographic and legal characteristics and prevalence of psychiatric disorders in HIV+ incarcerated women.
Method: Eighty-one HIV+ incarcerated women were interviewed using the Structured Clinical Interview for DSM-IV, Clinician Administered Post-Traumatic Stress Scale, and Addiction Severity Index.
Results: Women in this study had a mean age of 38.2 years (SD = 5.6 years). Twenty-four women were white (29.6%), 42 black (51.9%), and 15 Hispanic (18.5%). Most were single, unemployed, high school dropouts, who had at least one child. Nearly all of the women were dependent on alcohol and/or drugs (98.2%). The most common substances abused were cocaine, heroin, and alcohol. Lifetime major depression (60.5%), current major depression (19.7%), and dysthymia (9.9%) were prevalent. Posttraumatic stress disorder (PTSD) had high lifetime (74.1%) and current (17.3%) prevalence personality disorders were common (43.1%) with antisocial (18.5%) and borderline (9.9%) personality disorders predominating. Schizophrenia, schizoaffective disorder, bipolar disorder, and anxiety disorders other than PTSD had prevalence similar to those of community samples.
Conclusions: Incarcerated HIV+ women are likely to suffer complex psychopathology including addiction, current and lifetime PTSD, personality disorders and past and current major depression. These results suggest that HIV+ incarcerated women are a complex population likely to require careful psychiatric assessment and ongoing mental health treatment.

References:

NR755  Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Sildenafil Citrate Treatment for SRI-Associated Female Sexual Dysfunction
Supported by Pfizer Inc.
H. George Nurnberg, M.D., Health Science Center, University of New Mexico, 87131; Paula L. Hensley, M.D., Harry A. Croft, M.D., Maurizio Fava, M.D., Julia K. Warnock, M.D., Susan Paine, M.P.H.
NR756 Wednesday, May 21, 3:00 p.m.-5:00 p.m.
Atypical Antipsychotic Treatment of BPD: A 12-Week, Double-Blind, Placebo-Control Trial With Olanzapine Supported by Eli Lilly and Company

H. George Numberg, M.D., Health Science Center, University of New Mexico, 2600 Marble Avenue, NE, Albuquerque, NM 87131; Michael P. Bogenschutz, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be informed of the efficacy of atypical antipsychotic treatment in borderline personality disorder.

Summary:
Objective: Borderline personality disorder (BPD) is a prevalent, etiologically heterogeneous condition characterized by unstable relationships, impulsivity, affective instability, self-damaging behaviors, identity disturbances, and abandonment fears. Atypical antipsychotics with improved tolerability suggest a new treatment approach.

Methods: Forty male/female BPD patients were randomized (1:1) to olanzapine or placebo 2.5–20mg/day flexible dose. Structured Clinical Interview for DSM-IV-Axis II and Mini-International Neuropsychiatric Interview established diagnoses; schizophrenia, bipolar disorder, or current major depression were excluded. No concomitant psychotropic medications were allowed. Primary outcome was change in the total CGI-BPD score; nine BPD criteria each Likert score 1–7 at baseline, 2.4,8,12 weeks. Secondary measures: Overt Aggression Scale-Modified; Anger, Irritability, and Assault Questionnaire; Hamilton Depression/Anergy Inventories; Symptom-Checklist-90; Addiction Severity Index. LOCF-ITT a-priori analysis was ANCOVA comparing endpoint with baseline CGI-BPD as covariate.

Results: Olanzapine was superior to placebo as early as four weeks (p=0.03). Similar results were found for global-CGI. Other measures were nonsignificant at endpoint. Olanzapine effect size for primary CGI-BPD was 0.77 (Partial eta-squared = 0.139). Differences between men and women for baseline severity, time, or medication effect were non-significant. Patients generally tolerated the medication; weight gain associated with olanzapine treatment (8.25 v. 0.17 lbs; p=0.027) and premature discontinuation.

Conclusion: This study supports earlier reports of olanzapine efficacy for BPD, extending to both genders, including drug and alcohol use. Additional studies comparing atypical agents and BPD subtypes are needed.

References:
of status at long-term is relevant for women with CSA as they might be in need of further treatment.

References:


NR759 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Primary Care Perceptions: Peri-Partum Psychiatric Disorders

Diane S. Thompson, M.D., Psychiatry, University of Hawaii, 1356 Lusitana Street, Honolulu, HI 96813; Deborah Goebert, D.P.H., LeighAnn Frattarelli, M.D., Mai Ann Nguyen, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should understand the degree to which primary care physicians are aware of peri-partum psychiatric disorders, assessment tools and treatments, and the need for mental health professionals to engage in ongoing peri-partum education for primary care colleagues.

Summary:

Objective: Postpartum depression is a common and often overlooked condition. Validated screening tools for postpartum depression exist but are not commonly used. This study assessed psychiatric and primary care (Family Practice, Internal Medicine, Obstetrics and Gynecology) physicians' knowledge about postpartum depression.

Method: A brief survey was distributed at educational venues in Hawaii. The survey contained questions about rates for depression, the "blues", postpartum depression, and postpartum psychosis as well as questions about symptoms, medications, and treatment for depression during pregnancy and postpartum.

Results: One hundred providers completed the survey, of which 53 were attendees and 47 were residents. Screening varied significantly by specialization with 71% of obstetricians/gynecologists, 63% of psychiatrists and 20% of family practitioners/internal medicine physicians (x^2=18.9, df=4, p<0.001). Generally, physicians screened by asking, "How have you been feeling?" Less than 20% recognized validated screening tools. Seventy-six percent underestimated the occurrence of postpartum blues. Physicians had accurate understanding of risk factors as well as pharmacological and psychotherapeutic treatment modalities. Less than half (48%) was aware of referral sources and less than 30% felt these referral options were effective.

Conclusion: Continuing medical education on screening and treatment as well as consultation systems need to be developed and implemented.

References:


NR760 Wednesday, May 21, 3:00 p.m.-5:00 p.m.

Luteal Phase Dosing of Paroxetine Controlled Release Is Effective in Treating PMDD

Supported by GlaxoSmithKline

Michelle Gee, Ph.D., Psychiatry, Glaxo Smith Kline, New Frontiers Science Park 3rd Ave, Harlow Essex CM195AW, United Kingdom; Kevin M. Bellew, M.S., Fiona J. Holland, M.Sc., Elizabeth Van Erp, Philip Perera, M.D., James P. McCafferty
Educational Objectives:

At the conclusion of this presentation, the participant will understand the benefits of luteal phase dosing of paroxetine controlled-release in PMDD.

Summary:

Background: Paroxetine controlled-release (CR) has been shown to be a highly effective treatment for PMDD when administered daily throughout the menstrual cycle. The current study has evaluated the efficacy of luteal phase dosing (last 14 days of the menstrual cycle) of 12.5 mg and 25 mg paroxetine CR.

Methods: A multicenter, randomized, double-blind, placebo-controlled, three-arm, fixed-dose study of paroxetine CR intermittent dosing (luteal phase) in the treatment of PMDD. Study participants fulfilled DSM-IV criteria for PMDD, which were confirmed by prospective daily ratings for two consecutive cycles. There were 116 patients randomized to 25 mg, 130 patients to 12.5 mg, and 120 patients to placebo. The primary measure of efficacy was the change from baseline in the mean luteal phase VAS-Mood score and 120 patients to placebo. The primary measure of efficacy was the change from baseline in the mean luteal phase VAS-Mood score at the endpoint. The VAS-Mood scale is a valid and reliable instrument used to measure four core mood symptoms of PMDD (irritability, tension, affective lability, and depressed mood).

Results: At endpoint, subjects treated with intermittent paroxetine CR (12.5 mg and 25 mg) demonstrated significantly superior improvements on the VAS-Mood scores compared with placebo subjects (paroxetine CR 25 mg mean treatment difference versus placebo [95% C.I.]: -10.8 [-16.5, -5.1], p<0.001; paroxetine CR 12.5 mg mean treatment difference versus placebo [95% C.I.]: -7.7 [-13.3, -2.1], p<0.007).

Conclusion: Intermittent treatment (luteal phase dosing) with 12.5 mg and 25 mg of paroxetine CR is effective in the treatment of PMDD.

References:


**NR763**  
**Thursday, May 22, 12:00 p.m.-2:00 p.m.**  
**Generalized and Psychic Anxiety Symptoms: Cross-Disorder Prevalence and Responsivity to Sertraline Treatment**  
**Supported by Pfizer Inc.**

Larry Culpepper, M.D., *Family Medicine, Boston University, Dowling SS, 1 Boston Medical Center Place, Boston, MA 02118; Henry Chung, M.D., Rana Fayyad, Ph.D., Cathryn M. Clay, M.D.

**Educational Objectives:**

At the conclusion of this session, the participant should (1) understand that psychic anxiety is prevalent, and (2) understand that psychic anxiety symptoms are responsive to medication treatment.

**Summary:**

**Objective:** Psychic anxiety is a symptom cluster that commonly complicates the presentation of depressive and anxiety disorders. The goal of this investigation was to characterize the severity of psychic anxiety across disorders, and evaluate its responsivity to treatment with sertraline.

**Method:** Data were combined across multiple double-blind studies of sertraline in panic disorder (PD; four studies), PTSD (two studies), social anxiety disorder (SAD; one study), GAD (one study), and MDD (one study). The HAM-A total score, psychic anxiety score, and item 1 (anxious mood) were analyzed.

**Results:** Mean baseline HAM-A total and psychic anxiety factor scores, respectively, were highest in GAD (mean=25.13.7), PD (23/11.6) and MDD (16/10.8), lower in PTSD (20/13.4), and lowest in SAD (10/6.4). Psychic anxiety symptoms contributed a larger proportion of the baseline HAM-A total score in MDD (68%) and GAD (56%) vs. other disorders. Sertraline resulted in significant improvement vs. placebo in the HAM-A total score in PD (p=0.005, SAD (p=0.041), GAD (p=0.0001), but not PTSD. The differential effect of sertraline on psychic vs. somatic symptoms of anxiety will be presented and discussed.

**Conclusion:** Generalized anxiety, and most notably symptoms of psychic anxiety, are common across depressive and anxiety disorders, and are responsive to sertraline.

**References:**


**NR765**  
**Thursday, May 22, 12:00 p.m.-2:00 p.m.**  
**The ZMARS: A Proposed New Rating Scale for Anxiety in Clinical Trials**

Daniel L. Zimbroff, M.D., *Pacific Clinical Research, 1317 West Foothill Boulevard, Suite 200, Upland, CA 91786; George Mendez, B.S.

**Educational Objectives:**

At the conclusion of this session, the participant should be able to develop a sensitive, reliable and validated scale for assessing anxiety symptoms that transcends the limitations of the Hamilton Anxiety (Ham-A) rating scale.

**Summary:**

**Objective:** To evaluate the efficacy and tolerability of sertraline in GAD.

**Methods:** Outpatients with DSM-IV GAD were randomized to 12 weeks of double-blind treatment with placebo (N=188; female, 51%; mean age, 42 years; baseline HAM-A, 25) or flexible doses (50–150 mg) of sertraline (N=182; female, 59%; mean age, 40 years; baseline HAM-A, 25). Outcomes included the HAM-A and the CGI-improvement scale (CGI-I ≤ 2 were responders).

**Results:** ANCOVA analysis of the ITT-LOCF sample at endpoint showed mean (± se) Ham-A change scores for sertraline vs. placebo of 11.7 ± 0.6 vs. 8.0 ± 0.6 (p < 0.0001). Improvement was significant by week 4. Significant endpoint improvement was also obtained on both the HAM-A psychic factor 6.7 ± 0.4 vs. 4.1 ± 0.4 (p < 0.0001), and the HAM-A somatic factor 5.0 ± 0.3 vs. 3.9 ± 0.3 (p < 0.02). CGI-I responder rates were significant for both the completer sample (73% vs. 46%; p < 0.0001) and for the LOCF sample (63% vs. 37%; p < 0.0001). Overall sertraline was very well-tolerated with an attrition rate due to adverse events of 8.2% compared with 10.0% on placebo.

**Conclusion:** Sertraline appears to be a significantly effective and well-tolerated treatment for GAD.

**References:**

may better discriminate between patients with differing illness severity.

Conclusions: Preliminary validation evidence demonstrates that inter-rater reliability of the ZMARS is greater than the Ham-A among experts with extensive experience in using the Ham-A. This may be due to the ZMARS standardized anchor points which may be clearer for raters than the individualized, sentence-long anchor points of the Ham-A. Convergent validity using the Ham-A was demonstrated, and the ZMARS appears to better discriminate between patients with differing illness severity than the Ham-A. Further, large scale evaluation of the validity of the ZMARS is warranted, as it appears to offer advantages over the Ham-A which could have important implications for the study of anxiolytic agents.

References:

NR766 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Pregabalin in GAD: Influence of Depressive Symptoms on Anxiolytic Efficacy Supported by Pfizer Inc.
Mark H. Pollack, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC-812, Boston, MA 02114; Daniel L. Zimbrow, M.D., Kathy J. Tobias, M.D., Gwen L. Zornberg, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the anxiolytic efficacy of pregabalin in patients with and without comorbid depressive symptomatology.

Summary:
Objective: To evaluate the anxiolytic efficacy of the novel alpha-2-delta anxiolytic pregabalin (PGB) in patients with clinically significant depressive symptoms.
Methods: The analysis sample consisted of patients from five double-blind, placebo-controlled four- to six-week trials of PGB for the treatment of DSM-IV GAD. The primary outcome measure was the Hamilton Anxiety Rating Scale (HAM-A). Effect size was calculated to compare the improvement in endpoint HAM-A scores for patients with a baseline HAM-D total score ≥ 15 (hi-dep) vs. < 15 (lo-dep) across three treatment groups: PGB 150–200 mg (hi-dep, N=80; lo-dep, N=132), PGB 300–450 mg (hi-dep, N=164; lo-dep, N=278), and PGB 600 mg (hi-dep, N=107; lo-dep, N=210).
Results: Baseline clinical and demographic variables were similar across all treatment groups. For each of the three dosage ranges, in both hi-dep and lo-dep subgroups, PGB demonstrated significantly greater anxiolytic efficacy vs. placebo. The average effect sizes for hi-dep vs. lo-dep, respectively, were PGB 150–200 mg, 0.44 vs. 0.32; PGB 300–450 mg, 0.62 vs. 0.38; PGB 600 mg, 0.50 vs. 0.41. All three PGB dosages were associated with significantly greater improvement in HAM-A total scores compared to placebo.
Conclusions: PGB shows significant anxiolytic efficacy regardless of the presence of clinically meaningful comorbid depressive symptomatology.

References:

NR767 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Quality of Life and Disability in Patients Seeking Treatment for Social Anxiety Disorder Supported by Pfizer Inc.
Mark H. Pollack, M.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC-812, Boston, MA 02114; Michael R. Liebowitz, M.D., Henry Chung, M.D., Nicholas Demartinis, M.D., Michael W. Otto, Ph.D., Rana Fayyad, Ph.D., Cathryn M. Clary, M.D.

Educational Objectives:
At the conclusion of this session, the participant should (1) understand that social anxiety disorder is associated with baseline impairment in QoL, and (2) recognize the importance of depression symptoms in social anxiety.

Summary:
Objective: The goal of this investigation was to characterize the extent and correlate of QoL impairment in treatment-seeking patients with severe social anxiety disorder (SAD).
Method: The analytic sample comprised 415 patients (41% female, mean ± sd age, 35 ± 11 yrs) meeting DSM-IV criteria for SAD who were entering an acute treatment study. QoL and functional assessments included the Quality of Life, Enjoyment, and Satisfaction Scale (Q-LES-Q), the Sheehan Disability Inventory (SDI), and the Endicott Work Productivity Score (EWP).
Results: Mean baseline scores on the Q-LES Q were 70 ± 11; 31% reported normal QoL, while 58% of patients had a baseline Q-LES-Q score that was ≥ 1 standard deviation (SD) below the community mean, and 23% were ≥ 2 SDs below the mean. Mean HAM-D scores at baseline were 6.4 ± 3.3 for sertraline patients and 6.2 ± 3.4 for placebo patients. Results of a regression analysis identified subsyndromic depressive symptoms as the most significant predictor of QoL (Q-LES-Q, R²=0.20; p=0.0001) and work impairment (EWP, R²=15.5%; p=0.0001). Other functional and QoL results will be presented and discussed.
Conclusion: Patients entering an SAD treatment study reported significant baseline impairments in QoL and functioning. Contrary to expectations, the quality of life of patients with social anxiety disorder appeared particularly sensitive to relatively low levels of comorbid depressive symptomatology.

References:

NR768 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Open Trial of VNS in Severe Anxiety Disorders Supported by Cyberonics, Inc
Mark S. George, M.D., Department of Psychiatry, Medical University of South Carolina, 67 President Street, Room 502 North, Charleston, SC 29425-0720; Herbert E. Ward, M.D., Philip T. Ninan, M.D., Mark H. Pollack, M.D., Zsad Mahas, M.D., Wayne K. Goodman, M.D., James C. Ballenger, M.D.
Educational Objectives:

At the conclusion of this session, participants should be familiar with VNS therapy and understand the rationale for studying it as a potential anxiety treatment.

Summary:

Background: Vagus Nerve Stimulation (VNS) therapy is an effective anticonvulsant treatment. The vagus nerve is a major route for transmission of peripheral signals to brain regions important in anxiety regulation. This open, acute, 10-wk study, with long-term follow up, was conducted in patients with treatment-resistant anxiety disorders.

Methods: Ten adult outpatients with treatment-resistant anxiety disorders (7 OCD, 2 PTSD, 1 PD) were recruited. Patients were rated with their disease specific rating (Y-BOCS for OCD; PDSS for Panic Disorder; CAPS-SX for PTSD) as well as the HAM-A and CGI.

Results: Mean baseline HAM-A was 26 (+/-6). Three of 10 patients were acute responders on the HAM-A (>=50% reduction), with two of 10 patients responders at six months. As measured by the CGI, six of 10 patients showed acute improvement, with seven of 10 patients improved at six months. Three of seven patients with OCD (43%) met Y-BOCS response criteria (>=25% reduction) acutely and at six months.

Conclusions: In this cohort of 10 patients with treatment-resistant anxiety disorders, VNS therapy was generally well tolerated and was associated with symptomatic improvement. Further double-blind studies assessing the role of VNS therapy in treating anxiety disorders, particularly OCD, may be warranted.

References:


NR769 Thursday, May 22, 12:00 p.m.-2:00 p.m. Long-Term Clinical Outcomes Following Drug Treatment for GAD in Primary Care Supported by Merck & Co., Inc.

Vasilisa Sazonov Kocovan, M.Sc., Department of Pharmacy, Purdue University, 575 Stadium Hall Dr., Room 502, West Lafayette, IN 47907-2051; Susan Jick, Sc.D., Joseph Thomas, Ph.D.

Educational Objectives:

At the conclusion of this session, practitioners will gain knowledge about long-term clinical outcomes following drug treatment for patients with GAD, which will enable them to make a more rational treatment selection decision.

Summary:

Objectives: To estimate the likelihood and timing of clinical outcomes following treatment with benzodiazepines, serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), and beta-blockers among patients with generalized anxiety disorder (GAD) from the United Kingdom.

Methods: A 12-month retrospective study of GAD patients ages 18-65, followed in the General Practice Research Database during 1997-1999, estimated likelihood of, and time-to-treatment failure/success using multivariate logit and Cox-proportional-hazards models. Failure was defined as treatment switches/augmentation and/or mental disease-related referrals, hospitalizations, or emergency room visits. Success following GAD treatment was based on physician-indicated patient improvement in the records.

Results: Among 2,499 patients, 20.6% experienced some treatment failure. There were no differences in likelihood or time-to-treatment failure between drug classes after controlling for risk factors including age, gender, region, dose, prior mental or somatic illnesses, and health services utilization. Physician-rated improvement was more likely in patients treated with SSRIs (Odds Ratio=6.07[3.59-10.3],p<0.0001), TCAs (OR=2.80[1.56-5.03], p<0.0006), and beta-blockers (OR=1.74[1.03-2.94], p=0.0385) than in those treated with benzodiazepines after adjusting for risk factors. SSRIs also had higher improvement rates than TCAs and beta-blockers (both p<0.01).

Conclusions: Based on objective measures of treatment failure, no differences in long-term outcomes following GAD treatments exist, although physician ratings tend to favor SSRIs.

References:


NR771 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Decreased Plasma Immune Factors in OCD
Daamiaen Denys, M.D., Department of Psychiatry, UMC, Heidelberglaan 100, P.O. Box 85500, Utrecht 3508 GA, Netherlands; Annemieue Kavelaars, Ph.D., Cobi Heynen, Ph.D., Herman Westenberg, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that plasma immune parameters such as TNF-alpha, IL-6, and NK-cells are decreased in patients with OCD, compared with normal controls.

Summary:
Objective: This study was carried out to investigate immune parameters in obsessive-compulsive disorder (OCD).
Methods: Plasma levels of TNF-alpha, IL-4, IL-6, IL-10, IFN-gamma, monocytes, and NK-cells were measured in 60 medication-free outpatients with OCD, and 27 controls matched for age and gender.
Results: We found a significant decrease in TNF-alpha (p < 0.000), IL-6 (p = 0.017), and NK-cells (p=0.003) in comparison with matched controls. No significant differences were observed in the other immune variables. A strong correlation was found with NK-cells and the familial distribution of obsessive-compulsive symptoms: patients with first-degree relatives with OCD had significant lower NK-cell levels than patients who had not (p = 0.03).
Conclusion: Our results confirm the previous reported decrease of TNF-alpha in patients with obsessive-compulsive disorder, and suggest that OCD may be associated with an altered immune regulation.

References:

NR772 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Tiagabine Treatment of PTSD
Supported by Cephalon Inc.
Fletcher B. Taylor III, M.D., Rainier Associates, 5909 Orchard Street, West, Tacoma, WA 98467-3824;

Educational Objectives:
At the conclusion of the presentation, the participant should gain an increased understanding of the potential use of tiagabine for posttraumatic stress disorder.

Summary:
Objective: Some agents known to have GABAergic effects have been found to be useful in the treatment of anxiety disorders. Thus, the selective GABA reuptake inhibitor (SGRI) tiagabine was evaluated for posttraumatic stress disorder (PTSD).

Method: This open-label case series enrolled seven-female outpatients with longstanding refractory PTSD and comorbid disorders. Tiagabine 2 mg was given nightly as add-on therapy and increased by 2 mg/two-three days to achieve optimal response (≤12 mg). Clinical Global Impression of Change (CGI-C) and PTSD Checklist-Civilian Version (PCL-C) scales evaluated efficacy. Adverse events were recorded.
Results: Six of seven patients continued treatment with tiagabine. Final mean dosage was 7.3 mg/day (range: 4–12 mg). Improvements in overall clinical condition were reported one-three days after treatment initiation; all 6 patients were rated as 'markedly improved' on the CGI-C within two weeks. Mean total PCL-C score improved significantly from baseline at Weeks two and eight (P<0.001). Similar improvements were observed in intrusive (P<0.05), avoidance (P<0.001), and arousal (P<0.05) subscales. The distressing dreams item score decreased (P<0.05), although normal dreams occurred and normal sleep patterns resumed. Tiagabine was generally well tolerated, with only one patient discontinuing due to GI disturbances.
Conclusion: These preliminary data suggest that the SGRI tiagabine may be effective in PTSD.

References:

NR773 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Efficacy of Pregabalin in Treating Psychiatric and Somatic Symptoms in GAD
Supported by Pfizer Inc.
R. Bruce Lydiard, M.D., Department of Psychiatry, South East Health Consultants, 1 Poston Road, Suite 150, Charleston, SC 29407; Robert J. Bielski, M.D., Kathy J. Tobias, M.D., Gwen L. Zornberg, M.D.

Educational Objectives:
The presentation should improve participants' understanding of the specific range of anxiety symptoms targeted by pregabalin.

Summary:
Objective: To evaluate the efficacy of the novel alpha-2-delta axiolytic pregabalin (PGB) in treating both psychic and somatic symptoms of GAD.
Methods: The analysis sample consisted of patients from five double-blind, placebo-controlled four-six week trials of PGB for the treatment of DSM-IV GAD. The primary outcome measure was the Hamilton Anxiety Rating Scale (HAM-A). Endpoint change in the 7-item HAM-A psychic and somatic anxiety factors were compared for placebo (N=398) vs. three PGB dosage groups, PGB 150–200 mg (N=212), PGB 300–450 mg (N=440), and PGB 600 mg (N=317).
Results: Baseline clinical and demographic variables were similar across treatment groups, with a mean baseline HAM-A ranging from 24.3 to 26.0; the psychic factor contributed 56% to the total score. The mean endpoint change scores for the HAM-A psychic and somatic factors, respectively, were: PGB 150–200 mg, −6.0 and −5.5; PGB 300–450 mg, −6.5 and −5.7; and PGB 600 mg, −6.6 and −5.5. PGB differences from placebo were statistically significant on both psychic and somatic subscales at each dose range, and showed a similar magnitude of improvement on both factors.
**Conclusions:** PGB has broad-spectrum efficacy across the full range of GAD symptomatology, with similar efficacy in reducing both psychotic and somatic symptoms.

**References:**

**NR774 Thursday, May 22, 12:00 p.m.-2:00 p.m.**

**Escitalopram is Effective in Relapse Prevention in Social Anxiety Disorder**

**Supported by H. Lundbeck A/S**

Stuart A. Montgomery, M.D., Department of Psychiatry, Imperial College, P.O. Box 8751, 19 Street Leonard's Road, London W13 8PN, England; Natalie Durr-Pal, M.D., Henrik Loft, Ph.D., Rico Nil, Ph.D.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to appreciate that escitalopram 10–20 mg/day is highly effective in preventing relapse in patients with social anxiety disorder.

