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# NEW RESEARCH ABSTRACT BOOK

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SATURDAY MAY 05, 2012

**MS-RES Competition Poster Session****Competition Poster Session 1****PATIENT-ORIENTED AND EPIDEMIOLOGY****NR1-01****DEPRESSION AND ANXIETY CONTRIBUTING TO SUPER OBESITY: THE CASE REPORT OF A 1018-LB MALE***Chair: Steven Powell M.D.***SUMMARY:**

This case involves the extreme case of a 1018-lb male who presented to the hospital in medical distress. The pt. had depression and anxiety that contributed directly to a worsening eating disorder over several years. The patient was known to be near 500 lbs. two years earlier, but had become reclusive with rapidly increasing weight. After presenting to the hospital, the patient went into respiratory arrest requiring extreme measures to resuscitate him. The patient required transfer from New London Hospital, the rural hospital that he presented at, to Dartmouth Hitchcock Medical Center. Due to the patient's size, normal methods to transfer the patient were not possible. After considering a U-Haul truck, the National Guard, and the U.S Coast Guard, I contacted the National Air Force Rescue Center in Washington, DC that helped to coordinate a transfer using a Chinook Helicopter. The patient was transferred within 10 hours of his respiratory arrest. I was the Hospitalist on duty and organized the transfer and flew with the patient to Dartmouth. I was a combination Internal Medicine and Psychiatry resident at Dartmouth at the time, moonlighting in the Shaller Institution. The patient survived the incident, and is now down to 650lbs working toward bariatric surgery. He would not let me share his story for nearly two years due to shame, but is now allowing me to do so. He is working on his depression and issues with his father that have contributed to his obesity.

**NR1-02****DELUSIONAL PARASITOSIS AND POLYSUBSTANCE DEPENDANCE: A CASE REPORT***Chair: Vishwani Sabai, M.D.***SUMMARY:**

Delusional Parasitosis is a disorder in which sufferers hold a delusional belief that they are infested

with parasites. Stimulant drug abuse, particularly amphetamine and cocaine, can lead to delusional parasitosis. This condition is also referred to as "Morgellon's disease" by the patient and Ekblom Syndrome. It is named after a Swedish neurologist, Karl Axel Ekblom, who published cases of the disease in 1937 and 1938. The patient typically reports parasites to exist under the skin, around or inside the body openings and in the stomach or bowels. A person holding such a belief may approach doctors or dermatologists asking for treatment for the supposed infestation, and will often bring small particles, dust and other material for the doctor to inspect. The material may be carried in an envelope or matchbox, so this presentation is known as the "matchbox sign." As an example, a case is discussed of a 37-year-old woman who complained of Morgellon's disease. Ms. M has a history of polysubstance dependence which may be the cause of her delusional belief. This report elaborates on her past history along with her most recent hospitalization which was directly related to the delusion.

**NR1-03****QUALITY OF CARE PROVIDED BY THE CHILD & ADOLESCENT PSYCHIATRIST: A PARENT SURVEY-TO PROVIDE PHARMACOTHERAPY AND PSYCHOTHERAPY IN THE MANAGED CARE ERA***Chair: Nirupama Natarajan, M.D.; Author(s): Daniel Shreeve, M.D., Ph.D.***SUMMARY:**

**Objective:** This Quality Assurance Initiative examined the Quality of Care provided by Child and Adolescent Psychiatrists and Consumer Satisfaction in a Managed care setting – A comparison of integrated treatment (both pharmacotherapy and psychotherapy) with split treatment (pharmacotherapy only). **Methods:** A Satisfaction Survey comprising of 4 items was completed by 148 parents of patients aged 2 to 17 years with psychiatric disorders at the Carilion Clinic -Virginia Tech School of Medicine Outpatient Child & Adolescent Psychiatry Faculty Clinic. It was done after their appointment and covered the reason for the child's visit, length of the appointment, and their preference for the treatment **Results:** During the month long study done in March 2011, the survey was completed by 148 parents of patients seen by 3 Child and Adolescent Faculty Psychiatrists. Length of session: 10 (7%) parents thought the session was not long enough, 1 parent thought it was too long and 137 (93%) parents thought it was just right. Preference of parents: 8 (5%) parents wanted only psychotherapy, 34 (23%) parents wanted only pharmacotherapy and 106 (72%) parents

wanted both. Overall quality of care received from the Child's Psychiatrist: 98 (66%) parents thought it was excellent, 37 (25%) parents thought it was very good, 8 (5%) parents thought it was good, 4 (3%) parents thought it was fair and 1 parent thought it was poor. Conclusions: The results support the conclusion that Integrated treatment is the preferred form of Psychiatric care sought by parents from their Child and Adolescent Psychiatrist.

**NR1-04  
12 YEAR OLD AUTISTIC SPECTRUM MALE  
WITH COMPULSIVE OVERDOSES: A  
DIAGNOSTIC QUANDARY**

*Chair: Aghaegbulam Uga M.D.; Author(s): Shreedhar Kulkarni M.D., Jeffrey Bennett M.D.*