**Summary:**
- **Introduction:** Escitalopram is the most selective SSRI, whose efficacy and safety in the treatment of MDD have been established.
- **Objectives:** To determine the efficacy of escitalopram 10–20 mg/day in preventing relapse in patients with social anxiety disorder (SAD).
- **Methods:** This study was conducted in outpatients (18–80 years) with a primary diagnosis of generalised SAD (DSM-IV) and an LSAS > 70. After 12 weeks of open-label treatment (10–20 mg/day escitalopram), patients responding (CGI-I of 1 or 2) were randomised to 24 weeks of escitalopram (n=190) or placebo (n=181) treatment, to assess their relapse rate. The initial dose of 10 mg/day escitalopram could be doubled to a maximum of 20 mg/day, if clinically indicated, at Week 2, 4, or 8. Relapse was either an LSAS increase >10 or discontinuation due to lack of efficacy.
- **Results:** The risk of relapse was 2.8-times higher for placebo-treated patients than for patients continuing escitalopram treatment (log-rank, p<0.001). The cumulative relapse rate at Week 24 was 23% for the escitalopram group versus 56% for the placebo group. The favorable long-term side-effect profile of escitalopram treatment was confirmed, with only 4% of escitalopram-treated patients withdrawing due to adverse events.
- **Conclusion:** Escitalopram 10–20 mg/day is highly effective in preventing relapse in patients with SAD.

**References:**

**NR775 Thursday, May 22, 12:00 p.m.-2:00 p.m.**

**Pregabalin in GAD: Speed of Onset**

**Supported by Pfizer Inc.**

Stuart A. Montgomery, M.D., Department of Psychiatry, Imperial College, P.O. Box 8751, 19 Street Leonard's Road, London W13 8PN, England; Karl Rickels, M.D., Robert J. Blieski, M.D., Kathy J. Tobias, M.D., Gwen L. Zomberg, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should have increased understanding of the anxiolytic efficacy of pregabalin and what to expect in terms of its onset of action.

**Summary:**
- **Objectives:** Onset of efficacy differs for different classes of anxiolytics, with benzodiazepines acting by one week, while serotonergic anxiolytics (SSRIs and buspirone) typically have onset by two to three weeks. The goal of this investigation was to evaluate the speed of onset of efficacy for the novel alpha-2-delta anxiolytic pregabalin (PGB).
- **Methods:** The analysis sample consisted of patients from five double-blind, placebo-controlled four- to six-week trials of PGB for the treatment of DSM-IV GAD. The primary outcome measure was the Hamilton Anxiety Rating Scale (HAM-A). At least 30% improvement by week 1 in HAM-A total score was used as a criterion for early improvement. Early improvement was compared for placebo (N=398) vs. three PGB dosage groups, PGB 150–200 mg (N=212), PGB 300–450 mg (N=440), and PGB 600 mg (N=317).
- **Results:** Baseline variables were similar across all treatment groups. Baseline HAM-A across treatment groups ranged from 24.3 to 26.0. The proportion of patients achieving improvement by week 1 were: PGB 150–200 mg, 44%; PGB 300–450 mg, 51%; PGB 600 mg, 54%; and placebo, 30%.
- **Conclusions:** PGB demonstrates early onset of efficacy that is more rapid than the serotonergic anxiolytics, and exhibits a modest dose-response relationship.

**References:**

**NR776 Thursday, May 22, 12:00 p.m.-2:00 p.m.**

**Genetic Anticipation in OCD: Exploring Affected Parent-Child Pairs**

**Canadian Institutes for Health Research**

S. Evelyn Stewart, M.D., Mclean Hospital, Third East House, 115 Mill Street, Belmont, MA 02478-9106; Daniel A. Gellar, M.D., David L. Pauls, Ph.D., Colleen Farrell, B.A.

**Educational Objectives:**
The participants should be able to recognize the concept of genetic anticipation and how it applies to obsessive-compulsive disorder.

**Summary:**
- **Objective:** To determine whether the phenomenon of genetic anticipation occurs in OCD, thus causing earlier and more severe illness in children than their affected parents.
- **Introduction:** As a genetic disorder, OCD is the fourth most common psychiatric illness. Genetic anticipation causes increasing severity and earlier onset of illnesses in subsequent generations. Anticipation has not been studied to date in OCD.
- **Methods:** This Harvard OCD Family study conducted structured interviews and blinded reviews of child probands(N=98) and their parents(OCD-affected parents: N=34). Chi-square and multivariate logistic regression were used in analyses. Outcome measures were age of onset and lifetime/current severity, primarily in probands and their affected parents; secondarily in probands without affected parents.
Results: OCD onset occurred earlier in probands (9.1 y) versus their affected parents (16.5 y) (p<0.001). OCD current and lifetime severity was greater in probands versus affected parents (p=0.003<0.001). Current and lifetime severity were decreased in probands with versus without affected parents (p<0.001<0.001), but there were no differences in illness onset (p=0.58).

Conclusion: Genetic anticipation may be present in OCD. This has clinical applications for children of OCD sufferers.

References:

NR777 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Long-Term Outcome of Child and Adolescent-Onset OCD: A Review of the Literature
S. Evelyn Stewart, M.D., Mclean Hospital, Third East House, 115 Mill Street, Belmont, MA 02478-9106; Daniel A. Gellar, M.D., David Shaw, B.A., Michael A. Jenike, M.D., Benjamen Mullin, B.A., David L. Pauls, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the current state of scientific knowledge regarding the long-term outcome and course of child and adolescent-onset OCD

Summary:
Objective: To review extant literature on the long-term outcome of juvenile-onset obsessive-compulsive disorder (OCD), given that OCD is the fourth most common psychiatric illness (1), and among the ten leading global causes of disability.

Method: Systematic Medline and Psychlit database searches were performed for articles on long-term outcomes of child/adolescent-onset OCD. Inclusion criteria permitted all English studies of child/adolescent-onset OCD accepted by peer-reviewed journals, with a minimum twelve-month follow-up period. Iterative bibliography searches on the six identified studies yielded 25 articles and no pre-existing outcome reviews. Articles were categorized using AHRQ criteria.

Results: The 18 study samples (n=55–139; total=726 participants) in 25 studies had follow-up periods ranging between 1–15.6 years. Study designs were frequently level A, retrospective, in-patient clinical series. OCD and subclinical-OCD rates at follow-up typically ranged between 26–50% and 17–46%, respectively. Course types were described using terms 'waxing/waning', remission (9–75%), subclinical (17-40%), episodic (7–32%) and chronic (17–70%). Psychosocial outcomes indicated high rates of social problems (55–100%), singleness (52–100%), and unemployment (45%), although 30–70% completed college. Reported outcome predictors were inconsistent between studies.

Conclusion: Although full and partial remission rates of at least 50% are commonly reported, there is no clear consensus on the long-term outcome in child/adolescent-onset OCD. Future prospective long-term studies are required.

References:

NR778 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Use of Outpatient Services in the Severely Mentally Ill Post-Discharge
Geetha Jayaram, M.D., Johns Hopkins University School of Medicine, 600 North Wolf Street, M-101, Baltimore, MD 21287; David Edwin, Ph.D.

Educational Objectives:
At the conclusion of this session, participants will recognize patients with the need for most support and interventions post-discharge.

Summary:
One dimension of the quality of care for severely mentally ill (SMI) patients is the assessment of the degree to which patients use services to sustain desired outcomes after discharge from inpatient care. Severely mentally ill patients suffer from a range of difficulties that hamper adherence to post-discharge appointments, with resultant relapses. Demographic factors, illness severity, are linked to the use of psychiatric services post-discharge. In this paper, we describe the service use patterns of 86 severely ill patients in a community psychiatry sample of 109 people who were discharged from an acute treatment service. We prospectively collected data ascertaining patterns of service use from a central database for Baltimore city, a model heretofore not demonstrated. Using t tests and Chi-square analyses, we found that gender, age, severe mental illness, and addictive behavior posed significant risks for relapse. Possible interventions to enhance treatment adherence will be discussed.

References:

NR779 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Occupational Impairment of Primary Care Patients With Social Anxiety Disorder Supported by Pfizer Inc.
Steven Bruce, Ph.D., Psychiatry Department, Brown University, Box G-BH, Providence, RI 02906; Benjamin Rodriguez, Ph.D., Risa B. Weisberg, Ph.D., Maria E. Pagano, Ph.D., Larry Culpepper, M.D., Martin B. Keller, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that social anxiety disorder adversely effects occupational impairment at a significantly higher level than other anxiety disorders.

Summary:
Objective: The present research reports data from the Primary Care Anxiety Project (PCAP), a longitudinal study of anxiety disorders in primary care patients. In this investigation, occupational impairment in patients with social anxiety disorder were examined and compared with patients with other anxiety disorders.

Methods: 540 patients recruited from primary care clinics across the New England area are currently enrolled in the study with 179 participants meeting criteria for social anxiety disorder. Follow-up evaluations are conducted at 6-months, one year, and annually thereafter.

Results: Compared with other anxiety disorders, results indicate that patients with social anxiety disorder are significantly less likely to have an occupation in which they work with customers or clients
These findings emphasize the need for early identification and treatment selection, even when compared to other anxiety disorders. These findings emphasize the need for early identification and treatment to minimize potential complications that may further reduce quality of life.

**References:**


**NR780**

Thursday, May 22, 12:00 p.m.–2:00 p.m.

**Drug Treatments Among Primary Care Patients With GAD in the United Kingdom Supported by Merck & Co., Inc.**

Joseph Thomas, Ph.D., Pharmacy Prac, Purdue University, 575 Stadium Mall, West Lafayette, IN 47907-2051; Vasilisa Saznov Kocevar, M.S., Susan Jick, Sc.D.

**Educational Objectives:**

- At the conclusion of this session, the participant should understand drug treatment patterns including duration, dosing and switching, or augmentations among GAD patients, particularly the relationships between clinical/demographic characteristics and treatment selection.
- Conclusions: Social anxiety disorder negatively affects occupational functioning, even when compared to other anxiety disorders. These findings emphasize the need for early identification and treatment to minimize potential complications that may further reduce quality of life.

**References:**


**NR781**

Thursday, May 22, 12:00 p.m.–2:00 p.m.

**Association of Panic Disorder With the L/L Genotype of Catechol-O-Methyl Transferase**

Burn-Hee Yu, M.D., Department of Psychiatry, Samsung Medical Center, 50 Ilwon-Dong, Gangnam-Gu, Seoul 135-370, Korea; Jong-Min Woo, M.D., Kyung-Jeong Kim, B.S.C., Kyung-Sik Yoon, M.D., Young-Hee Choi, M.D., Kang-Sub Oh, M.D., Young-Sik Lee, M.D.

**Educational Objectives:**

- At the conclusion of this session, the participant should understand that COMT genetic polymorphism could help to evaluate the susceptibility of panic disorder, and treatment response in patients with panic disorder.

**Summary:**

- Objective: Abnormal functions of catecholamines have been suggested to be important in the pathophysiology of panic disorder. Catechol-O-methyltransferase (COMT) mainly catalyses catecholamines, thereby leading to their inactivation. COMT gene leads to a three- to fourfold difference in enzymatic activity and has been implicated to play a role in anxiety disorders like panic disorder. We investigated the genotype frequencies of the COMT gene and the relationship between COMT genotypes and clinical characteristics in patients with panic disorder.
- Methods: We measured COMT genotypes using the PCR techniques in 189 patients who met the DSM-IV criteria for panic disorder, and 188 normal control subjects. There was no gender and age difference between panic patients and control subjects.
- Results: We found a significant difference in the distribution of the COMT genotypes between two groups. The frequency of the L/L genotype was higher in panic patients than in control subjects (12.2% vs. 4.8%; x² = 6.93, p = 0.031). Panic disorder was significantly associated with L allele and L/L genotype. Furthermore, panic patients with L allele and L/L genotype showed higher anxiety level (F = 3.58, p = 0.03), more comorbid agoraphobia (x² = 6.76, p = 0.034) and poorer treatment response to paroxetine (F = 7.59, p = 0.001) than those with H/L and H/H genotypes.
- Conclusions: Our analysis suggests that COMT genetic polymorphisms could help to evaluate the susceptibility of panic disorder, and estimate severity of clinical symptoms and treatment response in patients with panic disorder.

**References:**

NR782 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Escitalopram in SAD: More Cost Effective, Lower Costs, and Improved Quality of Life
Supported by H. Lundbeck A/S
Dominique Servant, M.D., Department of Stress and Anxiety, Hospital Boulevard De Metz, Lille Cedex 59037, France; Stuart A. Montgomery, M.D., Clement Francois, M.S.C., N. Despiegel

Educational Objectives:
At the conclusion of this session, the participant should be able to appreciate that escitalopram is cost-effective in preventing relapse in social anxiety disorder.

Summary:
Introduction: social anxiety disorder (SAD) is a prevalent and chronic psychiatric disorder, but its economic consequences are not well known. SSRIs have been proven to be effective in the prevention of relapse, but further cost-effectiveness studies are required.
Objectives: To evaluate the cost-effectiveness of escitalopram in comparison with placebo in relapse prevention of SAD.
Methods: Use of medical services and days of sick leave were recorded in parallel with a double-blind, placebo-controlled, six-month relapse prevention clinical study. Health-related quality of life (SF-36) was assessed at baseline, and at weeks 12 and 24 of treatment. The study adopted a societal perspective.
Results: Patients treated with escitalopram experienced a better health-related quality of life compared to placebo-treated patients (better scores for all the mental health-related dimensions: social functioning, role emotional, mental health; p<0.05 and vitality, p<0.01). Total costs were 22.5% lower for patients treated with escitalopram compared with placebo (Euro 255 versus Euro 329; p<0.05).
Conclusion: Continuation of escitalopram treatment is effective in the prevention of relapse in SAD patients. Escitalopram is more cost-effective than placebo and the drug purchase costs are more than offset by a decrease in total costs.

References:

NR783 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Quality of Life in OCD
Jane L. Eisen, M.D., Butler Hospital, Brown University, 345 Blackstone Boulevard, Providence, RI 02906; Maria Mancebo, Ph.D., Steven A. Rasmussen, M.D.

Educational Objectives:
At the conclusion of this session, the participant will recognize the impact of OCD on quality of life and functioning.

Summary:
Background: Epidemiologic studies have shown that obsessive compulsive disorder (OCD) is one of the most common major psychiatric disorders, with a lifetime prevalence of 2% to 3% worldwide. A WHO study has listed OCD as the tenth leading cause of morbidity of all medical conditions. This is the first study to present data comparing multiple domains of quality of life in patients with OCD with norms from a community sample.
Method: The Quality of Life and Enjoyment and Satisfaction Questionnaire (Q-LES-Q), a self-report with demonstrated reliability and validity, was completed by 100 participants with DSM-IV OCD, as part of a larger baseline assessment for a prospective study of OCD course. The Q-LES-Q consists of 91 items grouped into eight summary scales.
Results: Almost one-third of the subjects eligible to work reported being unable to do so. Ninety five percent of a community sample scored above the mean score of the OCD sample on the general activities summary scale (personal communication, Jean Endicot). The mean score of the OCD sample was significantly lower than the community sample mean (55.3, SD 17.67 vs 78.1, SD 13.67, p=.000). Correlations between Q-LES-Q summary scores and the Yale Brown Obsessive Compulsive Scale (YBOCS) total scores were significant on all summary scales (r=.345-.710, p=.000-.022). All summary scores were significantly different for subjects with YBOCS scores greater than 16 compared with those with YBOCS scores less than 16. Age of onset was associated with social relationships (r=.354, p=.015).
Conclusions: These preliminary findings suggest that all domains of quality of life measured by the Q-LES-Q are significantly affected in OCD compared to community norms and are significantly associated with OCD symptom severity measured by the YBOCS.

References:

NR784 Thursday, May 22, 12:00 p.m.-2:00 p.m.
The Clinical Anxiety Scale (CAS) and the Physician Questionnaire (PQ): Validation of the Spanish Version
Supported by GlaxoSmithKline
Antoni Bulbena, M.D., Department of Psychiatry, Hospital Del Mar, Paseo Maritimo 25, Barcelona 08003, Spain; Julio B. Bobes, M.D., Antonio Luque, M.D., Rafael Dal-Re, M.D., Javier Ballesteros, M.D., Nora Ibarrar, M.P.S.

Educational Objectives:
At the conclusion of this session, the participant should recognize the usefulness of the Spanish versions of CAS and PQ.

Summary:
Objective: To validate the Spanish version of CAS and PQ for use in routine practice and clinical research.
Method: We conducted a prospective, observational cohort and multicentre study in clinically stable or unstable outpatients with DSM-IV diagnosis of anxiety disorders. The convergent and discriminant validity for both scales, and their reliability (internal consistency, test-retest and inter-rating) and sensitivity to change were assessed as well.
Results: We entered 161 patients from 15 psychiatry settings widely distributed in Spain. The CAS and PQ showed appropriate convergent validity when compared with Hamilton Anxiety Rating Scale scores (r ≥ 0.70) and were able to discriminate between different symptom severity levels as assessed by the Clinical Global Impression (CAS: F [2, 158] = 35.5, p < 0.0001; PQ: F [2, 158] = 11.5, p < 0.0001). Both scales showed appropriate values for internal consistency (Cronbach's α ≥ 0.70), 1-week test-retest reliability (intraclass correlation coefficient (ICC) > 0.80), inter-rating reliability (ICC > 0.90) and 6-weeks sensitivity to change (effect size ≥ 1.5).
Conclusions: Our results confirm the robust psychometric properties of the Spanish versions of CAS and PQ, and hence support their use in clinical practice and research.

References:


NR785 Thursday, May 22, 12:00 p.m.-2:00 p.m.

Does Pretreatment Anxiety or Insomnia Predict Acute Response to Bupropion SR?

Supported by GlaxoSmithKline

A. John Rush, M.D., Department of Psychiatry, University of Texas, SW Medical Center, 5323 Harry Hines Boulevard, MC9086, Dallas, TX 75390-9086; Thomas J. Carmody, Ph.D., Sidney Zisook, M.D., Carol B. Rockett, Pharm.D., Barbara R. Haight, Pharm.D., Robert Schmid, B.A.

Educational Objectives:

- At the conclusion of this session, the participant should recognize that pretreatment severity of anxiety or insomnia are not clinically useful in predicting which depressed outpatients will benefit from bupropion SR.

Summary:

**Background:** Some clinicians believe that noradrenergic/dopaminergic agents are less effective for depressed patients with substantial levels of pretreatment anxiety or insomnia. This retrospective analysis was conducted to determine whether higher levels of anxiety or insomnia at baseline were associated with poorer antidepressant response or slower onset of response to bupropion sustained release (SR).

**Method:** A retrospective analysis was conducted using data from an open-label, eight-week, acute-phase, multicenter study in 796 adult outpatients with recurrent, major depressive disorder who received bupropion SR (300 mg/day). Depressive symptom severity was measured by the 17-item Hamilton Rating Scale for Depression (HAMD-17). Anxiety symptoms were measured by the 14-item Hamilton Rating Scale for Anxiety (HAM-A). Insomnia was assessed by totaling the three HAM-D17 insomnia items (early, middle, and late insomnia).

**Results:** Overall, 67% (533/796) of patients responded to treatment (response defined as ≥50% reduction in baseline HAMD-17 total score) and 56% (442/796) achieved remission (exit HAMD-17 total score ≤7) (intent-to-treat sample). Neither baseline anxiety nor baseline insomnia was associated with the likelihood of antidepressant response. Furthermore, there was no relationship between time to onset of either anxiolysis or antidepressant response and severity of baseline anxiety or insomnia. However, baseline anxiety, but not insomnia, was related to the likelihood of remission.

**Conclusion:** Antidepressant response rates and time to onset of response were similar in outpatients with and without high levels of baseline insomnia or anxiety treated with bupropion SR. Pretreatment severity of anxiety or insomnia are not clinically useful in predicting which depressed outpatients will benefit from bupropion SR.

References:


NR786 Thursday, May 22, 12:00 p.m.-2:00 p.m.

Sertraline Versus Paroxetine in the Treatment of Panic Disorder

Supported by Pfizer Inc.

Borwin Bandelow, M.D., Department of Psychiatry, University of Goettingen, Von-Siebold-Str 5, Goettingen 37075, Germany; K. Behnke, M.D., G.J. Hendriks, S. Lenoir, M.D., T. Alkin, M.D., Claus Goebel, M.D.

Educational Objectives:

- The presentation should increase the participant’s knowledge of the comparative efficacy and tolerability profiles of sertraline and paroxetine as treatments for panic disorder, providing evidence-based information to assist the participant in medication decisions.

Summary:

**Objective:** To compare the efficacy and tolerability of sertraline and paroxetine in panic disorder (PD).

**Methods:** Outpatients with DSM-IV PD were randomized to 12 weeks of flexible dose sertraline (50–150 mg; N=112; female, 60%) or paroxetine (titrated up to 40–60 mg; N=113; female, 66%). Patients were tapered off medication over 3 weeks. Outcomes included the Panic and Agoraphobia Scale (PAS)1, panic attack frequency, and the CGI-Improvement scale (CGI-I ≤ 2 were responders).

**Results:** Sertraline and paroxetine had equivalent improvement on the PAS total score, as well as on all secondary outcome measures. 82% on sertraline vs. 78% on paroxetine were CGI-I responders at endpoint. Paroxetine was less well tolerated than sertraline, with higher attrition due to adverse events (18% vs. 12%; p < 0.05), and a higher proportion of patients reporting ≥ 7% weight gain (7% vs. < 1%; p < 0.05). Taper off paroxetine was associated with significant clinical worsening compared to sertraline: the percent panic-free increased during taper from 54% to 58% on sertraline, but decreased from 53% to 42% during paroxetine taper (p < 0.05).

**Conclusion:** Sertraline and paroxetine had equivalent efficacy in PD, but sertraline was better tolerated, and had less clinical worsening during taper.

References:


NR787 Thursday, May 22, 12:00 p.m.-2:00 p.m.

Sertraline Versus Paroxetine in the Treatment of Panic Disorder

Supported by Pfizer Inc.

Borwin Bandelow, M.D., Department of Psychiatry, University of Goettingen, Von-Siebold-Str 5, Goettingen 37075, Germany; K. Behnke, M.D., G.J. Hendriks, S. Lenoir, M.D., T. Alkin, M.D., Claus Goebel, M.D.

Educational Objectives:

- The presentation should increase the participant’s knowledge of the comparative efficacy and tolerability profiles of sertraline and paroxetine as treatments for panic disorder, providing evidence-based information to assist the participant in medication decisions.

Summary:

**Objective:** To compare the efficacy and tolerability of sertraline and paroxetine in panic disorder (PD).
Methods: Outpatients with DSM-IV PD were randomized to 12 weeks of flexible-dose sertraline (50–150mg; N=112; female, 60%) or paroxetine (titrated up to 40–60 mg; N=113; female, 66%). Patients were tapered off medication over three weeks. Outcomes included the Panic and Agoraphobia Scale (PAS), panic attack frequency, and the CGI-Improvement scale (CGI-I ≤ 2 were responders).

Results: Sertraline and paroxetine had equivalent improvement on the PAS total score, as well as on all secondary outcome measures. 82% on sertraline vs. 78% on paroxetine were CGI-I responders at endpoint. Paroxetine was less well tolerated than sertraline, with higher attrition due to adverse events (18% vs. 12%; p < 0.05), and a higher proportion of patients reporting ≥ 7% weight gain (7% vs. < 1%; p < 0.05). Taper off paroxetine was associated with significant clinical worsening compared with sertraline: the percent panic free increased during taper from 54% to 58% on sertraline, but decreased from 53% to 42% during paroxetine taper (p < 0.05).

Conclusion: Sertraline and paroxetine had equivalent efficacy in PD, but sertraline was better tolerated, and had less clinical worsening during taper.

References:

NR788 Thursday, May 22, 12:00 p.m.–2:00 p.m.
Clinical Predictors of Drug Response in Patients With OCD

Min-Seong Koo, M.D., Department of Psychiatry, Yongdong Severance, 146-92 Dogok-Dong, Kangnam-Gu, Seoul, Korea; Chan-Hyung Kim, M.D., Ho-Suk Suh, M.D., Yoon-Sik Shin, M.D., Hong-Shick Lee, M.D., Keun-Ah Cheon, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to (1) evaluate the use of nefazodone in the treatment of generalized social phobia; and (2) understand the differences in treatment outcome for a variety of serotonergic antidepressants for generalized social phobia.

Summary:
Objective: Numerous studies have demonstrated the efficacy of serotonergic antidepressants, particularly the selective serotonin reuptake inhibitors, in the treatment of social phobia. We evaluated the efficacy, safety and tolerability of nefazodone, a 5HT2 antagonist, in patients with generalized social phobia.

Method: One hundred and four patients with generalized social phobia (GSP) from four Canadian sites, were assigned randomly to nefazodone (300–600 mg/day, flexible dose) or placebo for 14 weeks of double-blind treatment. Primary efficacy outcomes were the Clinical Global Impression Scale, Global Improvement Item (CGI-I) and the Liebowitz Social Anxiety Scale.

Results: Preliminary analysis of the intent to treat sample revealed that 16 of 51 subjects (31.4%) taking Nefazodone and 12 of 51 subjects (23.5%) taking placebo were much or very much improved on the CGI-I at end point (X² = 0.79; p=0.38).

Conclusion: These findings suggest that nefazodone is not an effective agent in the treatment of generalized social phobia. This finding parallels that found in a recent study by Kobak et al, 2002, using fluoxetine in GSP. It also supports the idea that there may be neurotransmitter systems other than serotonin involved in the pharmacological response seen in GSP.

References:

NR790 Thursday, May 22, 12:00 p.m.–2:00 p.m.
Selective Loss of Affective Arousal for Pleasant Images in Male and Female Bosnian Refugees With PTSD
Aida Spahic-Mihajlovic, M.D., Psychiatry, Alexian Brothers, 850 West Bisterfield Road, Suite 3005, Elk Grove Village, IL 60007; John W. Crayton, M.D., Edward J. Neafsey, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that emotional numbing in Bosnian refugees with PTSD reduces subjective feelings of emotional arousal when viewing
pleasant pictures, and how this differs from PTSD in Vietnam veterans.

Summary:

Background: Emotional numbing is a prominent and important symptom in PTSD that nonetheless remains vague and poorly defined, despite that fact that it best distinguishes between those with and without PTSD.

Objective: To determine whether numbing is global, affecting both positive and negative affect equally, or whether it predominantly affects one or the other.

Method: Lang’s Looking at Pictures test, in which a series of pictures are rated for valence (pleasant-unpleasant) and arousal (high-low), was administered to 10 male and 11 female Bosnian refugees suffering from PTSD and to control groups of 11 male and 10 female Bosnian refugees with similar trauma exposure but without PTSD or any other major mental illness. All subjects were also characterized using Foa’s PTSD Symptom Scale and the Hamilton Rating Scale for Depression.