**SUMMARY:**

A 12-year-old white male with Asperger's Disorder, Attention Deficit with Hyperactivity Disorder (ADHD), Obsessive Compulsive Disorder (OCD) and Generalized Anxiety Disorder (GAD) was admitted to the pediatric ICU for a fourth potentially lethal overdose, this time with 95 tablets of 500mg acetaminophen. An admission acetaminophen level was 362.4, but other studies were normal. There were no prior genetic or neuroimaging studies. The patient's reason for repeated overdose attempts was that it got attention and also because he "feels safe in the hospital", although there were no apparent safety issues at home. He stated that he feels safe at home but felt safer in the hospital with people constantly watching him "in case anything happens". He noted a sense of impending danger. He denied ever being suicidal stating that he "did not intend to die" and was not depressed. His grandmother added that, since his childhood, he had been obsessed with doctors, nurses, hospitals, and emergency services. The patient had overdosed on large amounts of different medications four times within a 2 month period but there were no other identifiable precipitants to the overdoses. Prior to the overdoses, the patient had used other strategies for hospital admissions including dissimulating symptoms of a myocardial infarction or severe acute abdominal pain. His medical history was otherwise negative. As a child, the patient was diagnosed with ADHD, Autism, and later with Asperger's Disorder, OCD, and mild intellectual disability. He was treated with different medications including sertraline, olanzapine, clonazepam, clonidine, and melatonin with little response. The patient's father had alcohol dependence and his mother was severely depressed with opioid dependence. The patient had early developmental motor and speech delay. On exam, he did not endorse psychosis or vegetative abnormalities. Attention span was short and he exhibited stereotypic

head and hand gestures. His affect was bright. The patient was treated for acetaminophen overdose and subsequently released to residential placement. The differential diagnosis explaining his behavior is discussed including Autistic Spectrum Disorder, Generalized Anxiety Disorder, Obsessive Compulsive Disorder, Factitious Disorder, Impulse Control Disorder, and Delusional Disorder.

**NR1-05  
INTEGRATION OF MENTAL HEALTH  
AND PRIMARY CARE IN SCREENING AND  
TREATMENT OF POSTTRAUMATIC STRESS  
DISORDER IN THE VA CLINICAL SETTING**

*Chair: Elliot Lee, M.D.*

**SUMMARY:**

In an effort to create seamless, population-based, veteran-focused care, the Veterans Administration has integrated mental health care into the primary care setting. The integrated model depends on PTSD screening for all primary care patients, followed by further evaluation by primary care physicians for positive screens. In this model, psychiatrists are embedded in primary care and serve as consultants to primary care physicians. Subsequent mental health care delivery can occur in the primary care setting for uncomplicated cases or may subsequently occur in specialty mental health clinics. The integrated care approach has been studied in the treatment of depressed primary care patients, but less is known about the successful level of referral and engagement of this approach for Posttraumatic Stress Disorder (PTSD). In this study, we describe the care management of veterans who screened positive for PTSD in various VA primary care clinics. During the 1 year period of September 2009-2010, 804 veterans in primary care screened positive for PTSD using the 4 question PC-PTSD screen. One hundred and ten of the veterans were already enrolled patients in the mental health clinic. Sixty eight percent of the remaining 694 veterans had an integrated care evaluation by mental health staff in the primary care setting and 32% were diagnosed with PTSD. The use of telemental health allowed veterans at both rural and urban clinics to receive integrated care evaluation with equal likelihood in either setting. We analyzed the OIF/OEF veteran population separately to better understand the referral process for our newest veterans. Of the 305 OEF/OIF veterans who screened positive, 71.8% had an integrated care assessment and 67% of these veterans were subsequently referred to the mental health clinic. Ninety eight percent of veterans had documented assessment of a positive screen, with documented follow up from primary clinic or integrated care regarding

treatment of their mental health symptoms. This high rate of follow up of mental health symptoms is indicative of the success of screening and the integrated care approach in the primary care setting for OEF/OIF veterans with PTSD symptoms.

**NR1-06  
ASSOCIATIONS OF MENTAL AND MEDICAL  
ILLNESSES WITH AGAINST MEDICAL  
ADVICE DISCHARGES: THE NATIONAL  
HOSPITAL DISCHARGE SURVEY, 1988-2006**

*Chair: Rima Tawk, Ph.D.*

**SUMMARY:**

**Objective:** To examine the association of mental, and medical illnesses with the risk of leaving against medical advice (AMA) in a national sample of adult patients who left general hospitals between 1988 and 2006. **Methods:** This study used data from the National Hospital Discharge Survey (NHDS) and was limited to adults (18 years and older). AMA patients represented a weighted total of 4,985,960 (n= 46,261). Leaving AMA was first examined as a function of year and mental illness. Multiple logistic regression analysis was then used to adjust for patient and hospital characteristics when associating mental and medical illnesses with AMA discharges. **Results:** Leaving AMA was strongly associated with mental health problems (OR= 4.928; 95% CI 4.759, 5.104 p<.0001) as well as major medical diagnoses. However, the impact of mental illness was attenuated after excluding patients with substance abuse as well as after adjusting for patient and hospital characteristics (adjusted OR [AOR] = 2.792; 95 % CI 2.601, 2.998 p<.0001). The most significant predictors of AMA discharge included being younger in age (37-44 years old), (AOR=4.608; 95% CI=4.288,4.953 p<.0001), being self-pay (AOR=3.952; 95% CI=3.736,4.180 p<.0001), having Medicaid insurance (AOR=2.941; 95% CI=2.801, 3.089 p<.0001), being male (AOR=2.148; 95% CI=2.074, 2.226 p<.0001), and the regional location of the hospital (Northeast) (AOR=2.132; 95% CI=2.036, 2.233 p<.0001). **Conclusions:** The results may be of value to clinicians, and hospital administrators in helping to profile and target patients at risk for treatment-compliance problems. Prospective primary data collection that would include patient, physician, and hospital variables is recommended.

**NR1-07  
PATTERNS OF POSITIVE SYMPTOM  
EMERGENCE IN FIRST-EPISEODE PSYCHOSIS**

*Chair: Dawn Flosnik M.D.; Author(s): Michael T. Compton, M.D., M.P.H. Amy A. Potts, Ph.D. Claire E. Ramsay,*

*M.P.H.*

**SUMMARY:**

**Objective:** Relatively little data exists regarding the pattern of emergence of positive symptoms in first-episode psychosis. Through this exploratory analysis, the evolution patterns of delusions and hallucinations were examined. Based on these patterns, comparisons were made between groups using specific variables (such as insight, family history, and cannabis use) in an attempt to elucidate meaningful clinical differences among patients in their early, pre-treatment course. **Method:** A total sample of 159 patients participated in the analysis after being recruited over 6 years as part of two research studies examining first-episode nonaffective psychotic disorders. Participants were recruited from an urban, public-sector, university-affiliated hospital (133, 69.2%), the psychiatric emergency room of the same hospital (4, 2.5%) or a public-sector psychiatric crisis center in a neighboring suburban county (22, 13.8%). Individuals who were aged 18–40 years, spoke English, and were admitted for a previously untreated, nonaffective psychotic disorder were considered eligible. Following an extensive clinical interview by a trained research assessor, the date of onset of hallucinations, delusions, and prodromal symptoms was determined. Additional clinical measures of insight, family history, duration of untreated psychosis (DUP), duration of untreated illness (DUI), alcohol and cannabis use, and Global Assessment of Functioning (GAF) were also measured. **Results:** Four mutually exclusive groups were derived regarding the onset of hallucinations and delusions: (1) those with delusions only (n=29, 18.2%, DEL-ONLY); (2) patients with delusions that began at least one month before the onset of hallucinations (n=31, 19.5%, DEL-HALL); (3) individuals with an onset of hallucinations at least one month before the emergence of delusions (n=26, 16.4%, HALL-DEL); and (4) those in whom delusions and hallucinations emerged concomitantly, within the same month (n=73, 45.9%, DEL+HALL). Patients with delusions and hallucinations emerging concurrently within the same month had a shorter duration of untreated psychosis and duration of untreated illness than those in whom one psychotic symptom emerged greater than one month before the other. The delusions-only group had significantly less severe positive, but also less negative and general psychopathology, symptom scores. Those in whom delusions and hallucinations emerged within the same month had a lower likelihood of a family history of psychosis than patients in the other three groups. Patients in whom delusions began at least one month before hallucinations had a higher rate of alcohol abuse or dependence compared to participants in each of

the other groups. Conclusions: This data, along with future replicated studies, may further deepen the field's understanding of first-episode psychosis, and improve nosology, sub-typing, diagnosis, and treatment of psychotic disorders.

#### NR1-08

### PATIENT FACTORS ASSOCIATED WITH EXTENDED LENGTH OF STAY IN THE INPATIENT PSYCHIATRIC UNITS OF A LARGE COUNTY HOSPITAL

*Chair: Jason Cheng, M.D.; Author(s): Martha Shumway, Ph.D., Mark Leary M.D., James Dilley, M.D., Christina Mangurian, M.D.*

#### SUMMARY:

Background: Despite years of cost reduction, inpatient psychiatric services still account for 16% of all US mental health spending. (1) Mental health administrators are often focused on reducing inpatient length of stay (LOS) to reduce costs. Nonetheless, some patients experience extended LOS. Unfortunately, most studies on factors related to inpatient LOS are more than ten years old, and many are more than twenty years old. (2) Previously identified patient-specific factors include age, diagnosis, sex, ethnicity, previous admissions, global assessment of functioning, violence, and discharge location, as well as comorbid substance use, personality disorder, and medical conditions. (2) Unfortunately, because this data is dated and psychiatric inpatient LOS has been decreasing (3) mental health administrators have little up-to-date guidance to understand which factors may impact extended LOS. It might be especially useful to examine patients with the very longest LOS. Objectives: To determine patient-specific factors associated with the longest inpatient stays at a large county hospital. Methods: -Study Design: Descriptive study -Study Subjects: Psychiatric inpatients at San Francisco General Hospital (SFGH). Procedures: The electronic records for SFGH psychiatry inpatients were reviewed for patients discharged between 1/1/2009 and 6/30/2011. Demographic and other patient-specific variables previously identified in the literature (e.g., substance abuse, diagnosis) were collected. Subjects who had LOS of 60 days or more were considered the extended LOS cohort. These subjects were compared to a cohort of equal size, consisting of a random sample of inpatients with LOS of 30 days or less. Data analysis: Chi Square analysis and t-tests were conducted to determine any differences in patient-specific factors, categorical and continuous respectively, that might be associated with extended LOS. Results: SFGH had 4247 discharges from its inpatient units over this timeframe. There were approximately 80 unique patients with

LOS of 60 days or more. The study is currently in the data collection phase, so full results are pending. Conclusions: This study aims to provide administrators with data on patient-specific factors that might explain extended LOS in this vulnerable population. Ideally, quality improvement initiatives could be implemented to address some of these factors and reduce LOS at overburdened safety net hospitals. (1) Frank RG et al. *Health Aff* 2009; 28:649-59. (2) Tulloch AD et al. *Adm Policy Ment Health* 2011; 38:155-168. (3) Mechanic D et al. *Arch Gen Psychiatry* 1998; 55:785-791.

#### NR1-09

### MENTAL HEALTH SERVICE CONTACTS AMONG SEXUAL MINORITY AND HETEROSEXUAL GIRLS IN BOSTON PUBLIC SCHOOLS

*Chair: Jeremy Kidd, M.P.H.; Author(s): J. Lee White, M.P.H., Renee M. Johnson, Ph.D, M.P.H.*