Results: The mean valence ratings for each picture of both PTSD and control males and females were similar to normal valence ratings, as determined by simple linear regression ($R^2 = .90$ for males, $R^2 = .76$ for females). The mean arousal ratings for each picture of both control males and control females displayed the normal “U-shaped” quadratic regression relation to normal valence ratings, with both unpleasant and pleasant pictures considered arousing while neutral pictures were not ($R^2 = .39$ for control males, $R^2 = .49$ for control females, $R^2 = .42$ for normals). In contrast, the mean arousal ratings of both males and females with PTSD showed an abnormal and linear relationship to normal valence ratings, with unpleasant pictures rated arousing while pleasant pictures were not ($R^2 = .81$ for PTSD males, $R^2 = .82$ for PTSD females).

Conclusion: These data suggest that in Bosnian refugees diagnosed with PTSD, affective numbing is not global or indiscriminate but instead affects primarily arousal elicited by pleasant or positive stimuli.

References:


NR792 Thursday, May 22, 12:00 p.m.-2:00 p.m.

Improvement of Functional Impairment in Patients With Social Anxiety Disorder Supported by GlaxoSmithKline

Lee D. Ruggiero, B.S., GlaxoSmithKline, 2301 Renaissance Blvd., Philadelphia, PA 19406-2772; Sig Rasmussen, M.D., Jane St. Lambert, Ph.D., Timothy E. Rolfe, M.Sc.

Educational Objectives:

At the conclusion of this presentation, the participant will be able to evaluate the effectiveness of paroxetine CR on functional impairment in outpatients with social anxiety disorder.

Summary:

Objective: To evaluate the effect of paroxetine CR on functional impairment in patients with social anxiety disorder (SAD).

Methods: Paroxetine CR was evaluated in a multicenter, double-blind, placebo-controlled trial in outpatients with SAD. This 12-week study employed a flexible-dose regimen of paroxetine CR (12.5 mg–37.5 mg). Primary efficacy was measured by the change from baseline in LSAS total score and proportion of CGI-I responders. The Sheehan Disability Scale (SDS) was utilized to measure functional impairment in three domains: work, social life, and family life.

Results: Paroxetine CR was effective in treating SAD as measured by the LSAS total score (p<0.001) and the proportion of CGI-I responders (p<0.001). Statistically significant differences were also demonstrated in favor of paroxetine CR versus placebo for all three functional domains of the Sheehan Disability Scale [family life: adjusted mean difference = −0.64, 95% CI (−0.99, −0.29), p<0.001; work: adjusted mean difference = −1.10, 95% CI (−1.56, −0.65), p<0.001; social life: adjusted mean difference = −1.10, 95% CI (−1.57, −0.63), p<0.001].

Conclusion: Paroxetine CR is an effective treatment for SAD. The results support the clinical usefulness of paroxetine CR treatment in improving the functional impairment of patients with social anxiety disorder.
NR793 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Efficacy of Controlled-Release Paroxetine in the Treatment of Patients With Social Anxiety Disorder Supported by GlaxoSmithKline

Jane St.Lambert, Ph.D., Psychiatry, Glaxo Smith Kline, Third Avenue, Harlow CM19-5AW, United Kingdom; Sig Rasmussen, M.D., Lee D. Ruggiero, B.S., Timothy E. Rolle, M.Sc.

Educational Objectives:
At the conclusion of this presentation, the participant will be able to critically evaluate the efficacy of paroxetine CR in the treatment of outpatients with SAD.

Summary:
Objective: To evaluate the efficacy and safety of controlled-release paroxetine (CR) in outpatients with social anxiety disorder (SAD).
Methods: Multicenter, randomized, double-blind, placebo-controlled, flexible-dose study (paroxetine CR 12.5mg to 37.5mg) conducted in patients with SAD. Eligible patients were randomized to receive either paroxetine CR or placebo for 12 weeks. There were two primary efficacy measures, change from baseline in the LSAS total score and the proportion of responders defined by a CGI-Improvement score of 1 or 2. Secondary efficacy measures included CGI Severity of Illness, LSAS Fear and Avoidance scores, and Social Avoidance and Distress Scale.
Results: The ITT population consisted of 370 patients (186 paroxetine CR; 184 placebo). At study endpoint, the mean difference between paroxetine CR and placebo in LSAS total score was -13.33 points (95% confidence interval [-18.25, -8.41], p<0.001); 57.0% of paroxetine-treated patients were responders compared with 30.4% of placebo patients (odds ratio 3.12, 95% CI: [2.01, -13.33]). Paroxetine CR was statistically superior to placebo at endpoint for all secondary measures. Withdrawals due to AEs were similar in paroxetine CR and placebo patients (2.7% vs 4.83%, p<0.001). Paroxetine CR was statistically superior to placebo at endpoint for all secondary measures. Withdrawals due to AEs were similar in paroxetine CR and placebo patients (2.7% vs 4.83%, p<0.001).
Conclusion: These data clearly demonstrate that paroxetine CR is an effective and well-tolerated treatment for SAD.

References:

NR795 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Follow-Up Study With Nortriptyline in Panic Disorder Patients

Isabella Nascimento, M.D., Department of Psychiatry, Federal University Rio Janiero, Rua Prof Hermes Lima 364/103, Rio De Janeiro, RJ 22795-065, Brazil; Antonio E. Nardi, M.D., Alexandre M. Valenca, M.D., Lopes L. Fabiana, M.D., Marco A. Mezzasalma, M.D., Walter A. Zin, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that there is no association between family history of PD and hyperreactivity to a range of clinical parameters.

Summary:
Objective: To ascertain whether patients with obsessive-compulsive disorder (OCD) with hoarding symptoms display a distinctive phenotypical profile.
Methods: Ninety-six patients with OCD were initially assessed with a sociodemographic questionnaire, the SCID-I/P, the Yale-Brown obsessive compulsive scale (Y-BOCS), the Beck depression inventory, the Hamilton rating scale for depression, and the global assessment of functioning. Patients who reported hoarding symptoms in the Y-BOCS checklist were compared and contrasted with patients without those symptoms using the Mann-Whitney U test for continuous variables and the Pearson's goodness of fit Chi-square test for categorical ones; Fisher's exact test was employed when indicated.
Results: Hoarders (14.9% of the total sample) were characterized by higher educational levels (chi=7.49; df=2; p=.02), earlier age at onset (Z=-2.8; p=.004), and a distinctive pattern of predominant obsessive thoughts [with significantly higher rates of symmetry (chi=8.10; df=1; p=.01) themes], compulsions [with significantly greater frequency of rituals repetition (chi=5.78; df=1; p=.01) and ordering (chi=8.10; df=1; p=.01)] and comorbidity [with significantly higher rates of previous major depressive episodes (chi=7.80; df=1; p=.005)].
Conclusions: The presence of hoarding symptoms may be an important factor in subtyping OCD.

References:

NR794 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Patients With OCD and Hoarding Symptoms: A Distinctive Subtype?

Leonardo F. Fontenelle, M.D., Department of Psychiatry, IPUB-UFRJ, Rua Lopes Trovao 88 1501A Icarai, Niteroi, RJ 24220-071, Brazil; Mauro V. Mendowicz, M.D., Marcio V. Versiani, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that patients with OCD and hoarding symptoms may differ from their non-hoarding counterparts on a range of clinical parameters.

Summary:
Objective: To ascertain whether patients with obsessive-compulsive disorder (OCD) with hoarding symptoms display a distinctive phenotypical profile.
Methods: Ninety-six patients with OCD were initially assessed with a sociodemographic questionnaire, the SCID-I/P, the Yale-Brown obsessive compulsive scale (Y-BOCS), the Beck depression inventory, the Hamilton rating scale for depression, and the global assessment of functioning. Patients who reported hoarding symptoms in the Y-BOCS checklist were compared and contrasted with patients without those symptoms using the Mann-Whitney U test for continuous variables and the Pearson's goodness of fit Chi-square test for categorical ones; Fisher's exact test was employed when indicated.
Results: Hoarders (14.9% of the total sample) were characterized by higher educational levels (chi=7.49; df=2; p=.02), earlier age at onset (Z=-2.8; p=.004), and a distinctive pattern of predominant obsessive thoughts [with significantly higher rates of symmetry (chi=8.10; df=1; p=.01) themes], compulsions [with significantly greater frequency of rituals repetition (chi=5.78; df=1; p=.01) and ordering (chi=8.10; df=1; p=.01)] and comorbidity [with significantly higher rates of previous major depressive episodes (chi=7.80; df=1; p=.005)].
Conclusions: The presence of hoarding symptoms may be an important factor in subtyping OCD.

References:
They were induced to breath-hold for as long as possible four probands with PD who have never had a panic attack and 25.2% control subjects had a PA after the test (p=0.023). There was no heart rate, anxiety levels or breath-hold time differences among the groups. In this breath hold challenge test PD patients were more sensitive to breath-hold than first-degree relatives and normal volunteers. Our data suggest there is no association between family history of PD and hyperreactivity to a breath-holding challenge test. Cognitive variables may be considered in this association as symptoms of a PA and apnea overlap.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the mechanisms involved in CO2 - provoked anxiety and its influence on the pathophysiology of PD.

Summary:
Our aim was to observe the induction of panic attacks (PA) symptoms by a breath-hold challenge test in panic disorder (PD) patients (DSM-IV), and their healthy first-degree relatives. We randomly selected 26 PD patients, 28 healthy first-degree relatives of probands with PD who have never had a panic attack and 25 normal volunteers with no family history of PD or mood disorder. They were induced to breath-hold for as long as possible four times with a two-minute interval between them. Anxiety scales were applied before and after the test. Using specific panic attack criteria, 46.1% (n=12) PD patients, 7.1% (n=2) first-degree relatives and 4.0% (n=1) control subjects had a PA after the test (p=0.023). There was no heart rate, anxiety levels or breath-hold time differences among the groups. In this breath hold challenge test PD patients were more sensitive to breath-hold than first-degree relatives and normal volunteers. Our data suggest there is no association between family history of PD and hyperreactivity to a breath-holding challenge test. Cognitive variables may be considered in this association as symptoms of a PA and apnea overlap.

References:

NR796 Thursday, May 22, 12:00 p.m.-2:00 p.m.
A Breath-Holding Test in Panic Disorder Patients
Isabella Nascimento, M.D., Department of Psychiatry, Federal University, Rio Janeiro, Rua Prof Hermes Lima 364/103, Rio De Janeiro, RJ 22795-065, Brazil; Antonio E. Nardi, M.D.; Alexandre M. Valenca, M.D., Fabiana L. Lopes, M.D., Marco A. Mezzasalma, M.D., Walter A. Zin, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the mechanisms involved in CO2 - provoked anxiety and its influence on the pathophysiology of PD.

Summary:
Our aim was to observe the induction of panic attacks (PA) symptoms by a breath-hold challenge test in panic disorder (PD) patients (DSM-IV) and their healthy first-degree relatives. We randomly selected 26 PD patients, 28 healthy first-degree relatives of probands with PD who have never had a panic attack and 25 normal volunteers with no family history of PD or mood disorder. They were induced to breath-hold for as long as possible four times with a two-minute interval between them. Anxiety scales were applied before and after the test. Using specific panic attack criteria, 46.1% (n=12) PD patients, 7.1% (n=2) first-degree relatives and 4.0% (n=1) control subjects had a PA after the test (p=0.023). There was no heart rate, anxiety levels or breath-hold time differences among the groups. In this breath hold challenge test PD patients were more sensitive to breath-hold than first-degree relatives and normal volunteers. Our data suggest there is no association between family history of PD and hyperreactivity to a breath-holding challenge test. Cognitive variables may be considered in this association as symptoms of a PA and apnea overlap.

References:

NR797 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Improvement in Physical Symptoms in Select Anxiety Disorders
Supported by Wyeth Research
Rajiv Mallick, Ph.D., Research, Wyeth, 500 Arcola Road, Collegeville, PA 19428; Bo Gao, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the often neglected but nevertheless important physical and somatic symptoms reported by patients with panic disorder and social anxiety disorder; understand how effective antidepressant therapy may help alleviate these symptoms.

Summary:
Objective: To characterize patient-reported functionality and quality of life in panic disorder and compare treatment with venlafaxine extended-release (VEN XR), paroxetine, or placebo.

Methods: In a multicenter, double-blind trial, patients with DSM-IV panic disorder were randomized to VEN XR (150 mg or 75 mg), paroxetine, or placebo treatment for 12 weeks (N=577). Functional impairment was measured using the work, social activities, and family life subscales of the Sheehan Disability Scale (SDS) and quality of life using the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q).

Results: At baseline, 42% of patients were "markedly" or "very severely" impaired in social activities, 33% in work, and 21% in family life. VEN XR 150 mg was associated with greater improvement versus placebo at the scheduled week 12 and the final on-therapy assessments on work (P=0.002 and P=0.003, respectively), social activities (P<0.001 and P<0.001, respectively), and

References:

NR798 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Quality of Life and Functionality in Panic Disorder Improve With Treatment
Supported by Wyeth Research
Rajiv Mallick, Ph.D., Research, Wyeth, 500 Arcola Road, Collegeville, PA 19428; Bo Gao, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that panic disorder is associated with impaired function and patient-perceived quality of life; describe how effective treatments have the potential to reduce not only frequency of panic attacks but also related disability and impaired quality of life.

Summary:
Objective: To compare the effectiveness of venlafaxine extended-release (VEN XR), paroxetine, or placebo in alleviating patient-reported physical symptoms in panic disorder (PD) and social anxiety disorder (SAD).

Methods: Data were pooled from two randomized, double-blind, placebo-controlled studies (including one also included a paroxetine control group) of VEN XR (75 mg, 150 mg, or flexible dosages) during 10–12 weeks of treatment of patients with DSM-IV PD (N=958). Outcomes included the physical health/activities and nine other subscales of the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q). Data were pooled from four randomized, double-blind, placebo-controlled studies (including two paroxetine-controlled studies) of flexible-dose VEN XR during 10-week treatment of patients with DSM-IV SAD (N=1,372). Outcomes included the physiological arousal subscale of the Social Phobia Inventory (SPIN) and the total SPIN.

Results: In PD, VEN XR and paroxetine were associated with greater improvement versus placebo on the physical health/activities subscale (P<0.0001 and P=0.0004, respectively), and on most other subscales (VEN XR 8/9; paroxetine 5/9). In SAD, improvement on the physiological arousal sub-scale and total SPIN score (all P<0.0001) was greater with VEN XR and paroxetine than with placebo.

Conclusions: VEN XR and paroxetine were associated with significant improvement in self-reported physical complaints in panic and SAD.
family life (P<0.001 and P<0.001, respectively), as well as significantly greater improvement, relative to placebo, at both assessments, on seven of 10 subscales of the Q-LES-Q. Similar, albeit weaker, differences were observed for VEN XR 75 mg and paroxetine in comparison with placebo.

Conclusions: VEN XR significantly improved functionality and quality of life in patients with panic disorder.

References:

NR799 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Clinical and Demographic Characteristic in Treatment-Resistant OCD FAPESP, Sao Paulo Brazil
Marcio A. Bernik, M.D., Department of Psychiatry, USP Medical School, Ambulatorio de Ansiedade HCFMUSP, Sao Paulo CX3671 01060-970, Brazil; Fabio M. Corregiari, M.D., Sergio B. Cabral, M.D., Maria C. Bravo

Educational Objectives:
At the conclusion of this session, the participant should be able to discuss clinical or demographic variables of patients with OCD possible related with SSRI resistance.

Summary:
Objective: Presenting clinical and demographic data of patients with obsessive-compulsive disorder (OCD) resistant to treatment with serotonin reuptake inhibitors (SRI).
Methods: Patients with OCD diagnosed by SCID-I/P, aged between 18 and 65 years of both genders, were accessed through a self-administered questionnaire and the Y-BOCS.
Results: Eleven patients were considered SRI resistant after 20% or smaller reductions on Y-BOCS scale scores after three trials with SRI in maximal doses for 12 weeks.
Demographic variables: Gender: 90.9% of men; Age: 34±8.4 years-old; Race: 90.9% Caucasian; 9.1% others; Marital status: 100% singles; occupational status: 72.8% unemployed, 18.1% employed; 9.1% retired.
Clinical variables: Age of onset: 16.9±6.8 years; type of onset: 88.9% insidious 11.1% abrupt; Clinical course: 72.7% episodic with periods of incomplete remission, 27.3% episodic with periods of complete remission.
Conclusions: (1) 90.9% of treatment-resistant patients are male, which contrasts with the reported similar prevalence in both genders in OCD. (2) 81.9% are not working and 100% are single, indicating social and occupational incapacitation in this sample.

References:
Summary:

**Objectives:** PTSD has been linked with increased health complaints and medical morbidity. There is increasing evidence that PTSD goes unrecognized in persons with severe mental illness. This study examined the impact of co-morbid PTSD on self-rated health and medical morbidity in patients with a primary psychiatric disorder.

**Methods:** Data were collected from a sample of male veterans (N=164) with a primary diagnosis of schizophrenia or schizoaffective disorder, hospitalized on a VAMC psychiatric unit. PTSD diagnosis was based upon the PTSD Check List. Self-rated health and number of physician diagnosed medical conditions were collected via self-report. Analyses compared patients with co-morbid PTSD to those without PTSD.

**Results:** Eighty-one patients (49%) met criteria for PTSD, however, only 9% had a diagnosis of PTSD in their medical chart. Patients with co-morbid PTSD did not differ from those without PTSD in age, race, marital status, or severity of psychotic symptoms. Co-morbid PTSD was associated with poorer general and mental health. Results from adjusted poisson regression analyses indicated that co-morbid PTSD was associated with increased number of medical conditions.

**Conclusions:** PTSD is prevalent among VA patients with primary psychiatric disorders. The presence of co-morbid PTSD is associated with both decreased self-rated health and increased number of co-morbid medical conditions.

**References:**

**NR802 Thursday, May 22, 12:00 p.m.-2:00 p.m.**

**Dissociative Experiences in OCD and Trichotillomania: Role of Childhood Trauma**

Christine Lochner, M.A., Department of Psychiatry, University of Stellenbosch, P.O. Box 19063, Tyberberg, South Africa; Soraya Seedat, M.D., Dan J. Stein, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should have some understanding of the link between childhood trauma and dissociation in OCD and trichotillomania

**Summary:**

**Objective:** A link between dissociation proneness in adulthood and self-reports of childhood traumatic experiences has been documented. In addition, several studies have provided evidence for a definitive relationship between trauma and dissociative experiences in various psychiatric disorders, including posttraumatic stress, borderline personality, dissociative identity and eating disorder. Based on the relative paucity of data on the link between dissociation and trauma in obsessive-compulsive disorder (OCD) and trichotillomania (TTM), this study examined the association, if any, between trauma and dissociative experiences (DE) in these two groups.

**Method:** 110 OCD and 32 TTM patients were compared with respect to frequency of DE, with participants grouped on the Dissociative Experiences Scale into high (mean DES score >30) or low (mean DES score <30) dissociators.

**Results:** 16.4% of OCD patients and 18.8% of TTM patients were classified as ‘high’ dissociators. For both patients with OCD and TTM, significant positive correlations were found between mean DES scores and mean CTQ sub-scores of emotional abuse, physical abuse, sexual abuse and physical neglect. Stepwise multiple linear regression analysis showed that for OCD patients, ‘physical neglect’ was an independent predictor of variance in DES scores (R square = .135; p<.001) while for TTM patients, ‘emotional abuse’ accounted for 37.5% of the variance in the DES (R square = .376; p<.001).

**Conclusion:** High dissociative symptomatology may be present in a substantial proportion of patients with OCD and TTM. This study demonstrates a link between childhood trauma and DE in these two groups. Further work is needed to determine the impact of trauma and associated DE on treatment outcome in these disorders.

**References:**

**NR803 Thursday, May 22, 12:00 p.m.-2:00 p.m.**

**Nocturnal and Daytime Panic Attacks: A Phenomenological Comparative Study**

Fabiana L. Lopes, M.D., Institute of Psychiatry, University FED Rio Jan, Min Octavio Kelly 467, AP1204-B, Niterol, RJ 24220-300, Brazil; Antonio E. Nardi, M.D., Isabella Nascimento, M.D., Alexandre M. Valenca, M.D., Marco A. Mezzasalma, M.D., Walter A. Zin, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to compare the phenomenology of nocturnal and daytime panic attacks in relation to respiratory symptoms, cognition and personality traits.

**Summary:**

**Background:** Nocturnal panic attacks have been linked to a greater severity of the panic disorder (PD).

**Methods:** We performed a cross-sectional retrospective study at the baseline and a prospective longitudinal follow-up of the 57 PD patients. The sample was divided into nocturnal and daytime panic attacks (NDPA, DPA). They were compared on measures of PD severity, prominent respiratory symptoms, comorbidities response to the treatment, neuroticism, and cognition (Brown ADD Scale).

**Results:** The final sample consisted in 55.9% NDPA (n=33) and 40.5% DPA (n=24). There were no demographic differences between the groups (p=0.317) and both groups exhibited the same pattern of respiratory symptoms (57.8% NDPA, 50.3% DPA; p=0.954). There were no group differences (NDPA vs DPA) in terms of current comorbid diagnoses (p=0.396); scores of the Panic Disorder Severity Scale at the baseline (mean:20.8 vs 19.8; p=0.351) and at the follow-up (mean:9.181 vs 6.625; p=0.481); neuroticism (mean:17.0 vs 18.7;p=0.094); and attention deficit (mean:42.2 vs 48.0; p=0.527). 25% DPA patients underwent the cognitive behavior therapy, compared with 12.5% DPA patients.

**Conclusion:** The presence of nocturnal panic attacks do not represent a more severe form of PD.

**References:**

NR804 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Hyperactivity to Respiratory Challenge Tests in Panic Disorder
Alexandre M. Valenca, M.D., Department of Psychiatry, University Feder Rio Janeiro, Min Otavio Kelly 467 AP 1204 B, Niteroi, RJ 24220-300, Brazil; Antonio E. Nardi, M.D., Marco A. Mezzasalma, M.D., Fabiana L. Lopes, M.D., Walter A. Zin, M.D., Isabella Nascimento, M.D., Marcio V. Versiani, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to recognize that respiratory panic disorder subtype may be the most sensitive than any other group to a respiratory challenge test.

Summary:
- Background: Respiratory tests have been fruitful in generating hypotheses about panic disorder.
- Aim: to compare the clinical features of hyperventilations breath-holding induced panic attacks in panic disorder patients-DSM-IV.
- Methods: We examined 70 panic disorder patients previously submitted to a hyperventilation challenge test (HPA) and 25 panic disorder patients submitted to a breath-holding test (BHPA). The HPA were induced to hyperventilate (30 breaths/min) for four minutes, and the BHPA were induced to hold their breath for as long as possible four times with a two-minute interval between them. Anxiety scales were applied before and after the test.
- Results: The HPA and the BHPA group had a similar (p=0.562) presence of respiratory symptoms during a panic attack. The criteria for respiratory panic disorder subtype were fulfilled in 41 (58.6%) HPA patients and in 15 (60.0%) BHPA. Patients with four or more respiratory symptoms had significant more situational panic attacks than did the remaining patients (p=0.014).
- Conclusion: Our data suggest that there is an association between respiratory panic disorder subtype and hyperreactivity to respiratory challenge tests—hyperventilation and breath-holding.

References:

NR805 Thursday, May 22, 12:00 p.m.-2:00 p.m.
9/11 Disaster: Impact on GAD Research Population Supported by Pfizer Inc.
Rebecca G. Knapp, Ph.D., Biometry and Epid Department, Medical University of South Carolina, 171 Ashley Avenue, PO Box 250835, Charleston, SC 29425; Karl Rickels, M.D., Moira A. Rynn, M.D., Olga Brawman-Mintzer, M.D., Karen L. Wehls, M.D., Ram K. Shrivastava, M.D., Harvey A. Tilker, M.D., Angelo Sambunaris, M.D., William M. Patterson, M.D., Mark H. Rapaport, M.D., Naresh Emanuel, M.D., Renee Hebert, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to describe the effects of the 9/11 disaster on the conduct of anxiety clinical trials conducted in subjects immediately following the disaster.

Summary:
- Objective: Differences in baseline characteristics and treatment outcome between generalized anxiety disorder (GAD) patients participating in clinical trial before and after September 11, 2001, were examined.
- Methods: DSM-IV GAD subjects in a 10-week placebo-controlled sertraline treatment trial were classified post hoc into those completing prior to 9/11 (n=237) and those entering after 9/11 (n=75). Baseline characteristics and outcome variables were compared using standard statistical analyses.
- Results: Although no differences in age, education, ethnicity, gender, GAD duration, and completion rates were noted, significantly higher proportion after 9/11 were divorced (26.7% vs. 13.5%) and had history of psychiatric disorders (34.6% vs. 23.5%), particularly major depression (24% vs. 15.8%). Subjects after 9/11 had significantly higher baseline anxiety and depression (MADRS 12.3 vs 13.6; HAD 21.1 vs 23.0), and lower quality of life scores (Q-LES-Q 64.1 vs 61.3). Change in HAM-A total scores was significantly lower after 9/11 due primarily to increased placebo effect. Finally, prior to 9/11, subjects experienced more rapid decline in anxiety symptoms during the first week of treatment (30% vs. 16% with ≥20% reduction in HAM-A scores).
- Conclusion: The effects of a major national trauma are far-reaching and should be considered when examining clinical research studies conducted shortly following the 9/11 disaster.

References:

NR806 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Escitalopram 10 mg/day is Effective in the Treatment of GAD Supported by Forest Laboratories, Inc.
Wayne K. Goodman, M.D., Department of Psychiatry, Florida University, 100 Newell Drive, Suite L4100, Gainesville, FL 32610-0256; Anjana Bose, Ph.D., Qin Wang, Ph.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to evaluate the efficacy and tolerability of escitalopram in the treatment of generalized anxiety disorder.

Summary:
- Introduction: Three recently conducted randomized, double-blind, placebo-controlled trials of escitalopram in generalized anxiety disorder (GAD) patients were all positive. Results using data pooled across the three studies are presented below.
- Methods: All trials were of virtually identical design. The dose of escitalopram was fixed at 10 mg/day for the first four weeks, and could be increased to 20 mg/day after four weeks. The primary efficacy variable was HAMA total score. The HAMA psychic anxiety subscale, and the CGI-I and CGI-S were secondary efficacy variables.
- Results: At baseline, patients in the placebo group (N=419) and the escitalopram group (N=421) were demographically indistinguishable, with mean HAMA scores of approximately 23, indicative of moderate to severe GAD. By visit LOCF and OC analyses of the primary and secondary efficacy variables revealed significantly greater improvement (p<0.05) in the escitalopram group relative to placebo beginning at the end of week 1 and continuing through
the end of week 4 (while the escitalopram dose was fixed at 10 mg/day) and through study endpoint (week 8).