#### SUMMARY:

Objective: Although sexual minority (SM) adolescent girls are at high risk for suicidal behavior, very little is known about their use of mental health services (MHS). Therefore, we investigated the prevalence of suicidality and MHS utilization among SM girls in Boston (N=889). Methods: This study is a cross-sectional analysis of data from the 2008 Boston Youth Survey (BYS), a comprehensive survey of 9th-12th grade students in Boston Public Schools. A stratified random sampling procedure was used to select respondents (n=1,878). Surveys were self-administered in selected classrooms between January and April 2008. The BYS inquired about age, nativity, and sexual orientation identity in single items. Girls who described their sexual orientation as "mostly heterosexual", bisexual, "mostly homosexual," or lesbian were coded as sexual minority, and those who said they were heterosexual were coded as such. Girls who chose "not sure" (n=16) were coded as missing. MHS use was assessed with a single yes-no item: "In the past 12 months, did you visit a school counselor, therapist, or psychologist because you were feeling bad or were having some emotional problems?" In three yes-no items, students were asked about past 12-month suicidal ideation, suicide attempts, and deliberate non-suicidal self-harm. Those who endorsed any of the aforementioned three variables were coded as having high mental health need. We used chi-square tests to assess the statistical significance of group differences. To test whether SM status moderated the association between MHS use and mental health need, we entered mental health need, SM status, and the interaction term of the two into a regression model that predicted past 12-month MHS use. Results:

Because there were few SM boys in the sample (n=20), we restricted our analysis to girls (n=983). We excluded respondents with missing data on sexual orientation, MHS use, and MHS need; resulting in a final sample of girls (n=889). There were no demographic differences between those excluded and girls in the final analytic sample. Compared to heterosexual girls, SM girls (n=89) were substantially more likely to report suicidal ideation (33% v 12%,  $p<.0001$ ), suicide attempts (14% v 4%,  $p<.0001$ ), and non-suicidal self-injury (33% v 8.3%,  $p<.0001$ ) in the past 12 months. SM girls were also more likely to have reported a past 12-month MHS contact (54% v 26%,  $p<0.0001$ ); this finding held for those with and without a high level of mental health need. The interaction term was not statistically significant, indicating that SM status does not moderate the effect of mental health need on MHS use. Conclusions: SM girls are at increased risk for mental health problems. These results also indicate that SM girls – particularly those experiencing suicidality – are likely to report a MHS contact. Future research is needed to elucidate when/how SM girls come to use MHS and what types of services they are receiving.

**NR1-10  
GEOGRAPHIC VARIABILITY IN INTERNET SEARCHES FOR SUICIDE AND SUICIDE RATES IN THE UNITED STATES IN 2007**

*Chair: Matthew Burkey M.D.; Author(s): Jacob Taylor*

**Summary:**

Background: Internet search frequency has been shown to be a useful tool in predicting influenza and other infectious disease epidemics. Internet searches for suicide have been demonstrated to reflect time trend patterns of completed suicides in the United States. However, additional studies are needed to test the validity of using Internet search data as a predictor of suicidal behavior. The objective of this study is to assess the ecological geographic relationship between Internet searches for suicide and suicide rates by comparing state-by-state data in the United States. Methods: The relative frequencies of internet searches for “suicide” performed from January 1, 2007 to December 31, 2007 by state in the United States were assessed using Google Insights for Search, a publicly available search engine database of search trends. Weekly data were available for the number of searches for the term of interest (i.e., suicide) relative to the total number of searches performed on Google, yielding a 0-100 normalized index in which 100 indicates the highest relative search frequency during the time period of interest. 2007 suicide rates by state were abstracted from the National Vital Statistics Reports. Linear regression

was performed to evaluate the relationship between suicide rate (independent variable) and relative search frequency (dependent variable). Results: Univariate linear regression revealed a significant ( $p=0.038$ ) linear relationship with correlation coefficient of 0.15 (95% CI: 0.009 to 0.29) between relative search frequency and suicide rate by state in 2007. An increase in one point for normalized search rate for suicide was correlated with a 15% increase in suicide rate in 2007. Conclusions: There was a positive ecological geographic relationship between greater frequency of Internet searches for suicide and higher suicide rates in the 50 United States and the District of Columbia. This study adds to the literature suggesting a correlation between Internet search patterns and suicide frequency. Future studies evaluating the utility of internet search data in predicting suicide patterns or targeting suicide interventions are indicated.

**NR1-11  
WEIGHT CHANGE AND CARDIOMETABOLIC RISK WITH ANTIPSYCHOTIC POLYPHARMACY: META-ANALYSIS SHOWING IMPROVED OUTCOMES WITH CERTAIN ARIPIRAZOLE COMBINATIONS**

*Chair: Vishesh Agarwal M.D.; Author(s): Christoph U. Correll, M.D.*

**Summary:**

Background: While antipsychotic cotreatment (APC), used frequently in clinical practice, has been criticized for lack of evidence and additive adverse effects, open label data suggest that some combinations might improve cardiometabolic risk. Objectives: To investigate the cardiometabolic effects of specific APCs. Methodology: Data from randomized placebo controlled trials (RPCTs) of APC versus placebo in schizophrenia were meta-analyzed using random effects models. Primary outcome was change in weight or BMI. Secondary outcomes included other cardiometabolic and psychopathology outcomes. For dichotomous data relative risk (RR) and for continuous data Hedges’s  $g$  was calculated as effect size measures, each with 95% Confidence Intervals (CIs), and with number-needed-to-treat (NNT) and standardized/weighted mean difference (SM.D./WM.D.) as appropriate. Results: Eight RPCTs (n=786) lasting 8-16 weeks were analyzed. Compared with placebo, adding aripiprazole to clozapine or olanzapine (N=3, n=283) was the only APC associated with significant weight loss [SM.D.=-0.54 (CI:-0.78,-0.30),  $p<0.0001$ ; WM.D.=-1.69kg (CI:-2.79,-0.59),  $p=0.003$ ], greater weight loss >7% [N=1, n=206, RR:4.93 (CI:1.48,16.42),  $p=0.009$ ; NNT=9 (CI:6-25)] and significant reduction