**Conclusion:** Escitalopram 10 mg/day is effective and well tolerated in the treatment of GAD.

**References:**


**RR807 Thursday, May 22, 12:00 p.m.-2:00 p.m.**

**Risperidone Prevents and Restores Haloperidol-Induced Oxidative Stress-Mediated Brain Injury Supported by Janssen Pharmaceutical Products, L.P.**

Sahebarao Mahadik, Ph.D., Department of Psychiatry, Medical College of Georgia, 1515 Pope Avenue, Augusta, GA 30912; Vinay Parikh, Ph.D., Mohammed Khan, Ph.D., Pinky Salat, M.S., Abhishek Kalla, B.S., Peter F. Buckley, M.D.

**Educational Objectives:**

- At the conclusion of this session, the participant should be able to demonstrate the effects of risperidone on oxidative stress-mediated brain injury induced by a typical antipsychotic (haloperidol).

**Summary:**

**Objective:** We investigated the effects of risperidone on the indices of brain oxidative stress (antioxidant enzymes manganese-superoxide dismutase [MnSOD], copper-zinc superoxide dismutase [Cu/Zn-SOD]) and membrane damage (lipid peroxidation and hydroxyalkenals [HAE]) associated with haloperidol in rats.

**Methods:** For 45 days, adult Wistar rats (250–300 gm) received vehicle only (controls); 2 mg/kg/day of haloperidol followed by vehicle; 2.5 mg/kg/day of risperidone followed by vehicle; haloperidol followed by risperidone; or risperidone followed by haloperidol. Levels of antioxidant enzymes were determined by enzymatic activities (units/mg of protein) and immunohistochemical methods.

**Results:** Compared with controls, haloperidol but not risperidone significantly (P<0.01) reduced the levels of antioxidant enzymes (Cu/Zn-SOD from 6.6 to 3.1 and MnSOD from 10.3 to 6.1) and increased HAE levels (from 0.21 to 0.66 nmol/mg of protein). Risperidone significantly (P<0.01) restored the haloperidol-induced reductions in Cu/Zn-SOD (from 3.1 to 4.5) and MnSOD (from 6.1 to 7.6). Risperidone also tended to prevent the haloperidol-induced membrane damage (lipid peroxidation and hydroxyalkenals [HAE]). Immunohistochemical examination of cortical areas, striatum, and basal forebrain supported the changes in enzymatic activities.

**Discussion:** These findings provide a molecular mechanism for the neuroprotective actions of risperidone in preventing oxidative stress-mediated membrane damage.

**References:**


**RR808 Thursday, May 22, 12:00 p.m.-2:00 p.m.**

**Mirtazapine Treatment for Adult OCD Supported by Organon Inc.**

Lorin M. Koran, M.D., Department of Psychiatry, Stanford University, 401 Quarry Road, OCD Clinic #2363, Stanford, CA 94305-5721; Helen W. Chuong, M.S.

**Educational Objectives:**

- At the conclusion of this session, the participant should be able to discuss the potential use of mirtazapine to treat OCD.

**Summary:**

**Introduction:** From 20% to 40% of OCD patients fail to respond satisfactorily after SSRI treatment trials. A small, open-label trial suggested that mirtazapine, which increases both NE and 5-HT release, is effective in treatment-naïve OCD patients. We conducted a larger trial to investigate this possibility.

**Methods:** We enrolled 14 treatment-naïve, adult outpatients with DSM-IV-defined OCD of at least one year’s duration and a minimum Y-BOCS score of 21 in a (continuing) 12-week, open-label trial, followed by an eight-week randomized, double-blind, placebo-controlled phase to identify true drug response. Mirtazapine was begun at 30 mg/day and increased weekly by 15 mg/day to 60 mg/day as tolerated.

**Results:** The 14 subjects (8 men and 6 women) had a mean baseline Y-BOCS score of 27.9 (SD 3.3) and mean MADRS score of 11.0 (SD 8.8). Four patients discontinued for adverse events. After 12 weeks, mean Y-BOCS score (LOCF) was 22.2 (SD 6.3) (paired t = 2.68, p=0.019), mean MADRS was 7.2 (SD 8.2), and seven subjects (50%) were responders (Y-BOCS decrease ≥ 25%). Three lost the response in the double-blind phase.

**Conclusions:** At the study’s present stage, mirtazapine appears as effective as SSRIs for treatment-naïve OCD patients. Further studies are indicated.

**References:**


**RR809 Thursday, May 22, 12:00 p.m.-2:00 p.m.**

**Tiagabine for the Treatment of Anxiety and Comorbid Pain**

Daniel M. Gruener, M.D., 1128 Old York Road, Abington, PA 19001

**Educational Objectives:**

- At the conclusion of the presentation, the participant should recognize the potential use of tiagabine for treatment of anxiety and comorbid pain.

**Summary:**

**Objective:** Gamma-aminobutyric acid (GABA), the predominant inhibitory neurotransmitter, plays a role in anxiety and pain. Tiagabine, a selective GABA reuptake inhibitor (SGRI), enhances normal GABA tone and has been shown to reduce anxiety and improve pain. The effectiveness of tiagabine was evaluated in patients with anxiety or anxiety comorbid with pain.

**Method:** In this case study, 20 consecutive outpatients with anxiety (9 with comorbid pain) who were stabilized on current medications, but still symptomatic received tiagabine. Tiagabine was initiated at 2 mg nightly and titrated by 2 or 4 mg every 3–4 days until an optimal response was achieved (maximum dosage ≤16 mg bid). Efficacy assessments were the Hamilton Rating
ties could also be seen using uncorrected P values < 0.001 in left
the left parahippocampal gyrus in patients with PD compared to
healthy subjects (corrected P value < 0.05). Additional abnormali-
malisation.

Conclusions: These preliminary results suggest that the SGRI
tiagabine may be an effective agent for anxiety and comorbid pain.

References:
1. Meldrum BS: Basic mechanisms of Gabitril (tiagabine) and
future potential developments. Epilepsia 1999; 40(Suppl.
2. Zwanzger P: Tiagabine improves panic and agoraphobia in

NR810 Thursday, May 22, 12:00 p.m.–2:00 p.m.
Parahippocampal Gray Matter Decrease in Panic: A
Voxel-Based Morphometric Study
Guillem Massana, M.D., Psychiatry Department, Corporacio
Clinic, Villarreal 170, Barcelona 08036, Spain; Josep M. Serra-
Grabulosa, Ph.D., Pilar Salgado-Pineda, M.S., Cristobal Gasto,
Dr., Carme Junque, Ph.D., Joan Massana, M.D., Josep M.
Mercader
Educational Objectives:
At the conclusion of this session, the participant should be able
to have new insights in brain circuitry of panic disorder.

Summary:
Objective: To examine possible cerebral gray matter abnormali-
es in Panic Disorder (PD) patients.
Method: The Voxel-based morphometry approach was applied
to 18 PD outpatients and 18 healthy comparison subjects. The
3D MRI data sets were analyzed using SPM99 software, and the
T1-weighted images were transformed into standard MNI (Mon-
treal Neurological Institute) space using an automated spatial nor-
malisation.

Results: We found a decrease in the gray matter density of the
left parahippocampal gyrus in patients with PD compared to
healthy subjects (corrected P value < 0.05). Additional abnormali-
ties could also be seen using uncorrected P values < 0.001 in left
cuneus, right middle temporal gyrus, right inferior temporal gyrus,
hypothalamus, right parahippocampal gyrus, right thalamus, left
and right cerebellum, left middle temporal gyrus and left angular
gyrus.

Conclusions: Our results are relevant in view of previous neuroi-
maging findings in PD and provide further support for the involve-
ment of the parahippocampal area in the pathophysiology of PD.

References:
1. Ashburner J, Friston K: “Voxel-based Morphometry. The Meth-
2. Coplan JD, Lydiard RB: “The Neurobiology of Anxiety Disor-
ders. Brain Circuits in Panic Disorder.” Biol Psychiatry 1998;
44:1264–1276.

NR811 Thursday, May 22, 12:00 p.m.–2:00 p.m.
Reduced Amygdalar Volume in Panic Disorder: A
Volumetric Magnetic Resonance Study
Guillem Massana, M.D., Psychiatry Department, Corporacio
Clinic, Villarreal 170, Barcelona 08036, Spain; Josep M. Serra-
Grabulosa, Ph.D., Pilar Salgado-Pineda, M.S., Cristobal Gasto,
M.D., Carme Junque, Ph.D., Joan Massana, M.D., Josep M.
Mercader, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able
to have new insights in brain circuitry of panic disorder.

Summary:
Objective: It has been suggested that the pathophysiology of
panic disorder (PD) may involve abnormalities in several brain
structures, including the amygdala. To date, however, no study
has used quantitative structural neuroimaging techniques to ex-
mare amygdalar anatomy in this disorder.
Method: Volumetric magnetic resonance imaging (MRI) studies
of the amygdalas, hippocampi and the temporal lobes, were con-
ducted in 12 drug-free, symptomatic PD patients (6 females
and 6 males), and 12 case-matched healthy comparison subjects.
Volumetric MRI data were normalized for brain size.

Results: PD patients were found to have smaller left-sided and
right-sided amygdalar volumes than controls. No differences
were found in either hippocampi or temporal lobes.

Conclusions: These findings provide new evidence of changes
in amygdalar structure in PD and warrant further anatomical and
MRI brain studies of patients with this disorder.

References:
1. Gorman JM, Kent JM, Sullivan GM, Coplan JD: “Neuroanat-
omy Hypothesis of Panic Disorder, Revised.” Am J Psychiatry
York, 1996.

NR812 Thursday, May 22, 12:00 p.m.–2:00 p.m.
Pregabalin Improves Patient-Reported Work
Productivity in Patients With GAD
Supported by Pfizer Inc.
Thomas N. Taylor, Outcomes Research, Pfizer Inc., 2800
Plymouth Road, Ann Arbor, MI 48105; Douglas E. Feltner,
M.D., James Goodrich, M.S., Jerri Brock, M.S., Atul C. Pande,
M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able
to understand the reported effects of treatment with pregabalin on
patient-reported work productivity in a placebo-controlled, double-
blind trial among patients with GAD.

Summary:
Objective: Previous reports documented the efficacy of prega-
balin in the treatment of patients with generalized anxiety disorder
(GAD). This report presents the results of analysis of the Endicott
Work Productivity Scale (EWPS); a secondary endpoint.
Method: After completing a one-week screening phase, 465
patients with generalized anxiety disorder were randomized to
four weeks of double-blind treatment with pregabalin 300 mg/day,
pregabalin 450 mg/day, pregabalin 600 mg/day, alprazolam 1.5
mg/day, or placebo, all dosed TID. Patient-reported work produc-
tivity was assessed at baseline and week 4 using the EWPS, a
25-item, self-administered questionnaire. Patients were required
to have worked the week prior to completing the EWPS.

Results: Patients treated with pregabalin 600 mg/day reported
a significantly greater improvement in self-reported work produc-
tivity scores than patients receiving either placebo (p<0.02) or
alprazolam (p<0.02). Patients treated with other doses of prega-
balin also reported improvements in work productivity, though
these improvements were not significantly different from either
placebo or alprazolam. Patients treated with alprazolam reported
EWPS change scores that were not significantly different from placebo (p=0.99).

Conclusions: Patients treated with pregabalin 600 mg/day reported improved work productivity compared with patients treated with placebo or alprazolam 1.5 mg/day.

References:

NR813 Thursday, May 22, 12:00 p.m.-2:00 p.m.
The Development and the Effects of Experiential Cognitive Therapy for the Treatment of Panic Disorder With Agoraphobia
Young-Hee Choi, M.D., Psychiatry, Inge University, #85 Juv-Dong, Joong-Ku, Seoul 100-032, South Korea;

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the efficacy of brief cognitive-behavior therapy for panic disorder with agoraphobia and the rationale behind the exposure with virtual reality scene.

Summary:
In order to reduce the duration of treatment, the author developed the treatment protocol called Experiential Cognitive Therapy (ECT). This study had two objectives. The first was to introduce the process of developing ECT, which originally integrated traditional cognitive-behavior therapy with virtual reality exposure for the treatment of panic disorder with agoraphobia. The second objective was to test the efficacy of short-term (four sessions) ECT compared with traditional 12 sessions of Panic Control Program (PCP) for the treatment of panic disorder with agoraphobia. Forty patients who were diagnosed with panic disorder with agoraphobia by the diagnostic criteria of DSM-IV were randomly assigned to ECT and PCP groups of 20 patients each. Both groups had no significant difference in the demographic data. The treatment effects were measured with various self-report screening tools. Also, the author assessed the panic attack frequency, the clinical severity rating (CSR), the end-state functioning (ES), the success rate of stopping or reducing medication at post-treatment, and six-month follow-up. In all ratings, both the ECT and PCP group showed significant improvement after treatment compared with the pre-treatment scores and there were no significant differences between two treatments at post-treatment and six month follow-up. Four sessions of ECT showed the similar efficacy with 12 sessions of traditional PCP. ECT, which was using virtual reality exposure, proved to be an effective treatment modality for panic disorder with agoraphobia. This study might be the first pilot study to apply short-term cognitive-behavior therapy combined with virtual reality exposure to the treatment of panic disorder with agoraphobia.

References:

NR814 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Duration of Pharmacotherapy In Medicaid Recipients With PTSD Supported by Pfizer Inc.
M. Blakely Fox, Ph.D., Department of Management, Millsaps College, 1701 N. State Street, Jackson, MS 38210; David Harrison, M.A., Brain S. Nightengale, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that a significant proportion of Medicaid recipients with PTSD do not receive adequate courses of pharmacotherapy in accordance with recognized guidelines.

Summary:
Background: Consensus guidelines recommend that patients with PTSD receiving SSRIs be treated at adequate doses for ≥180 days.

Objective: To examine treatment duration in Medicaid recipients with PTSD.

Methods: Medical and pharmacy claims spanning from 1995–1998 from a state Medicaid program were analyzed. Patients were included if they received at least one prescription for fluoxetine, paroxetine or sertraline during the study timeframe, had an initial diagnosis of PTSD and were eligible for benefits for >180 days prior to and 360 days following the date of initiation of pharmacotherapy. Patients were excluded if they had a concomitant diagnosis of bipolar disorder or schizophrenia.

The proportion of patients completing ≥180 days of pharmacotherapy was determined using non-parametric survival methods. A logit model was used to evaluate the impact of age, gender, AFDC status and comorbidities.

Results: Of the 2,700 patients included in the analysis, 28.3% (std. error=0.89%) received medication for ≥180 days. AFDC and pregnant recipients were less likely to receive medication for 180 days (p=0.041 and 0.003 respectively) while patients with comorbid endocrine diagnoses were more likely to receive medication for 180 days (p=0.001).

Conclusions: A large proportion of Medicaid recipients with PTSD are not receiving adequate courses of pharmacotherapy.

References:
Summary:
Background: Consensus guidelines recommend that patients with PTSD receiving SSRIs be treated at adequate doses for ≥180 days.

Objective: To evaluate differences in treatment duration across agents in Medicaid recipients with PTSD.

Methods: Medical and pharmacy claims from 1995–1998 were analyzed. Patients were included if they received at least one prescription for fluoxetine, paroxetine or sertraline during the time-frame, had an initial diagnosis of PTSD and were eligible for benefits for >180 days prior and 360 days following the initiation of pharmacotherapy. Patients were excluded if they had a diagnosis of bipolar disorder or schizophrenia.

The proportion of patients completing ≥180 days of pharmacotherapy was compared using a Cox Proportional Hazard model. Covariates included age, gender, AFDC status and comorbidities.

Results: Patients in the sertraline (n=984) and fluoxetine (n=840) cohorts were significantly more likely to complete ≥180 days of pharmacotherapy compared to paroxetine (n=967) (p=0.011 and 0.017 respectively). AFDC and pregnant patients were less likely to receive medication for 180 days (p<0.05) while patients with comorbid endocrine diagnoses were more likely to receive medication for 180 days (p=0.003).

Conclusions: Medicaid recipients with PTSD receiving paroxetine were less likely to receive an adequate course of pharmacotherapy compared to sertraline and fluoxetine.

References:

NR817 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Bupropion Tolerability in Depressed Combat Veterans With PTSD
Neal A. Kline, M.D., Psychiatry, University of California San Diego, 8810 Rio San Diego Drive VA Clinic, San Diego, CA 92108;

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize that in the treatment of PTSD and comorbid depression, prescribing bupropion (immediate-release) may be a tolerable and efficacious intervention, though non-serotonergic bupropion is a noradrenergic/dopaminergic agent, while the two FDA-approved products for PTSD, to date, are both serotonergic psychotropes.

Summary:
Background: The pharmacotherapy of posttraumatic stress disorder (PTSD) has drawn broadly from the spectrum of antidepressants, mood stabilizers, anticonvulsants, and anxiolytics. Due to side effects such as sexual dysfunction, agitation, or over-sedation—with tricyclic antidepressants, SSRIs, nefazodone, and venlafaxine—we changed to bupropion immediate-release (IR) for 17 depressed male Vietnam combat veterans with PTSD, at our DVA PTSD outpatient clinic.

Method: Open-label bupropion IR was initially prescribed at 75 mg/day, with upward titration at two-week intervals, over 12 weeks, to a maximum of 300 mg/day, in divided doses, with final doses determined by considerations of tolerability and efficacy, utilizing the Clinical Global Impression Scale for Improvement (CGI-I).

Results: Within the first two weeks, three veterans (18% of 17) dropped out due to medication intolerability (psychomotor agitation), with CGI-Is of six (much worse). CGI-Is at week 12, for the 14 completers, clustered as follows: one (7% of 14) had a CGI-I of 1 (very much improved); three (21% of 14) had a CGI-I of 2 (much improved); seven (50%) a CGI-I of 3 (minimally improved); and three (21%) a CGI-I of 4 (unchanged).

Conclusion: With three (18% of 17) veterans finding bupropion intolerable (CGI-Is of 6), and four (25% of 14) completers finding bupropion IR efficacious (CGIs of 1 or 2), bupropion IR may warrant further study for PTSD and comorbid depression, using controlled, double-blind designs.

References:


NR816 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Tiagabine Treatment of Symptoms of Rage and Anxiety
Supported by Cephalon, Inc.
Daniel A. Hoffman, M.D., Neurotherapy Clinic, 8200 E. Belleview Avenue, Suite 600E, Greenwood Village, CO 80111-2808;

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize the potential of tiagabine for the treatment of symptoms of anxiety and rage.

Summary:
Objective: Rage is a symptom of several psychiatric disorders, treatment of which presents clinical challenges. The predominant inhibitory neurotransmitter, y-aminobutyric acid (GABA), has been implicated in treating anxiety and may play a role in the control of rage. Tiagabine the selective GABA reuptake inhibitor (SGRI), enhances normal GABA tone and has shown promise in the treatment of anxiety disorders. Tiagabine was evaluated in patients with symptoms of rage and anxiety.

Method: A retrospective chart review of 36 patients with anxiety, irritability, anger, or rage associated with one or more of the following disorders: bipolar, irritability, explosive, panic, posttraumatic stress disorder, major depression, or substance abuse. Patients, previously stabilized on medications yet still symptomatic, received 2 mg bid tiagabine and were titrated individually (maximum dosage ≤ 16 mg bid). The physician rated overall clinical response as excellent, good, minimal, or none.

Results: Twenty-eight patients were eligible for analysis (8 lost to follow-up/noncompliance). Tiagabine was effective in decreasing or eliminating symptoms of anxiety, irritability, anger, or rage in 20 patients (treatment duration range: 2–52 weeks). Tiagabine dosage

References:

NR818 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Tiagabine Treatment of GAD
Supported by Cephalon Inc.
Laszlo A. Papp, M.D., Psychiatry, Hillside Hospital, 75-59 263rd Street, Glen Oaks, NY 11004; Susan Ray, M.A.

Educational Objectives:
At the conclusion of this session, the participant should recognize the therapeutic potential of the SGRI tiagabine for the treatment of GAD.

Summary:
Objective: Tiagabine, a selective GABA reuptake inhibitor (SGRI), enhances normal GABA tone and reduced anxiety and improved sleep quality in preliminary reports. This study examined the benefits of tiagabine in patients with generalized anxiety disorder (GAD).

Method: Patients with DSM-IV GAD received open-label tiagabine for eight weeks; 2 mg bid during week 1, increased for optimum response by 2 mg/3 days to a maximum of 16 mg/day (bid dosing). Assessments included the Hamilton Rating Scale for Anxiety (HAM-A) and Pittsburgh Sleep Quality Index (PSQI). Last-observation-carried-forward methodology was employed.

Results: Eighteen patients have entered the eight-week study to date. Mean tiagabine dose was approximately 10 mg/day (range: 4–16 mg/day). Significant improvement in anxiety symptoms were observed (mean HAM-A total score±SEM: baseline, 28.1±1.4 vs. endpoint, 16.4±1.8; P<0.001). Sleep quality also improved significantly (PSQI: baseline, 10.6±0.98 vs. endpoint, 7.8±0.85; P<0.05). Symptoms improved within the first two weeks of treatment. Among the 18 patients exposed to tiagabine, the most commonly reported adverse events were asthenia, somnolence, and inability to concentrate. Four patients discontinued due to adverse events. Full dataset from the ongoing study will be presented.

Conclusion: These findings suggest that the SGRI tiagabine may be a therapeutic option for patients with anxiety.

References:

NR819 Thursday, May 22, 12:00 p.m.-2:00 p.m.
GAD: Gender Differences in Clinical Presentation and Response to Sertraline
Supported by Pfizer Inc.
Meir Steiner, M.D., Department of Psychiatry, MC Master University, 50 Charlton Avenue East, Hamilton, ON L8N 4A6, Canada; Christer Algulander, M.D., Arun V. Ravindran, M.D., Rana Fayyad, Ph.D., Carol Austin, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should have an improved knowledge of gender-related differences in the clinical presentation of generalized anxiety disorder, as well as a better understanding of the influence of gender on treatment response.

Summary:
Objective: To evaluate gender differences in GAD and response to sertraline treatment.

Methods: Outpatients with DSM-IV GAD were randomized to 12 weeks of double-blind treatment with placebo (N=188; female, 51%) or flexible doses (50–150 mg) of sertraline (N=182; female, 59%). Outcomes included the HAM-A and the CGI-Improvement scale (CGI-I ≥2 were responders).

Results: Clinical presentation of GAD was very similar in men and women, respectively, in terms of the severity of the HAM-A psychic anxiety factor (13.7 ± 2.8 vs. 13.6 ± 2.7), the somatic anxiety factor (10.6 ± 3.2 vs. 11.5 ± 3.3), and severity of concomitant depression symptoms as measured by the MADRS (10.8 ± 3.0 vs. 10.8 ± 3.2). Treatment with sertraline resulted in higher CGI-I responder rates compared to placebo from week 4 (males: 39% vs. 18%, p < 0.003; females: 33% vs. 21%, p = 0.054), through LOCF-endpoint at week 12 (males: 64% vs. 40%, p < 0.003; females: 62% vs. 34%, p < 0.001). The influence of gender on other aspects of treatment response will be presented. Overall sertraline was well tolerated.

Conclusion: Sertraline was an effective and well-tolerated treatment for GAD in both men and women.

References:

NR821 Thursday, May 22, 12:00 p.m.—2:00 p.m.
Escitalopram Treatment of GAD: A Double-Blind, Placebo-Controlled, Flexible-Dose Study
Supported by Forest Laboratories, Inc., and Integrated Therapeutics, Inc.
Jonathan R. T. Davidson, M.D., Department of Psychiatry, Duke University Medical Center South, Trent Drive, Room 4082B, Box 3812, Durham, NC 27710; Anjana Bose, Ph.D., Hongie Zheng, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the efficacy of escitalopram in generalized anxiety disorder.

Summary:
Objective: This study was designed to evaluate the efficacy and tolerability of escitalopram in the treatment of generalized anxiety disorder (GAD).
Method: Outpatients = 18 years meeting DSM-IV criteria for GAD with baseline HAMA scores, 18 were randomly assigned to double-blind treatment with escitalopram (10–20 mg/day) or placebo for eight weeks, following a one-week, single-blind, placebo lead-in period. The primary efficacy variable was mean change from baseline in total HAMA score at week 8.

Results: A total of 315 patients received treatment with escitalopram (N=158) or placebo (N=157). The escitalopram group showed statistically significant, and clinically relevant, greater improvement at endpoint compared with placebo in all prospectively defined efficacy parameters. Mean changes from baseline to week 8 on the HAMA total score using a LOCF approach were −11.3 for escitalopram and −7.4 for placebo (p<0.001). Treatment with escitalopram was well tolerated, with low rates of reported adverse events and an incidence of discontinuation due to adverse events not statistically different from placebo (8.9% vs. 5.1%; p=0.27).

Conclusion: Escitalopram is effective, safe, and well tolerated in the treatment of patients with GAD.

References:

NR823 Thursday, May 22, 12:00 p.m.—2:00 p.m.
Sertraline in GAD: HAM-A Item and Factor Analyses Supported by Pfizer Inc.
Alv A. Dahl, M.D., Department of Psychiatry, Aker University Hospital, Sognsvannsvein 21, Oslo N-0320, Norway; Arun V. Ravindran, M.D., Christer Allgulander, M.D., Rana Fayyad, Ph.D., Carol Austin, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should have an improved knowledge of the psychic and somatic symptoms that contribute to the clinical picture of GAD, and their differential response to sertraline treatment.

Summary:
Objective: To evaluate the differential efficacy of sertraline in treating GAD symptoms as measured by specific HAM-A factors and items.
Method: Outpatients with DSM-IV GAD were randomized to 12 weeks of double-blind treatment with placebo (N=188; female, 51%) or flexible-dose sertraline (50–150 mg) (N=182; female, 59%). The Hamilton Anxiety Rating Scale (HAM-A) was the primary efficacy parameter.

Results: Treatment with sertraline resulted in significantly greater LOCF-endpoint improvement than placebo on both the HAM-A psychic (−6.7 ± 0.4 vs. −4.1 ± 0.4; p < 0.0001) and somatic factor (−5.0 ± 0.3 vs. −3.9 ± 0.3; p < 0.02). Significant separation from placebo was seen from week 4 on the psychic factor, and at weeks 4 and 12 for the somatic factor. At week 12 (LOCF) there was greater reduction in the psychic (50%) vs. the somatic factor (45%) in the sertraline group. All seven items of the HAM-A psychic factor were significantly more improved on
sertraline vs. placebo, in comparison to three of seven items of the somatic factor. Effect sizes for the psychic and somatic factors were 0.54 and 0.26, respectively.