in total cholesterol [N=2, n=246, SM.D.=-0.43 (CI:-0.68,-0.18), p=0.0009], LDL-cholesterol [N=2, n=241, SM.D.=-0.34 (CI:-0.57,-0.11), p=0.002] and triglycerides [N=3, n=273, SM.D.=-0.35 (CI:-0.70,-0.00), p=0.05], but not of HDL-cholesterol (p=0.95) or glucose (p=0.41). No significant cardiometabolic effects were found with risperidone or fluphenazine augmentation of clozapine (N=3, n=119), aripiprazole augmentation of quetiapine or risperidone (N=1, n=290) or aripiprazole augmentation of haloperidol (N=1, n=54). No significant changes were found regarding total psychopathology (p=0.25-0.94), positive symptoms (p=0.30-0.99) or negative symptoms (p=0.19-0.94) with any APCs. Side effects were not significantly different with placebo vs. APC, except for significant prolactin decrease when adding aripiprazole to clozapine (p=0.0005) or quetiapine/risperidone (p<0.0001), while adding risperidone to clozapine raised prolactin significantly (p<0.0001). Conclusion: Specific APCs differ in their cardiometabolic safety. Short-term addition of aripiprazole to a high metabolic risk antipsychotic (olanzapine, clozapine), but not to a medium risk (quetiapine, risperidone) or low risk (haloperidol) antipsychotic significantly improved body weight and lipid parameters. Adding risperidone or fluphenazine to clozapine did not have any beneficial effect and none of the combinations benefited or worsened psychopathology or short-term adverse effects, except for increased prolactin when adding risperidone to clozapine, while aripiprazole addition to clozapine, quetiapine or risperidone lowered prolactin.

**NR1-12  
PSYCHIATRIC COMORBIDITIES IN  
TREATMENT AND TREATMENT PLANNING  
IN REFRACTORY CHILD AND ADOLESCENT  
PATIENTS IN A TERTIARY STATE HOSPITAL:  
A CASE SERIES**

*Chair: Meredith Weiss M.D.; Author(s): Ginny Mary Gerbino-Rosen, M.D., Zoe Blacksin, M.D.*

**SUMMARY:**

Background: Patients who failed multiple acute inpatient hospitalizations are commonly admitted to tertiary state hospitals because of “refractory” mental illness. We suggest that a primary psychiatric diagnosis refractory to treatment may, in fact, be complicated by overlooked and untreated comorbidities that need to be teased apart and addressed as independent elements contributing to a whole picture of inadequately treated mental illness. Therefore, comorbidities may be a legitimate issue for treatment and treatment planning and thereby require identification and consideration of unique pharmacologic and psychotherapeutic interventions.

Objective: 1) To identify unaddressed co-morbidities that may transform refractory illness into treatable disorders. 2) To study significant outcomes of patients admitted to a tertiary state hospital with refractory primary psychiatric illness after co-morbidities were identified, addressed and treated pharmacologically and psychotherapeutically. 3) To explore the implications and ramifications of identification and treatment of psychiatric co-morbidities. Methods: A retrospective review of the inpatient medical and psychiatric records of 10 patients, ages 7-17, from Bronx Children’s Psychiatric Center (BCPC), a tertiary state psychiatric hospital, who have failed multiple shorter term hospitalizations. Charts were chosen from child, young adolescent and older adolescent units. The primary Axis I psychiatric diagnoses identified included Affective Spectrum Disorders, Psychotic Spectrum Disorders, Pervasive Developmental Spectrum Disorders, and severe Attention-Deficit/Hyperactivity Disorder (ADHD) with aggressive outbursts. Comorbidities identified included trauma, substance abuse, previously undiagnosed or residual ADHD, previously undiagnosed seizure disorders, eating disorders and Communication Disorders. Moreover, issues of impulse control disorders, somatic complaints, intermittent explosivity and panic features were often part of these comorbidities, particularly in trauma cases. Results: Addressing comorbidities effectively, along with necessary psychoeducation of families and staff regarding these additional issues, yielded greater clinical improvement, better follow-up planning, greater compliance with aftercare, and lower rates of recidivism. Conclusions: Comorbid disorders can be identified and addressed and transform refractory illness into treatable disorders. Appropriate treatment and intervention of previously unidentified comorbid issues is essential in breaking the cycle of rapid relapse and hospitalization.

**NR1-13  
BATH SALT INTOXICATION: A LITERATURE  
REVIEW OF THE CLINICAL SIGNS,  
SYMPTOMS, PHYSIOLOGY, AND CURRENT  
TREATMENT RECOMMENDATIONS**

*Chair: Scott Yobo D.O.; Author(s): Curtis McKnight, M.D.; David Kasick, M.D.; Anne-Marie Duchemin, M.D.*

**SUMMARY:**

Introduction: “Bath Salts” are increasingly popular drugs. They contain mephedrone and other synthetic cathinones and are sold legally in many countries including the United States. As a consequence, psychiatrists are more and more often faced with a potential diagnosis of bath salt intoxication when treating patients using these designer drugs.

**Objective:** To review the current literature on clinical signs and symptoms of bath salt intoxication, the physiological effects of bath salt ingestion, and the current recommendations for treatment of acute bath salt intoxication. **Method:** This study consists of a literature review performed by searching PubMed using keywords: Bath Salt, Mephedrone, Cathinone, Methylenedioxypropylone, MDPV, and “meow meow”. Search for these terms resulted in 589 articles, ranging in publication date from 1927 to the present. Articles were reviewed based on relevance, content, and online availability. **Results:** Bath salts are still considered by many to be “legal highs” despite the recent legislation passed to help curb the distribution and use of these increasingly popular drugs. Bath salt intoxication has profound psychiatric effects which can present with symptoms of agitation, paranoia, and hallucinations, among others. Bath salts also have far reaching effects on other major systems of the body including cardiac, neurologic, gastrointestinal, pulmonary, and ear, nose and throat symptomology. Other symptoms are also prominent such as fever, diaphoresis, hyponatremia, and rash. The physiology of bath salts is not fully understood and varies in each specific synthetic compound but they appear to have amphetamine like effects. At this time, a cost effective, widespread method of screening for bath salt use does not exist. Bath salts do not register on routine urine or serum drug toxicology screens and present physicians across treatment settings with the dilemma of how to effectively determine what is causing the patient’s symptoms when presenting with suspected toxidromes. Treatment is mostly supportive and involves treating the patient’s symptoms in most cases. **Conclusions:** Understanding the clinical signs, symptoms, and physiology of bath salt intoxication can be valuable due to the lack of effective screening tests for these drugs. While more research is needed on bath salts and their effects on the body, there is data available to assist health care providers with diagnosis and treatment of patients with bath salt intoxication. A history of bath salt use should be investigated in patients presenting with possible symptoms of bath salt intoxication.

**NR1-14**  
**PATTERNS OF UTILIZATION OF PEDIATRIC EMERGENCY DEPARTMENT FOR PSYCHIATRIC EMERGENCIES**

*Chair: Polina Shats, D.O.; Author(s): Celine Wong, M.D., Alicia Garcete, M.D., Kathleen Malloy, M.D., Tarika Nagi, M.D., Theresa Jacob, Ph.D, M.P.H.*

**SUMMARY:**

**Introduction:** While the Emergency Department (ED) is only one of the clinical settings in which children and

adolescents may present for mental health concerns, ED visits for psychiatric needs have significantly risen in the past decade leading to potential overutilization of pediatric EDs. **Objective:** Our objective was to examine the patterns of utilization of the pediatric ED for psychiatric emergencies and to examine the demographic and clinical characteristics of children referred for psychiatric consultation, in a large, urban, independent academic medical center setting. **Methods:** An IRB-approved retrospective study was conducted of patients referred for psychiatric consultation in the Pediatric ED of Maimonides Medical Center, from January 1st, 2009 to December 31st, 2009. Analyzed variables included, demographics, reason for consult (aggressive behaviour, depression, psychosis, anxiety, deliberate self-harm, suicidal thought or attempts), past psychiatric history, diagnosis and final disposition. **Results:** Of the 350 children with ages ranging from 4-19 years (mean age±SD: 13.5±3.0 years; median age: 14 years), 55% were male. The most common mode of arrival was by ambulance (47%) and the predominant referral source was parent/relative (40%) while a fourth of the cases were referred from schools. Referral from physician for psychiatric consultation was significantly low in our setting (9.7%, p<0.05). The most common reason for consult was related to suicidality, with 11% referred for episodes described as suicide attempts (including overdose), 13% for suicidal ideations with plan, and 16% for suicidal ideations without plan. Aggressive behaviour/violence, anxiety, and psychosis accounted for 23%, 6%, and 3% patients, respectively. Nearly half the children were previously undiagnosed for any psychiatric ailment, and never had any psychiatric treatment, and 69% were not on any medication at the time of presentation. While hospitalization occurred in 10% of the total 350 patients, only a significantly small number ended up being admitted to a psychiatric unit (p<0.01). A third of the patients were dispositioned 2-4 hours after presentation. Preliminary analyses demonstrate that the most common Axis I psychiatric diagnosis was Adjustment Disorders (25%) in our patient population. **Conclusions:** Our data are consistent with those in previous reports in terms of consultation reasons and referral source. However, psychiatric-related visits to the pediatric ED did not have a high admission/transfer rate in our setting. Although suicidality and aggressive behavior/violence were the main reasons for the ED visits, most patients did not require admission to an inpatient unit, and were able to follow-up with outpatient providers. Hence more resources need to be allocated to outpatient child psychiatry services, including establishing crisis walk-in clinics to lessen the burden on already over utilized EDs.

## NR1-15

**SYSTEMATIC REVIEW OF THE PREVALENCE OF DELIRIUM IN INPATIENT PSYCHIATRIC SETTINGS AND FINDINGS FROM A GERIATRIC PSYCHIATRIC UNIT**

*Chair: Meera Balasubramaniam, M.B.B.S; Author(s): Dr. Yesne Alici, M.D.*

**SUMMARY:**

**Objectives:** The objectives of the study are to determine the frequency of delirium among patients admitted to an inpatient geriatric psychiatry unit of a state hospital and to determine factors that may contribute to misdiagnosis of delirium among these patients. **Methods:** A retrospective chart review of consecutive inpatient admissions between July 1st 2008 and November 15th 2010 to the geriatric psychiatry unit of Central Regional Hospital, NC was conducted. The two investigators independently reviewed patient charts, prior to which 10 randomly selected charts were reviewed to assess inter-rater reliability. Discharge summaries of all subjects were reviewed to determine the number of subjects who were diagnosed with delirium in the inpatient geriatric psychiatry unit or shortly before admission. Admission intake notes were then reviewed of patients diagnosed with delirium for completeness and accuracy with respect to the history of present illness, vital signs, physical examination, laboratory radiological investigations, collateral information and structured cognitive tests. IBM SPSS Statistics software (Version 18; SPSS Inc., Chicago, IL) will be used for all statistical analyses. Descriptive statistics will be used for data analysis. For simple comparisons, chi-square analysis will be performed for categorical data, and Wilcoxon rank sum tests will be used for continuous data. Items will be coded as missing if information is not available in the chart. Multivariable logistic regression will be performed to determine clinical variables that were independently associated with a diagnosis of delirium. **Results:** The charts of 116 consecutive admissions to the geriatric psychiatric unit were retrospectively reviewed and a preliminary analysis has been completed. 22 patients (18.9%) were diagnosed with delirium within 7 days of inpatient admission and 11 of these patients had a previous history of psychiatric illness other than dementia. The referral diagnosis in 14 of these patients was dementia. 10 out of 22 patients were referred from inpatient medical units. Almost all patients manifested hyperactive delirium. Urinary tract infection was the most common underlying medical etiology, followed by medications and an elevated BUN/ Creatinine ratio. 45% of patients diagnosed with delirium were transferred to a medical unit for management of their

medical conditions. Statistical analysis is in process. **Conclusions:** Our preliminary findings are in line with available scientific literature about the prevalence of misdiagnosed delirium among patients admitted to inpatient geriatric psychiatric units. Further research on factors contributing to misdiagnosis will be helpful for education of patients, families and health care professionals in judiciously diagnosing and optimally managing delirium.