Conclusion: Sertraline treatment resulted in significant improvement in both the HAM-A psychic and somatic symptom clusters in GAD.

References:

NR824 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Efficacy of Sertraline in PTSD After Interpersonal Trauma or Childhood Abuse
Supported by Pfizer Inc.

Dan J. Stein, M.D., Department of Psychiatry, University of Stellenbosch, P.O. Box 19063, Tygerberg, South Africa; Bessel A. Van Der Kolk, M.D., Cathryn M. Clary, M.D., Rana Fayyad, Ph.D., Carol Austin, M.D.

Educational Objectives:
At the conclusion of this presentation, the participant should be able to understand the impact of the index trauma on the clinical presentation in PTSD patients, and understand that sertraline is a useful treatment option in PTSD, irrespective of whether the index trauma involves interpersonal trauma or childhood abuse.

Summary:
Introduction: Posttraumatic stress disorder (PTSD) occurs after a range of different traumas, including interpersonal trauma (physical/sexual assault) and childhood abuse. There is evidence that the nature of the trauma, as well as the age of occurrence has substantial effects on psychobiological sequelae and treatment response.

Methods: Data from two randomized placebo-controlled multicenter trials of sertraline for the treatment of PTSD(1,2) were analyzed in order to determine whether response differed in patients with and without an index trauma that involved interpersonal trauma in general, or childhood abuse in particular.

Results: Interpersonal trauma and childhood abuse were both more common in females than males, and were associated with early age at time of index trauma and longer duration of PTSD, but not with PTSD symptom severity. Sertraline was significantly more effective than placebo on most primary efficacy variables, irrespective of whether patients had experienced interpersonal trauma or childhood abuse. Similarly, there were significantly more responders to sertraline than to placebo in PTSD patients with and without interpersonal trauma or childhood abuse.

Conclusions: These data demonstrate that sertraline is valuable for the treatment of PTSD, irrespective of whether the precipitating trauma involves interpersonal trauma in general, or childhood abuse in particular.

References:

NR825 Thursday, May 22, 12:00 p.m.-2:00 p.m.
A Comparison of Publication Trends on Avoidant Personality Disorder and Social Phobia
Supported by Faperj, Capes, and CNPq

Ivan L. V. Figueira, M.D., Department of Psychiatry, UFRJ, Rua Dona Mariana 182, BL1A 1503, Rio de Janeiro, RJ 22280-020, Brazil; Raphael J. Braga, M.D., Marcelo G. Land, M.D., Mauro V. Mendlowicz, M.D., Mariana Cabizvca, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to interpret publication trends on APD and SP.

Summary:
Objective: To ascertain the number of scientific articles published per annum on avoidant personality disorder (APD) and social phobia (SP) in the period from 1973 to 2001. We hypothesize that while annual publication rates on SP would exhibit a sound growth, the number of articles on APD published per annum would present a stagnant or declining trend.

Method: We performed a review of the literature on APD and SP using the MEDLINE, the PsycINFO, and the Web of Science. The references were gathered by means of the Reference Manager software, transferred to an SPSS database, and input into regression models with the goal of predicting future growth of the literature in these areas.

Results: The number of articles published annually on SP has steadily increased in the period from 1973 (1 article) to 2001 (118 articles). In contrast, the production of scientific literature on APD peaked in 1986 (5 articles) and subsequently declined.

Conclusions: Given the declining trend identified in this study, it is unlikely that the publication of articles on APD will provide the empirical evidence required to validate this disorder in a foreseeable future. The permanence of APD in the roll of the personality disorders should therefore be reassessed.

References:

NR826 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Screening Alzheimer's Disease: Mini-Mental State Versus Olfactory Test
Supported by Eli Lilly and Company

Roland M. Dardenne, M.D., CMME, University Paris 5, 100 Rue de la Sante, Paris 75014, France; Elisabeth Watrin-Bourbon, M.D., Anne-Sophie Rigaud, M.D., Jocelyne De Rotrou, Ph.D., Catherine Rouby, Ph.D., Gilles Sicard, Ph.D., Julien D. Gueff, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to better identify patients with probable Alzheimer's disease with olfactory assessment and to define a 2-steps strategy to optimize the allocation of time-consuming resources such as neuropsychologic assessment to the diagnosis.

Summary:
Objectives: To compare performances of the Mini-Mental State (MMSE) and the Clinical Olfactory Test (COT) in discriminating patients with probable Alzheimer's disease (AD).

Methods: 68 patients with memory complaints completed the COT and the MMSE. Patients were examined and classified ac-
cording to three categories—probable AD (DSM-IV criteria), Mild Cognitive Impairment (MCI), no cognitive impairment (NOCI). Receiver Operating Characteristics curves and Area Under Curves (AUC) were computed.

Results: 59 subjects (23 AD, 18 MCI, 18 NOCI) were included. AD made more errors of odor identifications and had lower MMSE scores compared to MCI and NOCI (8.1 vs 3.9 and 4.2, p < 0.05 and 23.0 vs 27.9 and 28.4, p < 0.05). When AD were compared to NOCI, AUC for the COT and the MMSE were similar (0.825 vs 0.840, ns). The best cutoff score was 2 errors for the COT and 24 for the MMSE. When AD and MCI were grouped together, performances of COT and MMSE were lower (AUC = 0.735 and 0.690 respectively, hit rate = 73% vs 53%, Fisher Exact Test = 0.035).

Conclusions: Substituting olfactory screening for the MMSE may increase the robustness of screening and give better access to resource-consuming neuropsychological batteries.

References:

NR827 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Donepezil Treatment Benefits Early-Stage Alzheimer's Disease
Supported by Eisai, Inc., Pfizer Inc.

Sharon Richardson, Ph.D., Medical Affairs, Eisai, Inc., 500 Frank W. Burr Boulevard, Teaneck, NJ 07666-6741; Ben Seltzer, M.D., Parvaneh Zolnouni, M.D., Margarita Nunez, M.D., Robert Goldman, Ph.D., Dinesh Kumar, M.S., John Ieni, Ph.D.

Educational Objectives:
At the end of this session, a participant should be able to recognize the impact of initiation of donepezil treatment in early-stage Alzheimer's disease.

Summary:
Objective: To evaluate donepezil treatment in patients with early-stage Alzheimer's disease (AD).
Method: A 24-week, randomized (donepezil/placebo, 2:1), double-blind, placebo-controlled study. Patients with probable AD and a global CDR of 0.5 or 1 received placebo (n=57) or donepezil (n=96.5 mg/d for first 42 days and 10 mg/d thereafter). The primary analysis was the least squares mean change from baseline on the ADAS-cog at endpoint. 73% and 81% of donepezil and placebo-treated patients completed.

Results: At baseline, approximately one-third of patients' CDR scores were 0.5 (the rest were CDR=1) and mean MMSE scores were approximately 24, confirming patients were in early-stage AD. Donepezil significantly improved ADAS-cog scores compared to placebo at Week 12 through endpoint (p<0.05). 42.9% of donepezil patients showed >3-point improvement in ADAS-cog score compared with 20% of placebo patients at endpoint (p=0.002). Donepezil significantly improved MMSE scores at Weeks 6 through endpoint (p<0.05). 51.7% of donepezil patients showed >1.5-point improvement on the MMSE compared with 29.1% of placebo patients at endpoint (p=0.012). Donepezil significantly improved performance on some subscales of the Computerized Memory Battery Test (p<0.05).

Conclusions: Donepezil significantly improved cognition in patients with early-stage AD versus placebo demonstrating the value of initiating treatment earlier in the disease course.

References:

NR828 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Memantine/Donepezil Dual-Therapy Is Superior to Placebo/Donepezil for Moderate-to-Severe Alzheimer's Disease
Supported by Forest Laboratories, Inc.

Pierre N. Tariot, M.D., Department of Psychiatry, University of Rochester, Monroe Hospital, 435 East Henrietta Road, Rochester, NY 14620; Martin K. Farlow, M.D., George T. Grossberg, M.D., Ivan Gergel, M.D., Stephen Graham, Ph.D., James Jin, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the safety and efficacy of memantine in combination with donepezil for the treatment of moderate-to-severe Alzheimer's disease.

Summary:
Objective: Memantine, a moderate-affinity uncompetitive NMDA-receptor antagonist, represents a novel Alzheimer's disease (AD) therapy in the U.S. and is approved in Europe. We conducted a 24-week, randomized, double-blind, parallel-arm, placebo-controlled trial in 37 U.S. centers to study memantine's safety and efficacy in moderate-to-severe AD patients treated with the cholinesterase inhibitor donepezil.

Method: Inclusion criteria: diagnosis of probable AD by NINCDS-ADRDA, MMSE 5–14, MRI/CT consistent with probable AD, six-month daily donepezil therapy. Primary assessments: SIB and ADCS-ADL (cognition and function measures, respectively). CIBIC-Plus global assessment also was performed. Analyses were performed on the ITT population using LOCF.
Results: Of 403 patients randomized and treated with memantine 10mg bid (n=202) or placebo (n=201), 85% of memantine-treated patients and 75% of placebo patients completed the trial. At week 24, memantine/donepezil patients improved significantly (p<0.001) in cognition (SIB) compared to placebo/donepezil patients, and declined significantly less (p=0.028) in function (ADCS-ADL). A significant difference favoring memantine/donepezil was seen on CIBIC-Plus (p=0.027). Memantine/donepezil was safe and well tolerated.

Conclusions: These results further support memantine's safety and efficacy for moderate-to-severe AD and demonstrate that memantine/donepezil is superior to donepezil alone. Treatment with memantine/donepezil improved cognition relative to baseline whereas donepezil alone was associated with continued cognitive decline.

References:
1. Parsons CG, Danyasz W, Quack G: Memantine is a clinically well tolerated N-methyl-D-aspartate (NMDA) receptor antagonist—a review of preclinical data. Neuropharmacology 1999; 38:735–767.
Dopamine Transporter Binding in Social Phobia

Franklin R. Schneier, M.D., Anxiety Clinic, New York State Psychiatric Institute, 1051 Riverside Drive, Unit 69, New York, NY 10032; Diana M. Martinez, M.D., Zhihong Zhu, Ph.D., Michael R. Liebowitz, M.D., Marc Laruelle, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be aware of recent brain imaging findings on dopamine system function in social phobia.

Summary:
Objective: Social phobia has been associated with dysfunction of the dopamine system, as evidenced by recent findings of low dopamine transporter (Tiihonen et al., 1997) and low D2 receptor availability in the striatum. The initial reports of these findings, however, have not yet been replicated.

Method: Binding availability of dopamine transporters was assessed in 12 unmedicated subjects with a principal diagnosis of generalized social phobia, and in 14 healthy comparison subjects matched for age and sex. Ratio of specific to nondisplaceable uptake (V3) of [123I]-β-CIT was measured at equilibrium using single photon emission computerized tomography (SPECT).

Results: Generalized social phobic subjects did not differ from healthy comparison subjects in respect to [123I]-β-CIT binding to striatal dopamine transporters (t = 0.53, df = 24, p = 0.60; mean = 7.7, SD = 1.1 vs. mean = 7.5, SD = 1.1). [123I]-β-CIT binding was not significantly associated with severity of social anxiety.

Conclusions: These findings do not replicate the prior finding of dopamine transporter binding in generalized social phobia. Findings are discussed in relation to prior studies of dopamine function in social phobia and related conditions.

References:

Memantine, a moderate-affinity, uncompetitive, NMDA-receptor antagonist, is approved in Europe for Alzheimer’s disease and under investigation in the U.S. Our objective was to determine whether an in vivo pharmacokinetic and pharmacodynamic interaction exists between memantine and the acetylcholinesterase inhibitor (ACHE) donepezil.

Method: In an open-label, multiple-dose study, 24 healthy subjects (18-35 years) received 10mg memantine orally on Day 1. Following a 14-day washout, subjects received 5mg donepezil orally once daily for seven days (outpatient). Beginning Day 22, donepezil dosage was doubled for 22 days, and the last donepezil dose was concomitantly administered with 10mg memantine on Day 43. Assessments included pharmacokinetic, pharmacodynamic (ACHE inhibition), and safety parameters (adverse event recording, ECG, vital signs, clinical laboratory tests).

Results: Memantine bioavailability was not significantly altered with donepezil daily-dosing, nor was the multiple-dose donepezil bioavailability altered with single-dose memantine. Percent maximum inhibition of ACHE activity by donepezil averaged 77.8% and was not statistically different upon memantine co-administration (81.1%). Two patients withdrew due to adverse events while treated with donepezil. Of 19 completers, single memantine doses administered with donepezil multiple-doses were well tolerated.

Conclusions: Memantine and donepezil did not interact pharmacokinetically or pharmacodynamically, suggesting that they can be safely co-administered.
References:

NR832 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Galantamine in the Management of Dementia With Lewy Bodies
Supported by Janssen Pharmaceutical Products, L.P.
Keith Edwards, M.D., Research Department, Alzheimers Diagnostic Center, 140 Hospital Drive Suite 210, Bennington, VT 05201; Linda Hershey, David Lichter, Edward Bednarczyk, Stewart Johnson, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate the effect of galantamine on cognition, behavior, global function, and activities of daily living (ADL) in patients with mild-to-moderate dementia with Lewy bodies (DLB).

Summary:
Objective: To ascertain effects of galantamine in patients with mild-to-moderate DLB.
Methods: A 24-week, multicenter, investigator-initiated, open-label study of galantamine (16 or 24 mg/day) in patients with DLB (DLB Consensus Criteria). Outcome measures included changes in cognition (MMSE, ADAS-cog), behavior (NPI-12, NPI-4), attention and visuospatial function (COGDRAS), global function (CGIC), and ADLs (ADCS/ADL). Twelve-week results are reported.
Results: Nineteen patients were enrolled (mean age: 76.9 ± 8.2 years; 68.4% male; mean baseline scores: MMSE, 19.84, ADAS-cog, 27.6, NPI-12, 20.5, UPDRS, 19.5). Results at 12 weeks indicated a mean change from baseline in NPI-12 of 4.0 points, with a 4.3-point change in NPI-4 (p = 0.02), and more than 70% of patients responded greater than 4.0 points. Patients demonstrated improvement in cognition (ADAS-cog) of 4.8 points. There was a 4.9-point improvement in ADLs and a 0.5-point improvement in global function.
Conclusions: This interim analysis suggests that galantamine is safe and effective in patients with DLB. Retention rates were higher, and adverse events lower, than those in previous trials of cholinesterase inhibitors in DLB.

References:

NR834 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Cognitive Enhancement With Donepezil for Neurocognitive Impairments After Traumatic Brain Injury
John C. Krusz, M.D., Anodyne Clinic, 5446 Glen Lakes Drive, Dallas, TX 75231; William K. Knoderrer, D.D.S., Alan Hopewell, Ph.D., Jack Thompson, M.S.

Summary:
Mild cognitive impairments (MCI) of frontal and temporal lobe functioning subserving attention, concentration and memory are seen commonly after traumatic brain injury (TBI). We have utilized donepezil (Aricept™) to treat cognitive dysfunctioning after traumatic brain injury in otherwise nondemented patients. We have employed a novel, brief, five-point rater to differentiate pre-treatment from post-treatment cognitive measures. We treated 42 patients with donepezil after a pretreatment. Our results show that there was statistical improvement in both aspects of the Selective Reminding Test (early and delayed) after treatment with donepezil. We have concluded from this open-label study that cognitive enhancement with donepezil is a useful strategy to help patients with cognitive dysfunctioning after TBI. In particular, immediate and delayed Selective Reminding Test was significantly better with donepezil therapy. This study represents the largest database of patients treated with donepezil in this clinical situation. Double-blind studies are definitely warranted based on these initial results.

References:

NR833 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Cognitive Enhancement With Donepezil for Neurocognitive Impairments After Traumatic Brain Injury
John C. Krusz, M.D., Anodyne Clinic, 5446 Glen Lakes Drive, Dallas, TX 75231; Alan Hopewell, Ph.D., Jack Thompson, M.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize new positive data on treatment of mild cognitive deficits after traumatic brain injury using donepezil. This initial data should point out to the clinician potential uses for this medication that can help a large potential pool of patients each year.

Summary:
Mild cognitive impairments of frontal and temporal lobe functioning subserving attention, concentration and memory are seen commonly after traumatic brain injury (TBI). We have utilized donepezil (Aricept™) to treat cognitive dysfunctioning after traumatic brain injury in otherwise nondemented patients. We have employed a novel, brief, five-point rater to differentiate pre-treatment from post-treatment cognitive measures. We treated 42 patients with donepezil after a pretreatment. Our results show that there was statistical improvement in both aspects of the Selective Reminding Test (early and delayed) after treatment with donepezil. We have concluded from this open-label study that cognitive enhancement with donepezil is a useful strategy to help patients with cognitive dysfunctioning after TBI. In particular, immediate and delayed Selective Reminding Test was significantly better with donepezil therapy. This study represents the largest database of patients treated with donepezil in this clinical situation. Double-blind studies are warranted.
NR835 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Long-Term Management of Vascular Dementia: Cognitive Efficacy After 24 Months of Galantamine Treatment
Supported by Janssen Pharmaceutica Products, L.P.
Alexander Kurz, M.D., Department of Psychiatry, Technische University, Moewistrasse 26, Munich 081675, Germany; Sean Lilienfeld, M.B.B.Ch.

Educational Objectives:
At the conclusion of this session, the participant should be able to evaluate long-term cognitive efficacy and safety of galantamine in patients with probable vascular dementia (VaD) for 24 months.

Summary:
Objective: To investigate long-term safety and efficacy of galantamine in patients diagnosed with VaD.

Methods: Patients with probable VaD or Alzheimer's disease with cerebrovascular disease who completed a six-month, double-blind, placebo-controlled study and a six-month, open-label extension (OLE) were eligible to enter this two-year, OLE trial with a fixed daily dose of galantamine 24 mg. Changes in cognition were assessed with the ADAS-cog/11. Safety was evaluated. Data were analyzed in VaD patients at Month 12 of the OLE (total treatment duration: 24 months).

Results: A total of 135 of 326 patients who entered the two-year, OLE had a diagnosis of VaD (60 had received galantamine continually for 24 months). Continuous galantamine treatment maintained cognitive levels close to baseline for 24 months (ADAS-cog/11 change from baseline: 0.8 ± 1.00; p = NS). The most frequently occurring adverse events were characteristic of those expected for an elderly population with dementia (depression, agitation, insomnia). Gastrointestinal symptoms decreased as therapy lengthened.

Conclusions: Long-term galantamine treatment in patients diagnosed with probable VaD is safe and effective in preventing cognitive decline for 24 months and has provided a treatment opportunity in this group with limited therapeutic options.

References:

NR836 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Six Months of Treatment With Donepezil and Cognition in Patients With Alzheimer's Disease
Alina Borkowska, Ph.D., Department of Psychiatry, University Medical School, Kurpińskiego 15, Bydgoszcz, Poland; Marzena Ziołkowska, M.D., Ewa Pilaczynska, M.D., Dionizy Fanzlav, M.D., Janusz K. Rybakowski, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to recognize a possibility of improving cognitive abilities in patients with Alzheimer disease by three to six month treatment with donepezil, 5–10 mg/day.

Summary:
Objective: One-hundred and twenty patients with mild to moderate stage of Alzheimer disease, aged 56–86 (mean 70) years, were treated with donepezil, 5–10 mg/day, (90 patients) or rivastigmine, 6–12 mg/day, (30 patients) for six months. Twenty-one patients were treated before with rivastigmine with poor therapeutic effect and were changed to donepezil.

Method: Clinical and cognitive measurements included: Trail Making Test, Verbal Fluency Test, ADAS-COG and MMSE as well as clinical interview with patient and caregiver. Neuropsychological assessment was performed before, after three and six months of treatment.

Results: Both after three and six months of treatment patients receiving donepezil showed significant improvement on MMSE (especially those with mild cognitive impairment), while in patients treated with rivastigmine such effect was observed only in patients receiving drug 12 mg/day. The results of neuropsychological tests were also significantly improved in patients treated with donepezil. In 21 patients with previous negative therapeutic effect during rivastigmine treatment, a significant improvement after treatment with donepezil on all cognitive tests was noted.

Conclusions: The results obtained suggest that the treatment with donepezil exerts more robust effect on cognition in patients with Alzheimer Disease, including patients previously treated with rivastigmine without positive therapeutic effect.

References:

NR837 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Cost Effectiveness of Memantine in the Treatment of Alzheimer's Disease in Norway
Supported by H. Lundbeck A/S
Robert Launois, M.D., University of Paris XIII, 74 Rue Marcel Cachin, Bobigny Cedex 93017, France; Chantal Guilhaume, Clement Francois, M.S.C., Eli Maehlum, M.Sc.

Summary:
Objective: Placebo-controlled clinical trials have demonstrated the efficacy of memantine versus placebo in moderately-severe and severe Alzheimer's disease. A modeling approach has been adopted to estimate costs and outcomes of memantine treatment in clinical practice in Norway.

Method: A Markov model simulated moderately-severe and severe patients' progression through levels of combination of severity, autonomy and setting over five years. Model inputs include clinical trial results and measurement of patient and caregiver resource utilisation from a societal perspective using literature and expert data. The main outcome measures are time spent in autonomy (patient's ability to accomplish activities using the ADCS-ADL scale) and time to institutionalisation.

Results: The time spent in autonomy is 10% higher for patients treated with memantine compared to donepezil and 25% higher without pharmacotherapy. Time to institutionalisation is 16% lower with memantine versus donepezil and 25% lower versus no treatment. Over a five-year period, patients treated with memantine showed a decrease of NOK37,208 and NOK85,171 in total health care costs, compared with donepezil and no treatment, respectively. Robustness of the results was validated by an extended-sensitivity analysis.

Conclusions: Memantine is more effective in improving time spent in autonomy and in reducing health care costs compared with donepezil or no pharmacotherapy.
Economic Burden of BPSD in a Nursing Home Population

Supported by Novartis Pharmaceuticals Corporation

Judith A. O'Brien, R.N., Caro Research Institute, 336 Baker Avenue, Concord, MA 01742; Amanda R. Patrick, B.A., Alexandria J. Ward, Ph.D.

Educational Objectives:

- At the conclusion of this presentation, the participants should be able to understand the extent of BPSD in a statewide nursing home population and its economic impact on that environment.

Summary:

Objective: To estimate the incremental cost of providing nursing home care for residents with Behavioral and Psychological Symptoms in Dementia (BPSD).

Method: In Minnesota, each nursing home resident is assessed as either "dependent" or "not" in eight activities of daily living (ADLs), and assigned to a management category (low 0–3 ADLs, medium 4–6 or high 7–8). Reimbursement is based on this category, as well as special nursing care and/or the presence of BPSD. The 1998 assessments for 12,901 residents diagnosed with dementia were analyzed (ICD-9-CM codes 290.00–290.99, 331.00). Residents requiring special nursing care or in a high dependency sub-category due to a neurological disorder other than dementia were excluded. Costs were compared for residents with and without BPSD (2002 US$).

Results: Care needs of 57% of residents were increased by BPSD, and fewer with BPSD had a low management category (18%) than without BPSD (32%). The mean annual cost per resident was $44,500, 10% higher than residents without BPSD. BPSD carried an annual incremental cost per resident in the low management category of $2,553, $2,396 in the medium, and $3,174 in the high.

Conclusions: BPSD is common amongst nursing home residents and increased the costs of providing care.

References:


Remission Rates Following Therapy With Buproprion or SSRIs

Supported by GlaxoSmithKline

Michael E. Thase, M.D., Department of Psychiatry, University of Pittsburgh-WPIC, Belli 843, Pittsburgh, PA 15260; Barbara R. Haight, Pharm.D., Nathalie E. Richard, M.S., Carol B. Rockett, Pharm.D., Melinda Mitton, Pharm.D., Younghua Wang, Ph.D.

Educational Objectives:

- At the conclusion of this session, the participant should recognize that remission is the optimal outcome of acute-phase antidepressant therapy for MDD and that duloxetine treatment results in high rates of remission.

Summary:

Objective: Complete remission is increasingly recognized as the optimal outcome of the acute phase of antidepressant therapy. Evidence suggests that therapy with dual reuptake inhibitors such as venlafaxine (at least at higher doses) may bring about higher rates of remission than SSRIs. Duloxetine is a dual reuptake inhibitor that has well-established efficacy and safety in clinical trials. Here, we examine the remission rates in controlled studies of duloxetine, using analytical techniques such as odds ratios and effect sizes.

Method: Pooled data from six randomized, double-blind, placebo-controlled clinical trials comparing duloxetine with an SSRI in the treatment of depression were analyzed. Remission was defined as a score of ≤7 on the 17-item Hamilton Rating Scale for Depression (HAMD17).


**Results:** Remission rates were 43% (300/697) for duloxetine, 38.3% (162/423) for SSRI and 28.4% (144/507) for placebo (χ² = 27.18, df = 2, p<.001). Odds ratios were 1.22 (95% confidence interval, CI: 0.95, 1.56) for duloxetine/placebo and 1.90 (95% CI: 1.49, 2.43) for duloxetine/placebo. The effect size was 0.3 for duloxetine vs. placebo, 0.2 for SSRI vs. placebo and 0.1 for duloxetine vs. SSRI.

**Conclusion:** Remission rates for duloxetine were greater than placebo or SSRI in controlled clinical trials.

**References:**

**NR841**

**Lack of Effect of Bupropion Sustained Release on Blood Pressure In Hypertensive Patients Supported by GlaxoSmithKline**

Michael E. Thase, M.D., Department of Psychiatry, University of Pittsburgh-WPIC, Bellt 843, Pittsburgh, PA 15260; Barbara R. Haight, Pharm.D., Jack G. Modell, M.D., Carol B. Rockett, Pharm.D., Afsaneh Asgharian

**Educational Objectives:**
At the conclusion of this session, the participant should be able to articulate the impact of bupropion SR on blood pressure as revealed in a randomized, double-blind, placebo-controlled study designed specifically to evaluate blood pressure effects.