## NR1-16

**TEMPORAL CHANGES IN INITIATION OF INJECTION DRUG USE, AND ASSOCIATED RISK FACTORS, IN HEROIN USERS IN MALAYSIA, 1968-1999**

*Chair: Emily Tejani, M.D.; Author(s): Richard Schottenfeld, M.D., Marek Chazwarski, Ph.D, Mahmud Mazlan, M.D.*

**SUMMARY:**

Malaysia has been experiencing widespread problems with injection drug use along with a growing HIV epidemic that has only recently stabilized. Historically the majority of heroin users in Malaysia administered the drug via intranasal use and smoking, but over the past four decades injection use has become widespread. An estimated 1.3% of the population engages in injection drug use, which is the highest in South-East Asia and among the highest in the world. Heroin is the most commonly injected drug. The transition from non-injection drug use to injection use among heroin users worldwide is common and well documented. The number of years from first heroin use to first heroin injection use (latency to injection use) varies greatly between regions. Although previous studies have documented latency to injection use, as well as changes over time in the proportion of new users switching to injection use, few studies have investigated how latency to injection use has changed over time. In addition, few studies have identified risk factors for switching to injection use or decreased latency to injection use, especially in developing countries. This study aims to describe how latency to injection use has changed over the past several decades in heroin users in Malaysia. We also aim to describe the proportion of heroin users who have switched to injection drug use during that time. In addition, we set out to find factors associated with switching to injection use and decreased latency to injection use. Some factors examined include: age at first drug use, history of physical or sexual abuse, and history of mandatory drug detention stays prior to first injection use. Understanding these patterns and associated factors may help to better target treatment and prevention efforts to those at highest risk of contracting disease, as transmission of HIV and HCV often occurs soon after

the initiation of injection use. Our study found that although virtually all (97%) heroin users in Malaysia initiate use via non-injection modes, the majority later transition to injection use. A trend of decreased latency to first injection use was found between each successive group of new heroin users; those that began using prior to 1979, between 1980-1984, 1985-1989, and 1990-1994. Each successive group also had increasingly greater proportions of heroin users who switched to injection use. For the group that began using heroin in 1995-1999, the latency to injection use did not change compared to the previous group (1990-1994). Surprisingly, there were actually fewer people who switched to injection use in this group (compared to 1990-1994 group). This pattern positively correlates with changes in heroin supply in South-East Asia during that time. As heroin supply increased greater numbers of heroin users switched to injection use, and did so at a faster rate, than when heroin supply was less or began decreasing. Other factors may also be responsible for this pattern.

**NR1-17**  
**INCREASED BODY MASS INDEX IN TOXOPLASMA GONDII POSITIVE PATIENTS WITH SCHIZOPHRENIA**

*Chair: Sara Mazaheri M.D.; Author(s): Olaoluwa Okusaga M.D., Gloria Reeves M.D., Ina Giegling Ph.D., Annette M. Hartmann Ph.D., Bettina Konte Ph.D., Marion Friedl Ph.D., Dan Rujescu M.D., Teodor T. Postolache M.D.*

**SUMMARY:**

**Background:** Evidence is accumulating that the prevalent neurotropic parasite *Toxoplasma gondii* (T. gondii) and schizophrenia are associated. Schizophrenic patients have also been shown to have an increased likelihood of being overweight or obese, important in the context of their potentially increased cardiovascular risk. Previously, obesity has been shown to be associated with immune activation, with a potential vicious circle between excess adipose tissue and mediators of inflammation. As T. gondii infection induces chronic low grade immune activation, and, as one report suggests, increased body weight in T. gondii infected rodents, we hypothesized that T. gondii seropositivity is associated with increased body mass index (BMI) in patients with schizophrenia. **Method:** BMI was measured in 1000 schizophrenic patients recruited in the Munich area for a larger "parent" study. Plasma was analyzed for T. gondii IgG antibodies using ELISA. BMI was compared in T. gondii seropositive vs. seronegative patients with ANOVAs adjusting for severity of illness by PANSS scores and for medication effects using chlorpromazine dose equivalent. **Results:** T. gondii positive schizophrenic

patients had significantly higher BMI than T. gondii negative group. (P: 0.045). **Conclusion:** Limitations include the cross sectional nature of the study, the lack of adjustment for socioeconomic factors, and the absence of biological markers to confirm a possible immune mediation. The results are consistent with previous data in rodents and require replication in a larger study specifically designed for this purpose.