**Summary:**

**Introduction:** Bupropion SR (BupSR) did not cause clinically significant changes in mean blood pressure (BP) in clinical trials, but there have been isolated reports of BupSR-associated BP increases occurring primarily among smokers. This randomized, double-blind study was designed to examine effects of BupSR on BP in mildly hypertensive patients.

**Methods:** Non-depressed outpatients with untreated Stage I hypertension received BupSR 150mg, 300mg, 400mg, or placebo for 4 weeks (n=74/group).

**Results:** BupSR did not differ from placebo in the primary endpoint of mean difference between pre- and post-treatment clinic diastolic or systolic BP (DBP, SBP). For BupSR 150mg, 300mg, 400mg, and placebo, the respective differences were −2.3, −1.9, −1.6, −2.4 mmHg for DBP and −6.5, −6.5, −6.5, −6.5 mmHg for SBP. The percentage of patients with any clinically significant increase in either DBP or SBP (increase of 6 or 10 mmHg, respectively) did not differ between any BupSR group (20% each group) and placebo (15%; p=0.52 each comparison). In addition, BupSR did not differ from placebo in mean change from baseline in average 24-hour BP at day 28. For each BupSR dose, changes in SBP were (respectively) 0.2, 2.3, 2.1 vs. 0.04 mmHg for placebo, and for SBP, 0.7, 1.8, 1.1 vs. −0.6 mmHg for placebo.

**Conclusions:** BupSR, a norepinephrine and dopamine reuptake inhibitor (NDRI), did not affect BP in this controlled study.

**References:**

**NR842**

**Long-Term Autonomic Reactivity in Terrorism’s Direct Victims: A Pilot**

Phoebe M. Tucker, M.D., Department of Psychiatry, University of Oklahoma, 920 Stanton Young Boulevard, WP3440 Box 26901, Oklahoma City, OK 73190; Betty Pfefferbaum, M.D., Carol S. North, M.D., Adrian Kent, M.S., Dorothy B. Wyatt, R.N., Akim Hossain, M.D., Christie Burcigl, Ph.D.

**Educational Objectives:**
At the conclusion of this session, (1) participants will be able to discuss implications of persistent autonomic reactivity in direct victims of Oklahoma City’s bombing, and (2) participants will understand low levels of PTSD, depression, family problems six to seven years after terrorism.

**Summary:**

**Objective:** Autonomic reactivity to trauma cues and subjective symptoms of PTSD and depression were assessed in 78 directly exposed survivors of Oklahoma City’s 1995 terrorist bombing and 69 adult community controls six to seven years post disaster.

**Method:** Direct victims from the Oklahoma Health Department’s official bombing registry and community controls were assessed for subjective symptoms of PTSD related to terrorism both in Oklahoma City and the World Trade Center with the IES-R, depressive symptoms with the BDI, and family issues with the Family Functioning Scale. Physiologic reactivity to trauma cues was compared for both groups through assessments of heart rate and systolic, diastolic, and mean arterial blood pressure changes (Biopac Instruments) for four minutes before and during a clinical interview regarding Oklahoma City’s bombing.

**Results:** Directly exposed survivors as a group did not have PTSD and depression symptoms in levels suggesting psychiatric illness, and their symptoms were not significantly different from community controls. However, directly exposed survivors had greater autonomic reactivity in measures of heart rate and systolic, diastolic, and mean arterial blood pressure (p<.001) compared to community controls.

**Conclusion:** Directly exposed survivors of terrorism assessed had persistent autonomic reactivity to trauma reminders despite having relatively low levels of subjective symptoms. Further study is needed to determine if enduring autonomic reactivity in directly exposed survivors of terrorism leads to greater medical illness, such as cardiovascular disease, or more somatization.

**References:**

**NR843**

**Personality Characteristics of Chronic Insomniacs**

Byuang-Joo Ham, M.D., Department of Psychiatry, Korea University Hospital, 126-1 5 Ga Anam Dong, Seoul 136-705, South Korea; Leen Kim, M.D., Kwang-Yoon Suh, M.D.

**Educational Objectives:**
At the conclusion of this session, the participant should be able to recognize the personality factors and the ways of coping to define the personality characteristics which is underlying the development of insomnia.
Summary:

Objectives: We investigated the personality factors and the ways of coping to define the personality characteristics underlying the development of insomnia.

Methods: The subjects were 21 chronic insomniacs and 26 normal controls. We diagnosed chronic insomnia by using the International Classification of Sleep Disorders. The diagnosis of chronic insomnia included psychophysiological insomnia, poor sleep hygiene, and hypnotics-dependent insomnia. Different aspects of personality were measured using 16 Personality Factors (PF) test and the Ways of Coping Checklist for both chronic insomniacs and normal controls.

Result: The chronic insomniacs showed significantly lower stability (C factor; 4.57 1.89 VS 7.38 1.83), intelligence (B factor; 3.76 2.23 VS 6.54 1.96), motivation distortion (B factor; 3.76 2.23 VS 6.54 1.96) factor scores, and higher guilt proneness (C factor; 6.67 2.11 VS 3.81 1.65), tension and anxiety (Q4 factor; 7.57 2.29 VS 3.46 1.88) factor scores than controls in 16 PF. The chronic insomniacs had significantly higher emotional-focused coping pattern (30.30 9.53 VS 24.52 5.71) and passive coping pattern scores (50.75 13.76 VS 43.26 8.73) than controls in the Ways of Coping Checklist.

Conclusion: It is suggested that chronic insomniacs are characterized by depressive mood and anxiety-proneness from low ego strength, high levels of anxiety and guilty feelings, and passive and emotion-concentrated coping pattern. These traits are supposed to be factors contributing to the state of emotional arousal and resultant physiological activation that has developed and maintained the insomnia.

References:

NR844 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Improving Sleep Disturbances With SSRI Therapy in Depression and Anxiety Disorders
Supported by GlaxoSmithKline
Jacquie Christie, Ph.D., Department of Psychiatry, GlaxoSmithKline, New Frontiers Science Park, 3 Roave, Marlow CM19SAW, United Kingdom; Jonathan R.T. Davidson, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize that sleep disturbance associated with depression and the anxiety disorders is a disabling symptom causing considerable distress to both the individual and their family. Results suggest that paroxetine is an effective agent in the treatment of sleep disturbances associated with depression and anxiety.

Summary:
Objective: To assess the efficacy of paroxetine in improving the sleep disturbances commonly occurring with depression and anxiety.
Method: Data were derived from short-term, clinical studies of paroxetine versus placebo and active comparators in depression, panic disorder, social anxiety disorder (SAnD), generalized anxiety disorder (GAD) and posttraumatic stress disorder (PTSD).
Sleep disturbance was measured for depression using MADRS item 4 (10 studies; n=1934), and HAM-D items 4, 5 and 6 (33 studies; n=5622); HAM-A item 4 scores for panic disorder, SAnD and GAD (10 studies; n=3141), and MADRS item 4, and items 2 and 13 on both CAPS-2 and DTS for PTSD (3 studies; n=1071). Sleep dysfunction was also assessed through the incidence of treatment-emergent insomnia across all short-term studies in all indications in depression and anxiety.

Results: Data from 46 studies (n=9834) across depression and the spectrum of anxiety disorders show that patients treated with paroxetine experienced a clinically and statistically significant improvement in sleep disturbance compared with placebo. Rates of treatment-emergent insomnia were similar to placebo. Data from all analyses will be presented.

Conclusions: The results suggest that paroxetine effectively treats sleep disturbances associated with depression and anxiety. Paroxetine has rates of treatment-emergent insomnia similar to those of placebo.

NR845 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Effects of Stress and Personality Characteristics on Sleep
Ho-Kyoyoung Yoon, M.D., Psychiatry, Korea Univ. Hospital, 126-1,5-Ga, Anam-Dong Sungbuk-Gu, Seoul 136-105, South Korea; Seung-Gui Kang, M.D., Byuang-Joo Ham, M.D., Leen Kim, M.D.

Educational Objectives:
At the conclusion of this session, the participants should be able to recognize stress and personality characteristics impair restorative effects of sleep by inducing arousal.

Summary:
Objectives: We have studied personality factors underlying the development of insomnia. One of our authors reported that chronic insomniacs were characterized by low ego strength, high levels of anxiety, and guilty feelings on 16 Personality Factor Questionnaire (16-PF), and minor stresses were highly correlated with symptoms of non-restorative sleep in normal persons. This study was aimed at investigating the correlations between stress and personality on sleep patterns.

Methods: A total 175 volunteers who were healthy college students participated in this study. They were selected after an interview, and completing a questionnaire on sleep habits, and Daily Stress Inventory before sleep on three consecutive days. They also completed 16-PF, BDI, and STAI.

Results: Minor stresses were associated with the symptoms of non-restorative sleep. And the O (guilty feeling), C (low ego strength) and Q4 (high anxiety) factors of 16-PF were highly correlated with these symptoms. BDI and STAI scores also correlated with above personality factors.

Conclusions: This study confirmed that minor stresses were associated with non-restorative sleep, not sleep schedule. The personality traits such as low ego strength, high levels of anxiety, and feelings of guilt were thought to be factors contributing to the changes of sleep quality from minor stresses.

References:

NR846 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Efficacy of Indiplon Solution in a Model of Transient Insomnia
Neurocrine Biosciences
Thomas Roth, Ph.D., Sleep Research, Henry Ford Hospital, 2799 West Grand Boulevard, CFP3, Detroit, MI 48202; James
K. Walsh, Ph.D., Joshua Burke, Roberta Rogowski, Bruce Campbell, Ph.D., Phillip Jochelson, M.D.

Educational Objectives:
At the conclusion of this session, participants should learn about the efficacy and tolerability of indiplon in healthy adults subjected to a well-accepted model of transient insomnia. Indiplon is a non-benzodiazepine GABA-A receptor modulator with sedative-hypnotic properties.

Summary:
Objective: This study explored the dose-related efficacy and tolerability of indiplon in healthy adults subjected to a laboratory model of transient insomnia.
Method: This was a randomized, placebo-controlled, parallel-group, dose-response study in 228 young healthy subjects with no history of insomnia. Transient insomnia was induced by a combined first night effect and two-hour phase advance of bedtime. Subjects were randomized to indiplon solution 15mg, 30mg, or placebo, and dosed 30 minutes before lights out. Hypnotic efficacy was evaluated via polysomnography and sleep questionnaires. The Digit Symbol Substitution Test (DSST), Symbol Copying Test (SCT) and Visual Analog Scale (VAS) of alertness, were conducted to evaluate next-day residual effects.
Results: Latency to persistent sleep was significantly improved with values of 34.1, 17.5 and 16.2 minutes for the 0/15/30mg dose groups (p<0.001). Subjective latency to sleep onset was also significantly improved with values of 31.1, 15.8, and 15.4 minutes for the 0/15/30 mg dose groups (p<0.001). There was no effect of indiplon on measures of total sleep time or on sleep architecture. DSST, SCT, and VAS in the indiplon groups were similar relative to baseline of placebo.
Conclusion: Indiplon solution appears to be an effective and well-tolerated hypnotic, with no next day residual effects.

References:

NR847 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Personality Disorders and Sexual Re-Offending
Peter Berger, M.D., Department of Psychiatry, University of Vienna, Waehringer Guertel 18-20, Vienna 1090, Austria; Wolfgang Berner, M.D.

Educational Objectives:
At the conclusion of this session, the participant should get more knowledge about the value of personality disorders as predictors of risk for relapse in sexual offenders.

Summary:
Introduction: Previous research on re-offending of sex-offenders had been focussed only on a limited number of personality traits such as psychopathy or antisocial traits, or did not use a structured method for the assessment of personality disorders.
Methods: Seventy male incarcerated sex-offenders were assessed for personality disorders according to DSM-III-R and ICD-10 with a structured interview, the IPDE. Further assessment included diagnoses on Axis I, type of a paraphilia, and criminological variables. Sixty of these subjects (30 rapists, 23 child molesters and seven with sexual homicide) had been released from prison and re-offending was determined by reviewing police reports after a mean follow-up time of seven years.

Results: Twenty of the 60 subjects (33%) had committed a new sex-offense and 11 (18%) a violent offense. Paraphilias but not personality disorders were associated with sexual re-offending. However, violent re-offending was associated with borderline personality disorder and antisocial personality disorder. Sexual re-offenders who had used substantial cruelty while offending had more sadistic personality disorder traits than others.

Conclusion: The results suggest that personality disorders are not negative predictors for sexual re-offending. In this regard deviant sexual preferences are more important. But re-offending is more severe if sadistic personality traits are present.

References:

NR848 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Manhattan’s Assisted Outpatient Treatment Program and Hospital Recidivism
Gary R. Collins, M.D., Department of Psychiatry, New York University - Bellevue, 462 First Avenue 21W30, New York, NY 10014; Andrew M. Kleiman, M.D., Joel R. Sneed, Ph.D., Angela Solimo, M.A.

Educational Objectives:
At the conclusion of this session, the participant should demonstrate a basic understanding of the Manhattan Assisted Outpatient Treatment Program, and recognize its possible benefits to the severely mentally ill person in terms of a decreased number of hospitalizations and a decreased total number of inpatient hospital days.

Summary:
Objective: To evaluate the effectiveness of an Assisted Outpatient Treatment (AOT) court order, with its concurrent increased number and intensity of psychiatric services, in reducing number of hospital admissions, and total number of inpatient hospital days in New York City’s severely mentally ill population.
Method: The authors examined the first 56 cases evaluated and treated in Manhattan under AOT. Of these, we analyzed 42 cases for which complete demographic and clinical data were available for the year prior to the initial AOT order and the year following the order.
Results: AOT clients were significantly less likely to be hospitalized and were hospitalized for significantly fewer days in the year following AOT enrollment compared with the year prior to AOT enrollment.
Conclusions: Although previous outpatient commitment laws have been studied, Manhattan AOT is unique because of its specific criteria and population. This initial study suggests that the court-ordered AOT Program was clinically beneficial to its clients, as evidenced by a decreased number of hospital admissions and total hospital inpatient days in the year following the entry into the program compared with the prior year.

References:

NR849    Thursday, May 22, 12:00 p.m.-2:00 p.m.
Predictors of the Occurrence of Amnesia in Neonaticidal Women
Supported by Faperj, Capes, and CNPq
Mauro V. Mendolowicz, M.D., Department of Psychiatry, IPUB-UFRJ, Rua Itiradentes 171 BL 02 AP 903, Niteroi, RJ 22420-071, Brazil; Leonardo Fontenelle, M.D., Pedro G. Coscarelli, M.D., Katia Mecler, M.D., Marcelo G. Land, M.D., Sander Fridman, M.D., Talvane M. Moraes, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to assess the nature of amnestic symptoms in neonaticide.

Summary:
Objective: This archival study investigates the role of psychiatric symptoms in neonaticide (i.e., the murder of a child by its mother on the day of its birth). We hypothesized that neonaticidal women (NW) who did not report amnesia for the crime would be younger, unmarried, less educated, would have lower educational level, and would lack social support. In contrast, NW reporting amnesia for the crime would exhibit symptoms associated with dissociative behavior such as denial of pregnancy, use of excessive violence, and failure to hide the corpse.

Method: Our cohort included 19 NW who spontaneously reported amnesia and 37 NW who did not. The socio-demographic characteristics, behavior during pregnancy, murder and post-murder, and the legal procedures for the groups were compared.

Results: Neonaticidal women reporting amnesia were more educated, had greater social support, and were more likely to be charged under the Brazilian Criminal Code of 1940. A logistic regression analysis indicated that being charged under the Criminal Code of 1940 was the best predictor of the occurrence of amnestic symptoms.

Conclusions: Our results argue against the existence of a dissociative basis for the amnesia associated with neonaticide and suggest that the reporting of amnesia by NW may be influenced by socioeconomic and legal factors.

References:

NR850    Thursday, May 22, 12:00 p.m.-2:00 p.m.
Does Performance of Professionals in Court Predict Court Decisions?
Supported by the State of Illinois Central Management Services
Jagannathan Srinivasaraghavan, M.D., Department of Psychiatry, Southern Illinois University, Chooe Mental Health Center, Anna, IL 62906; Alan R. Felthous, M.D., Wenona Whitfield, J.D., Sarah Andrew, Ph.D., Nancy Watkins, B.S.

Educational Objectives:
At the conclusion of this presentation, a participant will be able to appreciate the importance of psychiatric testimony and the role played by the opposing legal positions and the cumulative role in the outcome of court decisions involving petitions for psychotropic medications over objections.

Summary:
Objective: To test the hypothesis, combined ratings of the quality of testimony of the psychiatrist, performance of the state’s attorney and public defender can differentiate between two groups, cases where the petition for medication for psychotropic medications over objection was granted or denied.

Subjects: From 1991 to 2001 in Southern Illinois there were 17 denials and 136 granting of petitions for administration of psychotropic medications in Union County Court. This study involves all denials and randomly selected granted petitions; 48 transcripts were requested, 30 received, and 28 reviewed.

Method: From the court transcripts, any reference to the court decisions was deleted. An academic forensic psychiatrist and an academic lawyer rated the content and process of psychiatric testimony and performance of legal professionals, respectively, on a scale of one to four (poor, fair, good, and excellent).

Results: The review included nine psychiatrists, five State’s Attorneys and five defense attorneys. All but one case was ruled by the same judge. The combinations of the three independent variables correctly classified 16 of 28 cases (57%). A discriminant analysis produced a D squared statistic of .64052, which converts to a Hotelling T squared of 4.12 (statistically not significant).

Conclusion: Correlation for all subjects indicate positive correlations between psychiatrist and state’s attorney ratings and negative correlations between the defense attorney ratings and the other two.

References:

NR851    Thursday, May 22, 12:00 p.m.-2:00 p.m.
Neurological Soft Signs in Criminals and Schizophrenia Patients and Their Implications
Mary W.E. Ilaga, M.D., Department of Neuro-Psychiatry, University of St, Tomas Hospital, Manila 1008, Philippines; Aprillyn S. Reyes, M.D., Chona San Gabriel, M.D., Bernardo J. Conde, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to identify neurological abnormalities in patients with schizophrenia, and criminals.

Summary:
Several studies have been published claiming the association of neurologic abnormalities, criminality, and schizophrenia. The objectives are to identify and correlate neurologic deficits in criminals and schizophrenics. Group I are chronic schizophrenics, Group II are chronic schizophrenia with criminal offense, and Group III are criminals. Complete neurological examination and MMSE were done.

Results: a total of 134 male subjects. There was a significant difference among the three groups as to their mean MMSE score and presence of soft neurologic signs. The highest frequency of frontal signs belong to group II (70%). In the study we found that only soft neurologic signs were seen in all the groups. This were in the form of the following: glabellar, palmo-mental, hand mirror, ideomotor and paratonia. The presence of neurologic abnormalities might influence the violent dentencies of these individuals, thus, diminishing the liability of their acts.
References:


NR852 Thursday, May 22, 12:00 p.m.–2:00 p.m.

Binomial Forced-Choice Digit Recognition Test of Patients With and Without Compensative Traumatic Brain Injury in China

Beilin Gao, M.D., Shenzhen Kangning Hospital, Cuizhu Road #1080, Shenzhen Gungdon 518020, China; Rengang Liu, M.D., Chyi Hu, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to use Binomial Forced-Choice Digit Recognition Test for patients with head injuries.

Summary:

Objective: To explore the validity of Binomial Forced-Choice Digit Recognition Test (BFDRT) in detecting dissimulation of intellectual deficit.

Methods: 57 subjects with head injuries and with dissimulation of intellectual impairment were compared with 66 subjects without compensation. The differences of scores on BFDRT between two groups of malingering and non-malingering were compared. Distinguishing analysis was done in this study.

Results: There were significant differences in the scores of two dimensions and total score of BFDRT and the quotient of response bias between the malingering group and non-malingering group. The accuracy of distinction was 92.7%–100% with 0%–3% of false positive and 1.8%–14% false negative when the cutoff scores of BFDRT was 11 on easy items, 7 on difficult items, and 18 on total scores. The total score of BFDRT had a highest accuracy of distinction to dissipate intellectual deficit.

Conclusion: BFDRT is useful in detecting the dissimulation of intellectual impairment in patients with head injuries.

References:


NR853 Thursday, May 22, 12:00 p.m.–2:00 p.m.

Correlation Analysis of BFDMT and RSPM in the Patients With Financially Compensable Head Injuries

Beilin Gao, M.D., Shenzhen Kangning Hospital, Cuizhu Road #1080, Shenzhen Gungdon 518020, China; Rengang Liu, M.D., Chyi Hu, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to use Binomial Forced-Choice Digit Memory Test for detecting the true degree of the performance of intelligence test in patients with head injuries.

Summary:

Objective: To study correlation of Binomial Forced-Choice Digit Memory Test (BFDMT) and Raven’s Standard Progressive Matrices (RSPM) in patients with financially compensable head injuries.

Methods: 64 subjects with compensable head injuries were assessed by BFDMT and RSPM. The scores of BFDMT with the performance of RSPM in subjects with different ways of faking intellectual deficits and non-malingering were compared.

Results: (1) The scores on all dimensions, the total score, and the Intelligence Quotient (IQ) of RSPM in subjects with malingering were significantly higher than in those with no-malingering. (2) There were significantly differences on the total score and IQ of RSPM among all groups with different degrees for faking intellectual deficits and non-malingering. The less scores of BFDMT, the less scores of RSPM. (3) The scores of all dimensions and total score of BFDMT had significantly positive correlation with the scores of all dimensions, the total score and IQ of RSPM.

Conclusion: BFDMT is helpful for detecting the true degree of the performance of intelligence tests in patients with financially compensable head injuries.

References:


NR854 Thursday, May 22, 12:00 p.m.–2:00 p.m.

Residential Rehabilitation Treatment for Combat-Related PTSD-Outcome

Daniella David, M.D., Department of Psychiatry, Miami VAMC, 1201 N.W. 16th Street, Unit 116A12, Miami, FL 33125; Cathara Fuller, Ludmila B. De Faria, M.D.

Educational Objectives:

At the conclusion of this session, the participant should recognize that veterans with chronic PTSD respond to rehabilitation treatment, however symptom severity measures may not be the best outcome evaluations for this population.

Summary:

Objective: The outcome efficacy of intensive rehabilitation treatment for chronic, combat-related PTSD has been questioned in previous studies. While symptom severity measures do not necessarily show significant improvement, functional outcome measures have been reported to improve. The goal of this study is to evaluate the changes in severity of depression, anxiety and PTSD symptoms, and in mental and physical health perceptions and functionality, as reported by veterans who completed a residential rehabilitation program for chronic PTSD.

Methods: Subjects are 131 male veterans with a primary diagnosis of PTSD, who were admitted over a two-year period and completed the full length of the program. Mean age was 54.1 ± 6.4 years, 44.3% were white, 34.4% were black, and 21.4% were Hispanic. Patients completed the Beck Depression and Anxiety Inventories (BDI and BAI), the Mississippi scale for combat-related PTSD (M-PTSD), and the SF-36 upon admission to the program, at discharge and at four to six months follow-up. Follow-up data are presently being collected and scored. Differences in BDI, BAI, M-PTSD and SF-36 scores between admission and discharge were analyzed by paired t-tests. Once follow-up data are complete, ANOVA will be used to compare the three time points.

Results: No significant changes were found in BDI and BAI scores between admission and discharge, while the M-PTSD scores were higher on discharge (133.9 + 17.3 vs 136.5 + 18.8, t=2.1, df=115, p=.04). SF-36 subscales showed significant improvement in emotional role (21.9 + 3.0 vs 38.6 + 5.2, t=2.6, df=53, t=.01), mental health perception (24.5 + 16.6 vs 31.6 + 18.7, t=2.6, df=53, t=.01), and vitality (t=21.1 + 18.6 vs 27.2 + 20.6, t=2.6, df=53, t=.01).
2.1, df=53, \( t=0.04 \)), and worsening in physical health perception (41.8 + 27.7 vs 34.0 + 27.4, \( t=2.9, \) df=55, \( p=0.006 \)).

Conclusion: Residential treatment for chronic, combat-related PTSD is associated with no change or worsening in symptom severity measures and physical health perception. However, functional measures of mental health show significant improvement. Possible explanations for these findings will be discussed.

References:

NR855 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Community Terror: Hospital Staff Responses to a Series of Sniper Shootings
Thomas A. Grieger, M.D., Department of Psychiatry, Uniform Services University, 4301 Jones Bridge Road, Bethesda, MD 20814; Robert J. Ursano, M.D., Carol S. Fullerton, Ph.D., David M. Benedek, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the psychological and behavior changes associated with the terrorism of random sniper shootings.

Summary:

Introduction: This study determined emotional and behavioral effects on hospital staff following a three-week series of sniper shootings in the Washington, D.C. area.

Method: Employees of a large tertiary care hospital were anonymously surveyed regarding their attitudes, perception of safety, symptoms of acute stress disorder (ASD), depression, and alcohol use the week following capture of the suspects.

Results: There were 382 participants, 55% female, average age 39.0 years, 62.1% were married, and 60.5% had children. Twenty-four (6.3%) met criteria for ASD, 13 (3.4%) endorsed increased alcohol use, and 31 (8.1%) were depressed. Risk factors for ASD were female sex, increased alcohol use, comorbid depression, lower perception of safety, high levels of perceived threat, and higher levels of peri-traumatic dissociation, and decrease in activities outside the home. Those with depression were more likely to endorse increased alcohol use, lower perception of safety and higher levels of peri-traumatic dissociation.

Conclusions: The sniper shootings resulted in substantial changes in perceived safety and threat assessment as well as decrease in behaviors outside the home in an employed, highly educated, hospital staff. Levels of ASD were similar to levels of PTSD in New York City following the 11 September 2001 terrorist attack.

References:
Response rate was 80%. The questionnaire included question on demographics, sickness absence, as well as questions based on the General Nordic Questionnaire for Psychological and Social Factors at Work.

Results: Majority (86%) of the employee were women, middle aged, with 33% in the age range of 40 to 49 year of age. Never absent from work in the past 12 months due to sickness were 25% of the employees. Complaining of stress was associated with sickness absence (p<0.0001). However, variable work-pressure was very significantly associated with increased sickness absence (p=0.002). Furthermore, harassment was significantly associated with sickness absence. Relaxed and comfortable work-morale was associated with reduced sickness absence (p<0.001).

Conclusions: Reducing mental distress in general, with special efforts in fighting harassment at work and variable work-pressure is likely to improve mental health in general and reduce number of sick-days.

References:

NR859 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Decision-Making Impairment in Suicide Attempters Supported by Lilly-France
Fabrice Jollant, M.S., Department of Psychiatry, Lapeyrone Hospital, 371 Avenue Du Doyen G Giraud, Montpellier Cedex 34295, France; Frank Bellivier, M.D., Regis Verdier, M.D., Marion Leboyer, M.D., Alain Malafosse, Ph.D., Didier Castelnau, M.D., Philippe Courtet, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to admit a neuropsychological vulnerability to suicidal behavior.

Summary:
Suicidal behavior (SB) remains incompletely understood. The stress-diathesis model suggested that a deficit in serotonergic projections to orbitofrontal cortex is involved in the vulnerability to SB. This specific area has been implicated in decision making, a cognitive function concerned with complex choices that could be under serotonergic modulation. We aimed at assessing decision making in suicide attempters.

Method: We used the Iowa Gambling Task to investigate patients with a history of violent (N = 32) or non-violent (N = 37) SB, patients suffering from affective disorders without a history of SB (N = 25), and healthy controls (N = 82). All patients were seen out of a current Axis-I disorder.

Results: Both suicide attempters groups had significantly lower scores than healthy controls, and violent suicide attempters performed significantly worse than affective controls (p = 10\(^{-6}\)). There were no significant differences between each suicide attempters group and between each control group. The differences in performances could not be explained by gender, age, NART, level of education, number of SB, age of first SB, Axis-I diagnosis, or medications.

Conclusion: A decision-making impairment could represent a neuropsychological deficit in some suicide attempters and an intermediate phenotype in further genetic studies. Replication is needed.

References:
NR861 Thursday, May 22, 12:00 p.m.-2:00 p.m.
5HT Transporter Polymorphism and Suicidal Behavior in Brazil
Humerto Correa, M.S.C., Department of Pharmacology, UFMG-ICB/Biological Institute, AV Antonio Carlos 6621, Belo Horizonte, MG 31280-907, Brazil; Ana C. Campi-Azevedo, M.Sc., Melissa Machado, M.D., Luis A. Marco, Ph.D., Victor V. Lima, M.D., Wolfgang Boson, Marco A. Romano-Silva, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize the importance of genetic factor in suicide behavior.

Summary:
Central serotonergic dysfunction and genetic factors are associated with suicidal behavior in psychiatric patients. The objective of this study was to examine the association between suicidal behavior and a functional polymorphism within the promoter region of the serotonin transporter, where the presence of the short allele (S), as compared with the long allele (L), was found to be associated with a lower level of expression of the gene. Subjects were 131 schizophrenic, 45 with a lifetime history of suicide attempt (34.3%), 106 major depressed, 48 with a lifetime history of suicide attempt (45.2%), and 75 healthy controls. Diagnoses were based on a structured interview (MINI-PLUS), according DSM-IV criteria, and patients underwent a semi-structured interview for suicide history assessment. Chi-square was used to compare frequencies. We could find that the presence of the short allele genotypes (Ls + SS) was significantly associated with violent suicide attempt: LL (7/33, 21.2%) versus LS + SS (31/60); P = 0.004. The short allele genotypes were also associated with more lethal suicide attempts (scores greater than 2 in the Beck suicide attempt lethality scale): LL (11/33, 33.3%) versus LS + SS (33/60, 55%); p<0.05. These data show that a change in expression of the gene encoding the 5-HT transporter may be involved in violent and more lethal suicide behavior.

References:
4. We are indebted to the patients and their families for their participation in this study.
5. The study was supported by a grant from the National Institute of Mental Health (MH 48546).
NR865 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Depression in Elderly Patients With Attempted Suicide
Carlos A. Finkelsztein, M.D., Department of Psychiatry, Hospital Italiano, Gascon 450, Buenos Aires, Argentina; Daniel Matusevich, M.D., Eugenia Dabi, M.D.

Educational Objectives:
- At the conclusion of this session, the participant should be able to demonstrate the misdiagnoses and wrong treatment of Depression in elderly patients at high risk for commit suicide in Argentina population.

Summary:
- Objective: We analyze the presentation and duration of symptomatology and the treatment received by depressed patients prior to their suicide attempt.
- Method: This is a retrospective study using data from the medical records of patients -over 60- who were hospitalized for attempted suicide in Hospital Italiano, Buenos Aires (1999 to 2002).
- Diagnoses: DSM-IV criteria (by 2 trained GPs) and MMPI, Rorschach, and HDS.

Results:
- Initial symptomatology was: asthenia, weight loss, anhedonia and hopelessness. 83% with one to six months of duration. Patients who were under treatment with a psychiatrist (45.8%) were receiving: seven adequate antidepressant doses (100% with SSRI), 3 insufficient doses (Tricyclic), and one no AD at all. 100% were on BDZ. 63% with neuroleptics. Of the remaining 13 patients, 11 were under treatment with a GP. This group were receiving: two the right antidepressant therapy (SSRI), 1 insufficient doses of Amtriptyline, and eight were under no antidepressant therapy (72.7%). Six of these eight patients received BDZ and 1 was medicated with haloperidol.

Conclusions: The entire group taken into account, were not receiving the right treatment for Major Depressive Disorder. The duration of the depressive symptomatology prior to the attempt was long enough to be detected.

References:
NR867 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Post-Traumatic Symptoms in a Sample of the Kosovar Population
University Hospitals of Geneva
Ariel Eytan, M.D., Department of Psychiatry, Hug-Belle-Idee, 2 CH Petit-Bel-Air, Geneva 1225, Switzerland; Patrick A. Bovier, M.D., Marianne Gex-Fabry, M.Sc., Letizia Foscani, M.D., Louis Loutan, M.D., Liza Deroo, M.Sc.

Objectives: To describe the relationship between adverse childhood experiences and unexplained medical symptoms in adult patients in primary care.

Summary:
At the conclusion of this session, the participants should be able to describe the relationship between adverse childhood experiences and unexplained medical symptoms in adult patients in primary care.

References:

NR868 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Adverse Childhood Experiences and Unexplained Medical Symptoms
Daniel P. Chapman, Ph.D., Health and Aging Branch, Center for Disease Control, 4770 Buford Highway N.E., MS K45, Atlanta, GA 30341; Robert F. Anda, M.D., Maxia Dong, Shanta R. Dube, M.P.H., Valerie J. Edwards, Ph.D., Vincent J. Felitti, M.D.

Educational Objectives:
At the conclusion of this session, the participants should be able to describe the relationship between adverse childhood experiences and unexplained medical symptoms in adult patients in primary care.

Summary:
At the conclusion of this session, the participants should be able to describe the relationship between adverse childhood experiences and unexplained medical symptoms in adult patients in primary care.

NR866 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Acute Cognitive Effects of Hydrocortisone in PTSD Supported by the National Institute of Mental Health
Robert A. Grossman, M.D., Department of Psychiatry, Mt. Sinai Medical Center, One Gustave Levy Place, Box 1230, New York, NY 10029; Rachel Yehuda, Ph.D., Julia A. Goller, M.D., Philip D. Harvey, Ph.D., Nelly Santa Maria, Ph.D., Sarah Halligan, Ph.D.

Educational Objectives:
At the conclusion of this session, the participants should be able to recognize the traumatic impact of war-related events on a civilian Kosovar population sample two and a half years after the end of the conflict.

Summary:
A cross-sectional survey was conducted among 300 households in eight municipalities of Kosovo between September and November 2001. A total of 996 persons over age 15 agreed to participate. Prevalence of PTSD was established using the Mini International Neuropsychiatric Interview (MINI) locally translated in Albanian. Questions about traumatic events were adapted from the Harvard Trauma Questionnaire (HTQ). A total of 234 individuals (23.5%) fulfilled the diagnostic criteria for current PTSD. Presence of this disorder was significantly associated with exposure to combat situation, having been close to death, murder of family member or friend, forced separation from family, and to combinations of such events. Other factors significantly associated with current PTSD were being female, coming from the municipality of Decani (which was especially affected by guerilla war), low education level, low economic status, and low perceived general health. We compared for traumatic stress reactions those who remained in Kosovo throughout the conflict with those who sought temporary asylum in a safe country. The impact of asylum on symptoms is complex and is probably linked with living conditions and duration of stay in host country. These results will be discussed in the light of contemporary conceptual frameworks of trauma related to torture and mass human rights violations.

References:
of childhood abuse or household dysfunction they reported. Unexplained medical symptoms were defined as symptoms noted in the patient’s medical record under a standardized review of systems without a corresponding disease diagnosis.

Results: Across all five organ systems assessed (respiratory, gastrointestinal, central nervous system, cardiovascular, and musculoskeletal), mean ACE scores were positively associated with the number of unexplained medical symptoms (p<.001), the number of organ systems involved in unexplained medical symptoms (p<.001), and with the mean number of doctor visits in the preceding year (p<.001).

Conclusions: These results suggest assessment for adverse childhood experiences could prompt earlier referral for evaluation of symptoms which may have their roots in traumatic stressors of childhood.

References:

NR869 Thursday, May 22, 12:00 p.m.-2:00 p.m. 
Sleepless in America: Population Prevalence and Correlates
Daniel P. Chapman, Ph.D., Health and Aging Branch, Center for Disease Control, 4770 Buford Highway N.E., MS K45, Atlanta, GA 30341; Matthew M. Zack, M.D., David C. Morlarity, B.S.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the prevalence of impaired sleep and identify its correlates in the general population.

Summary:
Objectives: Sleeplessness is associated with a variety of psychiatric disorders and treatments and with impaired health and functioning in affected individuals. Although the deleterious consequences of sleeplessness have been widely studied in clinical samples, less is known about its prevalence and correlates in the general population.

Method: Subjects were 42,632 adults aged 18 years and older who responded to the Health-Related Quality of Life Module of the 1995–1997 Behavioral Risk Factor Surveillance System, a telephone survey assessing demographic, behavioral, and health characteristics. Respondents reported the presence of activity limitations and their cause and duration. Respondents also estimated the number of days during the past 30 days when they did not get enough rest or sleep, experienced pain, depression, or anxiety.

Results: Respondents reported an average of 7.6 days affected by sleeplessness, with the mean number of days varying inversely with age. Respondents aged 18–24 years reported an average of 10.0 sleep-impaired days, while those aged 75 years and older reported 3.9 days. Activity limitation caused by depression or other emotional disorder was associated with a greater number of sleep-impaired days (13.4) than activity limitations caused by cancer, arthritis (11.0, 8.8, respectively) or no activity limitation (7.2).

Conclusions: Sleeplessness is widely reported in the U.S. population and is associated with demographic and health-related characteristics. The elevated number of sleep-impaired days among respondents reporting activity limitation due to depression or other emotional disorder provides population-based corroboration of the importance of monitoring sleeplessness in the clinical management of psychiatric disorders.

References:

NR870 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Neurosteroids and Suicidality in PTSD
Supported by VA Health Services Research and Development
Marian I. Butterfield, M.D., Department of Psychiatry, Duke-Durham VAMC, 508 Fulton Street, Suite 116A, Durham, NC 27705; Karen M. Stechuchak, M.A., Courtney Mackven, Jonathan R.T. Davidson, M.D., Christine E. Marx, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to (1) define neurosteroids and discuss potential alterations in PTSD, and (2) discuss potential relationships between neurosteroids and suicidality in PTSD.

Summary:
Objectives: Recent studies suggest neurosteroids (steroids synthesized de novo in the brain) may be altered in PTSD. It is not clear if these alterations are related to PTSD symptoms. Because high rates of suicidality are noted in PTSD, we examined neurosteroid levels and correlations to suicidality in veterans with PTSD.

Methods: Veterans (n=130) with PTSD were consecutively enrolled from a psychiatric inpatient unit. We assessed whether study participants had experienced suicidal ideation or had attempted suicide during the six months prior to study interview. Serum from morning blood draws was used to determine neurosteroid levels across one biosynthetic pathway (dehydroepiandrosterone (DHEA) → androstenedione → testosterone → estradiol) using standard radioimmunoassays. Bivariate associations between neurosteroids and suicidality were examined by Wilcoxon rank sum statistics. Control variables considered in the analyses were age, alcohol use, childhood sexual and physical trauma, and smoking. Logistic regression analyses were conducted.

Results: High rates of suicidality were noted: 70% had suicidal thoughts and 26% had attempted suicide. Those who had attempted suicide compared to those who had not demonstrated significantly higher levels of DHEA (16.6 vs 11.7 ng/ml, p=0.02) and estradiol (28.2 vs 23.8 pg/ml, p=0.03). Younger age was associated with attempted suicide (p=0.02); no relationship was observed for smoking status, alcohol disorder or childhood trauma. After adjusting for age in the logistic model, DHEA remained associated with attempted suicide (p=0.0556).

Conclusions: This research suggests that higher levels of DHEA may be linked to suicidality in veterans with PTSD.

References:
Bartenders and Hairdressers as Natural Helpers After 9/11

Daniel Z. Lieberman, M.D., Department of Psychiatry, George Washington University, 2150 Pennsylvania Avenue, N.W., Washington, DC 20037; James C. MacIntyre II, M.D., Lawrence S. Wissow, M.D., Rebecca A. Powers, M.D., David B. Pruitt, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to describe the ways in which the terrorist attacks of 9/11 impacted bartenders and hairdressers in terms of their role as natural community helpers.

Summary:

Objective: Pathological emotional responses to trauma can paradoxically lead to reluctance to engage in treatment. Some people may feel more comfortable discussing emotional reactions with members of the community, such as bartenders or personal service providers, who are referred to as "natural helpers," and can serve as de facto caregivers. The purpose of this study was to learn more about the role of these helpers, and their reactions, following the attacks of 9/11.

Method: A brief questionnaire was developed. Bartenders and hairdressers were contacted by telephone, and asked how the 9/11 attacks affected their business, their interactions with customers, and whether they suffered adverse reactions to filling the role of natural helper in a disaster environment. Librarians were used as a control.

Results: 37 bartenders, 48 hairdressers, and 48 librarians agreed to participate in the study. Compared with librarians, significantly more hairdressers and bartenders reported that their customers wanted to talk about their emotional reactions to the attacks, that it was difficult for them to talk to so many people about this topic, and that they tried to avoid the topic with others because of so much exposure at work. Hairdressers reported missing significantly more days of work compared with librarians because the work environment reminded them of 9/11.

Conclusion: Bartenders and hairdressers reported an increased desire among their customers to talk about their emotional reactions to the 9/11 attacks, and experienced some adverse emotional effects.

References:


The Long-Term Follow-Up of the Survivors of a Major Disaster: The Impact of the Media and Legal Proceedings

Alistair M. Hull, M.B., Department of Research, Center for Trauma, Royal Cornhill Hospital, Aberdeen 4401224, Scotland; David A. Alexander, Ph.D., Susan Klein, Ph.D.

Educational Objectives:

At the conclusion of this presentation participants will understand the impact of media and legal proceedings after major traumatic events.

Summary:

Objective: To identify the impact of media and legal factors on the long-term outcome of survivors of a major offshore disaster.

Method: All survivors of the Piper Alpha oil platform disaster were invited for interview, and completed questionnaires (GHQ-28, IES-R, PTSS-12 & HS), a diagnostic interview (CAPS-DX) and a semistructured interview ten years after the disaster. 46 survivors were located (78%) and 36 (78%) completed the study.

Results: Survivors with feelings of hopelessness at follow-up were significantly more likely to have been made to feel guilty about compensation (p=0.01) or to have read the legal inquiry report (p=0.03). 92% of survivors gave interviews and whilst no specific aspect of media experience was statistically associated with outcome 42% describing the media as very intrusive, and 40% regretted giving an interview.

Conclusions: The media and legal proceedings play important roles in societies response to traumatic events. These results confirm the overall negative effect of the media, compensation proceedings and legal inquiries after a disaster. Those involved in the response to traumatic events must be aware of all areas that may effect outcome of survivors of major disasters.

References:


NR874 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Terror at Sea: Dissociation and PTSD After the Near Sinking of a Research Submarine
Jennifer S. Berg, M.D., Department of Mental Health, Naval Medical Center, 34800 Bob Wilson Drive, Suite 108, San Diego, CA 92134-5000; Thomas A. Grieger, M.D., James L. Spira, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to describe the emotional and behavioral effects on submarine crew members following the flooding and near-sinking of their submarine and dangerous rescue.

Summary:
Objective: This study examined posttraumatic stress disorder, depression, alcohol use, and perceived safety in 20 submariners who survived the flooding and near-sinking of their submarine.

Methods: Volunteers were anonymously surveyed to assess the effect of past experience, trauma exposure, initial emotional response, and peritraumatic dissociation on probable PTSD, depression, alcohol use, and perceived safety.

Results: The 20 subjects were all male, average age 22 years. Over 30% experienced an initial reaction of physical danger, a fear of death on the ship, and an initial fear of drowning. 35% were injured. Seven months following the trauma 10% (N=2) met criteria for PTSD, 5% (N=1) endorsed a temporary increase in alcohol use, and 0% endorsed depression. Only 15% reported their perception of safety aboard the submarine as "moderate or less". In comparing the PTSD subjects with the others, there were no statistical differences (due to the small number). Descriptive differences occurred.

Conclusions: Despite a high level of exposure to physical danger and possible death, only two of 20 survivors rescued from the ocean report PTSD. All subjects denied depression, and 85% reported high sense of safety, possibly due to unit cohesion and emergency training.

References:

NR875 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Thyroid Hormone Levels and Psychological Symptoms in Sexually Abused Girls
Mark G. Haviland, Ph.D., Department of Psychiatry, Loma Linda University, 11374 Mountain View Avenue, Loma Linda, CA 92354-3842; Janet L. Sonne, Ph.D., Donald L. Anderson, M.D., Jerome C. Nelson, M.D., Clare Sheridan, M.D., Joy M. Gardner, B.S., Esther I. Carlton, M.T., William G.C. Murdoch, M.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to understand the relationship between thyroid hormone concentrations and psychological symptoms (depression, general distress, and post-traumatic stress disorder) in sexually abused adolescent girls.

Summary:
Objective: To examine the power of peritraumatic dissociation, posttraumatic distress, and acute stress in predicting PTSD symptoms in a sample of industrial disaster survivors.

Method: An explosion of a factory caused the death of 30 people and injured 2,798. A total of 224 injured survivors were hospitalized in two emergency departments. Severity of exposure was assessed with an item measuring physical proximity to the explosion (1=other places; 2=within a few blocks of the factory; 3=inside the factory). The Injury Severity Score (mean ISS=3.9±3.6) was obtained from medical reports. The 224 participants were assessed with the Stanford Acute Stress Reaction Questionnaire 5–10 weeks posttrauma. They were reassessed six months posttrauma with the Peritraumatic Dissociative Experiences Questionnaire.

References:

NR876 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Predictors of PTSD Symptoms in a Sample of Industrial Disaster Survivors
Philippe J.R., Birnes, M.D., Department of Psychiatry, Hospital Casselardit, 170 Avenue De Casselardit, Toulouse F-31059, France; Dominique Coppin-Calmes, M.D., Alain Brunet, Ph.D., Nathalie Vinnemann, M.D., Henri Juchet, M.D., Dominique Lauque, M.D., Laurent J. Schmitt, M.D.

Educational Objectives:
At the conclusion of this session, the participant should recognize peritraumatic and acute traumatic predictors of PTSD symptoms.

Summary:
Objective: Among the neurobiological changes following extreme stress are thyroid hormone alterations. The purpose of the present study was to evaluate thyroid hormone concentrations and explore the relationships between these hormones and psychological symptoms in adolescent girls who have experienced sexual abuse.

Method: The sample included 22 adolescent girls ranging in age from 12 to 18 years. In addition to having their blood drawn, subjects completed three psychological tests (depression, general distress, and posttraumatic stress disorder [PTSD]).

Results: Girls' average free T4 total T4, free T3, total T3, and TSH levels were within laboratory reference limits, as were most individual concentrations. Free and total T3 concentrations, however, were correlated with several psychological test scores. The strongest correlations were between free T4 and PTSD total score, PTSD—avoidance/numbing, and general distress (respective rs = –0.50, –.49, and –.48; ps < .05) and between total T4 and depression, general distress, and PTSD—arousal (rs, respectively = –.46, –.45, and –.44; ps < .05).

Conclusion: Variations in thyroid hormone levels—even those within standard reference range limits—may have important clinical correlates. Moreover, these findings are consistent with interpretations of prisoner of war data where adaptation appears to be toward conservation-withdrawal versus fight-flight.
naire, the Peritraumatic Distress Inventory, and the Posttraumatic Stress Disorder Checklist Scale. Correlational analyses and a multiple linear regression were conducted.

Results: All of the early predictors were significantly correlated with later PTSD symptoms. Together, peritraumatic dissociation, peritraumatic distress, and acute stress symptoms accounted for 66% of the variance in PTSD symptoms.

Conclusion: This replicates the findings that peritraumatic dissociation, peritraumatic distress, and acute stress are robust predictors of PTSD. Such symptoms may be useful for identifying an early stage individuals at highest risk of remaining symptomatic.

References:

NR877 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Self-Esteem in Eating Disorder Patients and Social Phobia Patients

Renate Eiber, M.D., Psychiatry I, General Hospital, 100 rue Leon Cladel BP 765, Montauban, France; Luis Vera, Ph.D., Christine Mirabel-Sarron, M.D., Julien D. Guelfi, M.D.

Educational Objectives:
At the conclusion of this session, participants should be able to recognize different aspects of self-esteem in eating disorders and social phobia and focus cognitiv and behavioural treatment

Summary:

Background: Low self-esteem is a transnosographical concept, a core feature in eating disorders (ED). Aims: Assessing self-esteem and levels of anxiety and depression in anorectic and bulimic patients. Addressing qualitative differences of self-esteem between ED and social phobia patients (SPP).

Methods: 33 restrictive anorectics, 34 anorectics-bulimics, 36 bulimics and 26 SPP diagnosed according DSM IV criteria and investigated by the Self-Esteem Inventory Set (Coopersmith), the Rathus scale, the Fear Survey Schedule FSS III (Wolpe) and the Beck Depression Inventory (BDI).

Results: Self-esteem is reduced in the two patient groups. 86.1% of the total sample and 84.5% of the ED patients have a very low self-esteem. ED patients have significantly higher scores in the Social (p=0.016) and Professional (p=0.0225) sub-scales of the SEI, on the Rathus scale (p=0.0013), on the BDI (p=0.0003), and lower FSS III scores (p=0.0001) than SPP. ED patients with depressive cognitions do not differ from SPP with depressive cognitions by self-esteem. Self-esteem is not influenced by the Body Mass Index (BMI).

Conclusion: This new research included anorectics patients. The two previous studies concerned only a small sample bulimia nervosa. We have also compared the ED patients to social phobia: they differ significantly from SPP in their characteristics of social phobia and self-esteem.

References:

NR878 Thursday, May 22, 12:00 p.m.-2:00 p.m.
The Effects of Cognitive-Behavior Therapy Training on Clinical Practice

Hinda F. Dubin, M.D., Institute of Psychiatry, University of Maryland, 701 West Pratt Street, Baltimore, MD 21215-1023; Lisa B. Dixon, M.D., Erika Warten, M.D.

Educational Objectives:
At the conclusion of this session, the participant recognize the impact of a formal cognitive-behavioral therapy (CBT) training program in producing psychiatrists who will actively practice the highly effective modality of CBT.

Summary:

Introduction: Cognitive-behavioral therapy (CBT) is an evidence-based treatment for anxiety and depression. The ACGME now requires that residents demonstrate competency in CBT resulting in increased CBT training. Whether this additional training will translate to greater delivery of CBT in practice is uncertain. This study thus assessed and compared CBT training of psychiatrists and psychologists and the extent to which CBT training correlated with clinical practice.

Method: A 12-item questionnaire assessing amount of CBT training and percentage of time spent practicing CBT was sent to 200 randomly selected members of the Maryland Psychiatric Society and Maryland Psychological Association. The response rate was 50% for M.D.s and 57% for Ph.D.s.

Results: Ph.D.s reported receiving far more hours of CBT training than M.D.s (p<0.0001). Ph.D.s were more likely to report using CBT in practice (83% vs. 47%, p<0.001). Both M.D.s and Ph.D.s who currently practiced CBT reported more training in CBT, both early in their training period and after their formal training period was completed (p<0.01). The most common barrier preventing use of CBT by M.D.s was lack of training.

Conclusions: These data suggest that CBT training for psychiatrists will lead to greater use of this effective psychotherapeutic modality.

References:

NR879 Thursday, May 22, 12:00 p.m.-2:00 p.m.
The Effectiveness of Behavioral Treatment for Weight Loss in Patients With Schizophrenia

Supported by Janssen Pharmaceutica Products, L.P.

Rohan Ganguli, M.D., Department of Psychiatry, UPMC Health System, 3900 O’Hara Street, Pittsburgh, PA 15213-2593; Gahan J. Pandina, Ph.D., Sally A. Berry, M.D., Ibrahim Turkoz, M.S., Ramy A. Mahmoud, M.D., Jaspreet Brar, M.D.

Educational Objectives:
At the conclusion of this session, participants should be able to evaluate the effectiveness of a non-pharmacological, group-based behavioral treatment program for weight reduction that can be incorporated into most outpatient settings that treat patients with chronic psychotic illnesses.

Summary:

Objective: To evaluate the efficacy of a group-based behavioral treatment for weight loss in overweight and obese patients suffering from schizophrenia.

Methods: Seventy-two overweight/obese patients (BMI > 26) with DSM-IV schizophrenia or schizoaffective disorder were en-
rolled in a 14-week, multicenter weight reduction study. Patients were randomly assigned to either receive behavioral treatment for weight reduction (BT, n= 35) or usual care (UC, n = 37). Those assigned to the BT group attended 20 group sessions, during which they were taught various calorie intake reduction techniques. Those assigned to the UC group were weighed at baseline and at four-week intervals, but were given no special advice about weight reduction.

Results: Mean weight loss was numerically but not significantly higher in the BT versus the UC group (BT = −1.95 kg ± 3.79, non-BT = −1.08 kg ± 3.11). There was a trend for a larger proportion of patients in the BT group to lose ≥5% of their body weight versus the non-BT group (n=32.1% vs. 10.8%, p= 0.082). This trend was stronger for completers (36.0% vs. 16.0%, p=0.062).

Conclusion: This pilot study demonstrates that this behavioral treatment may be an effective non-pharmacological alternative for weight reduction in patients with chronic psychotic illnesses.

References:

NR880 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Rivastigmine Treatment With Slow Titration Improves Behaviors in Alzheimer’s Disease
Supported by Novartis Pharmaceuticals Corporation

Steven G. Potkin, M.D., Department of Psychiatry, University of California, Irvine, BIC Irvine Hall, Room 166, Irvine, CA 92697-3960; Barbara Kouramases, M.D., Arian Robinowicz, M.D., James S. Lee, Ph.D.

Educational Objectives:
At the conclusion of this session, the participant should be able to demonstrate that most behaviors improve significantly with rivastigmine treatment over 6-months with a slow titration schedule in mild to moderately severe Alzheimer’s disease

Summary:
Introduction: Alzheimer’s disease patients frequently present with prominent behavioral disturbances causing significant distress for patients and caregivers. These behavioral symptoms are usually progressive and play a key role in the decision to institutionalize.

Methods: The behavioral efficacy of rivastigmine was evaluated in a 6-month, or en-label, multi-center study employing a four-week minimum titration schedule. 147 outpatients aged 50 to 85 (mean 75) with mild to moderately severe Alzheimer’s disease were enrolled. Following a minimum of four weeks at the initial dose of 1.5 mg capsules bid, patients were titrated to their highest tolerated dose, ≤12 mg/day. The Behavioral assessment instrument was the NPI-12.

Results: Baseline mean NPI-12 score was 11.5. Preliminary results show statistically significant improvement in NPI-12 scores compared to baseline at Months 3 and 6. Improvement in behaviors at Month 3 was a mean change from baseline in total NPI-12 score of −1.9 points (p=0.02). At Month 6, sustained benefits were observed, with mean change from baseline in total NPI-12 score of −2.3 points (p=0.01). Also at Month 6, 11/12 symptoms indicated improvement or no decline from baseline.

Conclusion: These preliminary data indicate that most behaviors improve significantly with rivastigmine treatment over six months with a slow titration schedule.

References:

NR881 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Donepezil’s Global Benefits in Vascular Dementia Versus Patients With Alzheimer’s Disease
Supported by Eisai Inc., Pfizer Inc.

Stephen P. Salloway, M.D., Department of Neurology, Butter Hospital, 345 Blackstone Boulevard, Providence, RI 00290; Raymond D. Pratt, M.D., Carlos A. Perdomo, M.S.

Educational Objectives:
At the conclusion of this session, the participant should recognize differences in the treatment response to donepezil versus placebo in patients with Alzheimer’s disease compared with those with vascular dementia, as assessed by the CIBIC-plus.

Summary:
Introduction: The CIBIC-plus is a global assessment designed for Alzheimer’s disease (AD), which evaluates cognition, behavior, and activities of daily living (ADL), on a seven-point scale. Since disease progression in AD differs from vascular dementia (VaD), outcomes on the CIBIC-plus may also vary.

Methods: Data are presented for two 24-week studies in patients with probable or possible VaD (NINDS-AIREN criteria), and 10 similar studies in patients with probable AD (NINCDS-ADRDA criteria). Patients were randomized to receive placebo, or 5 or 10 mg/day donepezil.

Results: Most placebo-treated VaD patients showed no change on the CIBIC-plus, with similar proportions improved or worsened at Week 24 (Table 1). Conversely, most placebo-treated AD patients worsened. In the donepezil-treated groups, a greater proportion of VaD than AD patients improved, whereas more AD than VaD patients worsened.

Conclusions: Donepezil-treated AD and VaD patients demonstrated significant benefits in cognition, behavior and ADL, as assessed by the CIBIC-plus, compared with placebo. The lack of deterioration in placebo-treated VaD patients means, in contrast to AD, treatment benefits in VaD are driven by improvement rather than stabilization or decreased decline.

References:
Table 1: CIBIC-plus scores following 24 weeks of treatment with donepezil or placebo

<table>
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<tr>
<th></th>
<th>Placebo (n=322)</th>
<th>5mg/day (n=327)</th>
<th>10 mg/day (n=306)</th>
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<td>Improvement (%)</td>
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<td>41**</td>
<td>33†</td>
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<tr>
<td>No change (%)</td>
<td>41</td>
<td>38</td>
<td>40</td>
</tr>
<tr>
<td>Worsening (%)</td>
<td>30</td>
<td>21</td>
<td>27</td>
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AD

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<tr>
<th></th>
<th>Placebo (n=468)</th>
<th>5mg/day (n=457)</th>
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<tr>
<td>Improvement (%)</td>
<td>16</td>
<td>31**</td>
<td>27**</td>
</tr>
<tr>
<td>No change (%)</td>
<td>35</td>
<td>32</td>
<td>37</td>
</tr>
<tr>
<td>Worsening (%)</td>
<td>49</td>
<td>37</td>
<td>35</td>
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</table>

†P=0.072; **P<0.001 versus placebo

NR882 Thursday, May 22, 12:00 p.m.-2:00 p.m.

Donepezil Provides Significant Benefits in Patients With Vascular Dementia
Supported by Eisai Inc., Pfizer Inc.

Stephen P. Salloway, M.D., Department of Neurology, Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906; Raymond D. Pratt, M.D., Carlos A. Perdomo, M.S.

Educational Objectives:

At the conclusion of this session, the participant should appreciate the cognitive and global benefits of donepezil treatment in patients with vascular dementia.

Summary:

Introduction: Vascular dementia (VaD) accounts for approximately 10% to 20% of all dementia cases. There are currently no approved treatments for the cognitive symptoms of VaD. However, there is evidence that patients with VaD may benefit from treatment with cholinesterase inhibitors such as donepezil.

Methods: A combined analysis of two randomized, 24-week clinical trials of donepezil in VaD patients. Patients received placebo, donepezil 5 mg/day or donepezil 10 mg/day (5 mg/day for the first 28 days and 10 mg/day thereafter). Results are reported for intent-to-treat observed cases.

Results: A total of 1219 patients were enrolled (placebo n=392, donepezil 5 mg/day n=406, donepezil 10 mg/day n=421). Both donepezil-treated groups showed significant improvements in cognitive function compared with placebo (ADAS-cog least-squares (LS) mean change from baseline score at Week 24: placebo, -0.10; donepezil 5 mg/day, -1.18; P<0.001; donepezil 10 mg/day, -2.38, P<0.001). Significant benefits versus placebo in global function were observed in the donepezil 5 mg/day group (CIBIC-plus, % patients showing improvement at Week 24: placebo, 23%; donepezil 5 mg/day, 41%, P<0.001; donepezil 10 mg/day, 53%, P=0.07, overall P=0.001) and the donepezil 10 mg/day group (CDR-SB, LS mean change from baseline score at Week 24: placebo, 0.10; donepezil 5 mg/day, -0.11; donepezil 10 mg/day, -0.33, P=0.002).

Conclusions: Significant benefits of donepezil compared with placebo treatment were observed on measures of cognition and global function. These results indicate that donepezil may have an important role in the management of patients with VaD.

References:

NR883 Thursday, May 22, 12:00 p.m.-2:00 p.m.

Donepezil Is Well-Tolerated in Patients With Vascular Dementia
Supported by Eisai Inc., Pfizer Inc.

Stephen P. Salloway, M.D., Department of Neurology, Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906; Raymond D. Pratt, M.D., Carlos A. Perdomo, M.S.

Educational Objectives:

At the conclusion of this session, the participant should recognize that donepezil is well tolerated in both vascular dementia (VaD) and Alzheimer’s disease (AD) patients.

Summary:

Introduction: There is evidence to suggest that patients with vascular dementia (VaD) exhibit a cholinergic deficit similar to that observed in Alzheimer’s disease (AD). Therefore, patients with VaD may benefit from treatment with cholinesterase inhibitors, such as donepezil.

Methods: Incidences of adverse events (AEs) across placebo, donepezil 5 and 10 mg/day groups were compared using combined data from two randomized, double-blind, 24-week studies in VaD patients, and ten similar studies in patients with AD.

Results: Withdrawals due to AEs were low in VaD (placebo n=392, 10%; donepezil 5 mg/day n=406, 11%; and donepezil 10 mg/day n=421, 19%), and in AD (placebo n=893, 6%; donepezil 5 mg/day n=821, 6%; and donepezil 10 mg/day n=662, 14%). The proportions of VaD patients with AEs were: placebo, 88%; donepezil 5 mg/day, 90%; and donepezil 10 mg/day, 93%. The equivalent figures in AD patients were: placebo, 62%; donepezil 5 mg/day, 65%; and donepezil 10 mg/day, 83%. The most commonly reported AEs in donepezil-treated VaD and AD patients (i.e. nausea and diarrhea) were consistent with the cholinergic effect of donepezil. Cardiovascular AEs were more common in both placebo- and donepezil-treated VaD patients (placebo, 20%; donepezil 5 mg/day, 20%; and donepezil 10 mg/day, 20%) than AD patients (placebo, 7%; donepezil 5 mg/day, 7%; and donepezil 10 mg/day, 8%).

Conclusion: VaD donepezil- and placebo-treated groups showed a higher incidence of AEs than corresponding AD groups, indicating that VaD patients are generally “sicker” as a group than AD patients. Nevertheless, these results demonstrate that donepezil is well tolerated in VaD and AD patients.

References:

NR884 Thursday, May 22, 12:00 p.m.-2:00 p.m.

Long-Term Cognitive Effects of Galantamine in the Treatment of Mild-to-Moderate Alzheimer’s Disease: Evidence From 48 Months of Treatment
Supported by Janssen Pharmaceutica Products, L.P.

Atul R. Mahableshwarkar, M.D., Code #3A, Janssen Pharmaceuticals, 1125 Trenton-Harbourton Road, Titusville, NJ 08560; Gordon Wilcock, M.D., Luc Truyen, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the long-term safety and efficacy of galantamine in patients with mild-to-moderate Alzheimer’s disease (AD).
Summary:

Objective: To evaluate the safety and efficacy of galantamine in mild-to-moderate AD for 48 months.

Methods: Open-label extension of two double-blind studies of galantamine and open-label extensions with a total duration of 48 months. Patients received galantamine 24 mg/day for a further 12 months, making the total treatment duration 48 months. Cognitive change was evaluated by the ADAS-cog. Safety was assessed by adverse events (AEs) and changes in ECG, vital signs, and laboratory measurements.

Results: Patients treated continuously with galantamine for up to 48 months demonstrated an approximate increase in ADAS-cog score of 12.8 ± 0.863, compared with an estimated decline (increase in score) of 24 to 36 points for untreated patients. No clinically relevant ECG or laboratory changes were observed.

Conclusions: Long-term treatment with galantamine is safe and well tolerated, and delays cognitive decline by an estimated year or longer in patients with mild-to-moderate AD.

References:


NR885 Thursday, May 22, 12:00 p.m.-2:00 p.m.
The Effect of Galantamine on Behavior: Maintenance of Effects With Treatment in Vascular Dementia and Alzheimer’s Disease With Cerebrovascular Disease Supported by Janssen Pharmaceuticals, L.P.

Howard Feldman, M.D., Department of Neurology, UBC Vancouver Hospital, S192 2211 Wesbrook Mall, Vancouver BC V6T 2B5, Canada; Sean Lilienfeld, M.B.B.Ch., Atul R. Mahabaleshwar, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the effects of galantamine on behavioral disturbances in patients with vascular dementia (VaD) or Alzheimer’s disease with cerebrovascular disease (AD + CVD).

Summary:

Objective: To evaluate the effect of galantamine on behavior in VaD and AD + CVD patients.

Methods: Randomized, double-blind, parallel-group, placebo-controlled, six-month trial undertaken in multiple centers in Europe and Canada. Following a six-week escalation phase, patients were randomized to placebo (n = 196) or galantamine 24 mg/day (n = 396). Behavioral changes were assessed using total Neuropsychiatric Inventory (NPI) scores. Unadjusted mean changes in 10 NPI individual items compared with baseline levels are reported. Adverse events were monitored.

Results: At six months, the galantamine group had a significantly better outcome on total NPI than the placebo group (1.2 vs 1.0 points, p = 0.011). Treatment with galantamine 24 mg/day was superior to placebo on all items except two, with statistical significant differences (p < 0.05) for anxiety, apathy/indifference, and delusions. Most adverse events from galantamine were gastrointestinal in nature, of mild-to-moderate severity, and were mainly confined to the dose-escalation period.

Conclusions: Galantamine delays the emergence of behavioral symptoms in patients with VaD or AD + CVD. Delaying behavioral symptoms may enhance quality of life, ease caregiver burden, and postpone placing the patient in a long-term care facility.

References:


NR886 Thursday, May 22, 12:00 p.m.-2:00 p.m.
Donepezil Has Significant Benefits on Behavior in Patients With Severe Alzheimer’s Disease Supported by Pfizer Inc and Elsai Co, Ltd

Howard Feldman, M.D., Department of Neurology, UBC Vancouver Hospital, S192 2211 Wesbrook Mall, Vancouver BC V6T 2B5, Canada; Serge Gauthier, M.D., Bruno Vellas, M.D., Jane Hecker, M.D., YiKang Xu, Ph.D., John Jeni, Ph.D., Elias Schwam, Ph.D.

Educational Objectives:

At the end of this session, the participant should appreciate that the significant benefits of donepezil treatment on behavioral symptoms of patients with Alzheimer’s disease, extend into the severe stage of the disease (sMMSE score 5–12).

Summary:

Objective: To investigate the effects of donepezil on behavior in patients with severe AD.

Methods: In this randomized, double-blind trial, 145 patients classified as having severe AD (sMMSE score 5–12) received donepezil, 5 mg/day for the first 28 days and 10 mg/day thereafter per the clinician’s judgment (n=72), or placebo, for 24 weeks (n=73). Behavioral symptoms were assessed using the 12-item Neuropsychiatric Inventory (NPI).

Results: Baseline patient demographics were similar between treatment groups. Mean NPI baseline scores (± SD) were 21.1 ± 2.1 for donepezil- and 23.7 ± 2.2 for placebo-treated patients. Mean change from baseline scores on the NPI total improved throughout the study for the donepezil group and were significantly different from placebo at Weeks 4, 18, 24, and at Week 24 LOCF (mean difference = 6.9, P=0.0062). Benefits in 11/12 NPI items were observed with donepezil, compared with placebo at Week 24 LOCF, with significant differences for depression (P=0.016), anxiety (P=0.036) and apathy (P=0.028). For 8 NPI items more patients treated with donepezil showed a reduction in baseline symptoms (depression and anxiety P<0.05). Adverse events were similar between groups and generally rated as mild or moderate.

Conclusions: These data suggest donepezil is a safe and effective treatment for improving neuropsychiatric symptoms in patients with severe AD.

References:


The Effect of Galantamine on Behavior: Maintenance of Effects With Long-Term Treatment of Mild-to-Moderate Alzheimer's Disease

Supported by Janssen Pharmaceutica Products, L.P.

Jeffrey L. Cummings, M.D., Department of Neurology, UCLA/Reed Neurosciences Center, 710 Westwood Plaza, Los Angeles, CA 90095; Sean Lilenfeld, M.B.B.Ch., Atul R. Mahabshewarkar, M.D.

Educational Objectives:

At the conclusion of this session, the participant should be able to discuss the sustained behavioral effects of galantamine in patients with mild-to-moderate Alzheimer’s disease (AD) up to 18.5 months.

Summary:

Objective: To assess long-term behavioral effects of galantamine in mild-to-moderate AD patients.

Methods: Patients completing a five-month, double-blind, placebo-controlled trial followed by a six-week withdrawal trial (N = 699) were escalated to a 24-mg dose (12 mg bid) of galantamine and treated for 12 months (total treatment duration 18.5 months). Behavior was measured by the Neuropsychiatric Inventory (NPI) scale.

Results: Of 699 patients enrolled, 288 were randomized for treatment with galantamine continuously throughout the 18.5-month study. For most subjects, many of the 10 NPI domains were rated as absent (score = 0) throughout the trial. Overall, there was little change from baseline to the end of Month 5 among galantamine-treated patients and a trend toward small increases (worsening) in mean total NPI scores from baseline to later time points; the galantamine group treated continuously for 18.5 months experienced the least decline (1.75 ± 0.92) at study end. Patients initially treated with placebo deteriorated more slowly upon initiation of galantamine treatment.

Conclusions: Galantamine therapy was associated with delayed emergence of behavioral disturbances compared with expected decline in this first long-term evaluation of behavioral benefits of an approved therapy for mild-to-moderate AD.

References:


The Effect of Insight Meditation on the Level of Anxiety by Thai Stress Test

Sujira Charutsilp, M.D., Department of Psychiatry, HRH Medical Center, Ranesitnakonrayok, Nakornnayok 26120, Thailand

Educational Objectives:

To recognize the practice of insight meditation and its role in reducing anxiety level in normal Thai population (n=156), evaluated by the "Thai stress test" before and after the study.

Summary:

Objective: To study the effect of insight meditation practice on levels of stress.

Method: There were 166 normal subjects participating in an insight meditation training program for seven consecutive days. All took the Thai stress test before and after this program. The data were analyzed by using non-parametric test to compare the anxiety levels at the beginning and the end of the practice.

Results: Percentages of subject with mild and severe stress was reduced after practicing insight meditation from 63.4% to 34.0% and this reduction was statistically significant (Wilcoxon signed rank test, p-value < 0.001). The decrease of stress level was found in all subgroups categorized by sex, age, education, occupation, and income. The differences of stress level reduction were not found among the subgroups.

Conclusion: Practice of insight meditation shows a reduced effect on levels of stress. This effect was independent of sex, age, education, occupation, and income. It might be interesting to apply insight meditation for stress prevention and psychotherapy in patients with anxiety.

References:


NR890  Thursday, May 22, 12:00 p.m.-2:00 p.m.
The Role of Cognitive-Behavioral Therapy and Fluoxetine in Prevention of Recurrence of MDD

Timothy J. Petersen, Ph.D., Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114; Jonathan E. Alpert, M.D., Jaqueline Buchin, Psy.D., Amy H. Farbaugh, Ph.D., John D. Matthews, M.D., Andrew A. Nierenberg, M.D., Joel A. Pava, Ph.D., Maurizio Fava, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will be able to understand the role of CBT in preventing depressive recurrence.

Summary:

Background: Studies show that maintenance treatments with pharmacotherapy and/or psychotherapy (more specifically, interpersonal psychotherapy or cognitive behavioral therapy—CBT) significantly reduce MDD recurrence rates relative to treatment controls. The objective of this study was to compare rates of MDD recurrence during maintenance phase treatment for remitted MDD patients randomized to four treatment groups.

Methods: This was an eighty-week, randomized, parallel-group comparison of four maintenance treatment groups: CBT + placebo, CBT + 40mg fluoxetine, 40mg fluoxetine only, and placebo only. All patients entering this maintenance phase treatment (n=52; 54% women; mean age: 43.6) had completed two prior study phases. The first phase was an acute, open, eight-week, fixed dose of fluoxetine at 20mg/day (n=391 patients; 55% female; mean age 39.8 ± 10.6). Remitters following this acute phase treatment (n=132) (remission=HAMD-17 ≤ 7 for three consecutive weeks) were randomized to one of two 28-week continuation treatment groups: increase in fluoxetine to fixed dose 40mg/day or the same increased fixed dose plus 12 weekly and seven biweekly CBT sessions. Completers of the continuation phase who were still in remission were then eligible for entry into the maintenance study. Subjects were required at baseline to meet criteria for chronic or recurrent MDD.

Results: The primary outcome of this study was rate of recurrence, which was not significantly (p>0.05) different across the four treatment groups: CBT + placebo = 5/11 (45%); CBT + meds = 4/11 (36%); meds only = 4/14 (29%); placebo = 8/16 (50%). The overall MDD recurrence rate on meds (with or without CBT) was 32% (8/25), and was non-significantly (p>0.05) lower than the recurrence rate on placebo (50%). Kaplan-Meier survival curves were constructed with results censored at end of maintenance phase or at study discontinuation for reason other than recurrence, and showed no difference between groups (log-rank X² = 2.368, df= 3, p=0.4997). Only three patients discontinued the study during the 80 weeks of maintenance phase of treatment.

Conclusions: Our findings show a modest, non-significant prophylactic effect of continued antidepressant treatment (with or without CBT), with an 16% lower MDD recurrence rate than on placebo, and are consistent with those of recent antidepressant studies among chronic and recurrent MDD populations. The relatively small sample size of our study is likely to account for the lack of statistical significance of these findings.

References:


NR891  Thursday, May 22, 12:00 p.m.-2:00 p.m.
The Impact of Comorbid Anxiety on the Costs of Employees With Depression

Supported by Eli Lilly and Company

Nicole R. Yurgin, Ph.D., Department of Economics, University of Toledo, 2801 W. Bancroft, Suite 922, Toledo, OH 43606; Martin Marciniak, Ph.D., Ronald P. Landbloom, M.D., Eduardo Dunayevich, M.D., Lee Bowman, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to recognize that comorbid anxiety adds significantly to the medical and productivity cost of employees with depression.

Summary:

Objective: This retrospective study measures how comorbid anxiety impacts medical costs, productivity costs, and total costs of employees diagnosed with depression.

Method: The analysis was performed using a large 1999 employer database with medical claims, pharmaceutical, absenteeism, and short-term disability data. Employees diagnosed with depression (N=3,382) were compared with a control group of employees not diagnosed with depression (N=6,374). The control group is a 2:1 match using age, sex, industry, zipcode, and msa or at study discontinuation for reason other than recurrence, and showed no difference between groups (log-rank X² = 2.368, df= 3, p=0.4997). Only three patients discontinued the study during the 80 weeks of maintenance phase of treatment.

Results: The primary outcome of this study was rate of recurrence, which was not significantly (p>0.05) different across the four treatment groups: CBT + placebo = 5/11 (45%); CBT + meds = 4/11 (36%); meds only = 4/14 (29%); placebo = 8/16 (50%). The overall MDD recurrence rate on meds (with or without CBT) was 32% (8/25), and was non-significantly (p>0.05) lower than the recurrence rate on placebo (50%). Kaplan-Meier survival curves were constructed with results censored at end of maintenance phase or at study discontinuation for reason other than recurrence, and showed no difference between groups (log-rank X² = 2.368, df= 3, p=0.4997). Only three patients discontinued the study during the 80 weeks of maintenance phase of treatment.

Conclusions: Our findings show a modest, non-significant prophylactic effect of continued antidepressant treatment (with or without CBT), with an 16% lower MDD recurrence rate than on placebo, and are consistent with those of recent antidepressant studies among chronic and recurrent MDD populations. The relatively small sample size of our study is likely to account for the lack of statistical significance of these findings.

References:


NR892  Thursday, May 22, 12:00 p.m.-2:00 p.m.
Screening for Principal Versus Comorbid Conditions in Psychiatric Outpatients With the PDSQ

Mark Zimmerman, M.D., Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905; Thomas Sheeran, Ph.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to describe why it is important to consider the distinction between principal and comorbid conditions when screening for psychiatric disorders.
Summary:

Background: In examining the performance of screening scales, a distinction should be made between principal and additional diagnoses. In mental health settings, diagnostic recognition should be adequate for the principal disorders for which patients seek treatment (i.e., related to the chief complaint), whereas the recognition of comorbid disorders that are not the principal reason for seeking treatment may be problematic. If a scale is an effective screening tool only for principal disorders, and not for comorbid conditions, then its clinical utility would be limited. The Psychiatric Diagnostic Screening Questionnaire (PDSQ) is a brief, psychologically strong self-report scale designed to screen for the most common DSM-IV Axis I disorders encountered in outpatient mental health settings. Previously, we described the overall diagnostic performance of the PDSQ in an outpatient setting. In the present report, we compared the performance of the PDSQ in identifying principal and comorbid disorders.

Methods: Seven hundred ninety-nine psychiatric outpatients completed the PDSQ and were interviewed with the Structured Clinical Interview for DSM-IV.

Results: The sensitivity and negative predictive values of the PDSQ subscales were similar for principal and additional diagnoses.

Conclusions: The PDSQ performs as well in screening for comorbid disorders as it does in screening for principal diagnoses.

References:

NR894 Thursday, May 22, 12:00 p.m.–2:00 p.m.
Is Full Recovery of Executive Functions Possible in Remitted Schizophrenia Patients? A Preliminary Study
Saba Ghassen, Unite' d'hospitalisation Psychiatrique Romain, E.P.S. de Ville Ervand, 5, Rue du Docteur Delafontaine, Saint Cloud 92210, France; Claire M. Verdorn, Virginie Moulier, Gilles Dumortier, Khalid Kalalou, Jean F. Rocamora, Rene Benadissa, Laurence Stamatiadis, Dominique Januel

Summary:

Introduction: Several studies of cognitive functions in schizophrenic patients have shown impairment of executive functions during acute phase. Such impairment may be present prior to the onset of symptoms. This is thought to persist during periods of remission and linked to poor outcome and psychosocial difficulties after recovery. Few studies have explored the outcome of cognitive functions and especially executive functions in remitted schizophrenic patients. As executive function has been associated with psychosocial functioning in schizophrenia, we wanted to investigate if remitted schizophrenic patients may exhibit full recovery of executive functions. This concern about cognitive functions during remitted phase emerge from our clinical findings that some patients may totally recover and have good psychosocial functioning.

Aim of the study: The aim of this study is to assess the outcome of executive functions in schizophrenic patients during remitted phase. Executive functions were assessed in 20 remitted (R) schizophrenic patients (at least three months in remission), 25 schizophrenic patients during acute phase (A), and 15 healthy volunteers (C). Schizophrenic symptoms were assessed using Positive and Negative Syndrome Scale (PANSS). Wisconsin, Hanoi tower and GO no GO were used to evaluate executive functions.

Results: PANSS (Positive, negative, and general subscale) scores were statistically lower in the remitted group. Remitted schizophrenic (R) patients performed as well as control (C) in all the executive functions (Wisconsin correct answers, Hanoi tower and GO no GO), while there were statistical differences between A and C groups at Wisconsin and GO no GO performances (p < 0.05). All the groups showed a similar pattern of performance at Hanoi tower task. Perseveration and errors at the Wisconsin test were significantly higher in A and R groups. On the other hand, statistical analysis showed a positive correlation between negative...
Conclusion: Our preliminary study showed that remitted schizophrenic patients may fully recover from their executive function impairment during acute phase. These findings are inconsistent with those found in the literature except for negative symptoms that may predict poor outcome. However, questions remain, including:

- Insufficient number of patients recruited.
- Duration of remission (three months) is short. However, we can expect that a longer duration of remission could favour a better improvement of executive functions.
- The effect of medication should be taken into account although it doesn’t seem to interfere with the performance during these cognitive tasks.

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