**NR1-18**  
**DEPRESSION AND AMYLOIDOSIS: CURRENT FINDINGS AND FUTURE DIRECTIONS**

*Chair: Janet Shu M.D.; Author(s): John Berk, M.D. and David Seldin, M.D.*

**Summary:**

Amyloidosis, a rare disease, affects multiple organ systems, and has a poor prognosis, particularly for the hematologic AL type (1). With limited public knowledge of the disease, amyloid patients may feel more isolated than other populations, and be uniquely at risk for depression affecting prognosis. There is limited literature on the link between depression and amyloidosis (2), although one study found that stem cell transplant improved quality of life for amyloid patients (3). Significant research has shown that there is a correlation between depression and increased risk of mortality in patients undergoing stem cell transplant (4, 5). In most of these studies, patients had a variety of blood disorders, including leukemia, multiple myeloma, and amyloidosis. The familial form of amyloidosis, AF, may lead to further distress because of the implications of carrying a gene for a hereditary disease. This case report illustrates how a 60 year-old woman's depression may have increased her morbidity and mortality in the context of familial amyloidosis, and describes future directions in exploring the correlation between depression and amyloidosis, including an ongoing study retrospectively comparing the mortality rates of a cohort of depressed versus non-depressed amyloid patients receiving stem cell transplant (6). 1. Merlini G et al. "Amyloidosis: Pathogenesis and New Therapeutic Options." J Clin Oncol 2011, May 10; 29(14):1924-33 2. Wells DA and SR Lennon. "Major depression and amyloidosis." Gen Hosp Psychiatry. 1989 Nov; 11(6):425-6. 3. Seldin et al. "Improvement in quality of life of patients with AL amyloidosis treated with high-dose melphalan and autologous stem cell transplantation." Blood Sep 15; 104(6):1888-93. 4. Prieto JM et al. "Role of depression as a predictor of mortality among cancer patients after stem-cell transplantation." J Clin Oncol 2005, Sep 1; 23(25):6063-71. 5. Loberiza FR Jr et al. "Association of depressive syndrome and early deaths among patients after stem-cell transplantation

for malignant diseases." *J Clin Oncol*, 2002 Apr 15; 20(8):2118-26. 6. Shu and Seldin, ongoing research, unpublished.

### **NR1-19**

#### **THE POTENTIAL METABOLIC MEDIATION OF REDUCED REMISSION RATES IN AFRICAN AMERICANS WITH SEASONAL AFFECTIVE DISORDER TREATED WITH BRIGHT LIGHT**

*Chair: Olaoluwa Okusaga M.D.; Author(s): Gloria M. Reeves, M.D., Soren Snitker, M.D., Patricia Langenberg, Ph.D, Monika Acharya, M.D., Hyacinth Uzoma, M.D., Mary A Johnson, Ph.D, Teodor T Postolache, M.D.*

#### **SUMMARY:**

Background: 51 African Americans (19 men, 32 women, mean age 43.1 ± 10.3) and 27 Caucasians (14 men, 13 women, mean age 47.0 ± 10.1) with a diagnosis of Seasonal Affective Disorder (SAD), recently participated in a clinical trial of daily bright light treatment for 6 weeks. African Americans had a lower remission (defined as a score =8 on the Structured Interview Guide for the Hamilton Rating Scale for Depression- SAD version) in comparison with Caucasians (46.3% vs.75%;  $p = 0.02$ ). The reason for lower remission rates in the African American patients with SAD, as well as non-seasonal depression (previously reported) is currently unknown. Hypotheses: Lower remission rate in African Americans is mediated by metabolic factors such as lower vitamin D levels, increased insulin resistance, elevated ghrelin and leptin levels. Methods: This is an add-on study to identify biomarkers of poor remission in the context of a clinical trial of light treatment for SAD. Pre- and post-treatment data on vitamin D, insulin resistance, ghrelin and leptin levels were gathered for all subjects. Statistical analysis included crude t test comparisons between the two groups. Multivariable and mediation analyses will be further performed. Results: African American participants had mean lower vitamin D levels at baseline (16.0 vs. 24.4,  $p= 0.003$ ) and after 6 weeks (14.4 vs. 22.6,  $p= 0.002$ ) of light treatment. Unadjusted values for insulin resistance, ghrelin and leptin did not differ between groups. Additional multivariable and mediation analyses are ongoing and results will be presented. Conclusions: Confirming a metabolic mediation of reduced remission after light treatment for SAD in larger studies could further the understanding of mechanisms involved in the poorer antidepressant outcome in African Americans.

### **NR1-20**

#### **MEASURING EMPATHY, EMOTIONAL INTELLIGENCE, AND ANGER IN RESIDENT PHYSICIANS OF INDIA AND USA: FINDING**

### **PREDICTORS OF VARIATIONS IN SCORES**

*Chair: Deshmukh Parikshit M.D.; Author(s): Abhijeet Faye M.D., David Kemp M.D., M.S.*

#### **SUMMARY:**

Background: Research literature suggests that physician's level of empathy, emotional intelligence (EI), and anger has significant impact on patient care [1-3]. However, the research studies assessing these levels and understanding the contributing factors are scarce. Method: A survey was administered in resident physicians of various specialties in India and USA. The survey included standardized and well validated scales such as Multi-Dimensional Emotional Empathy scale, Emotional Quotient Self-Assessment Checklist, and Clinical Anger Scale. Scores for each responding resident physician are getting correlated with his/her demographic factors and factors assessing personal, familial, occupational and social life experiences. Results: Survey administration has been completed in India but not in USA yet. As per the 150 surveys collected in India, the level of EI was found to be poor in 70% of respondents. 10.6% scored moderate to high in Clinical Anger Scale. Male gender, married status, older age, experience of major life problem, regular contact with family members, more time for recreational activities and exercise, and less patient work load had statistically significant ( $p < 0.05$ ) correlation with higher scores in EI and empathy. EI and empathy correlated negatively with clinical anger. Survey results of the American resident physicians will be analyzed when more than 500 surveys will be available. Result from both countries will be compared. Conclusion – As the research project is not completed yet, final results and conclusions are not available. Conclusions will help understating predictors for these three domains and thus will help with taking appropriate actions during residency training in order to improve patient care as well as life of resident physicians. The final results and conclusions will be sent to American Psychiatric Association no later than February 15th, 2012. References: 1. Weng HC, Hung CM, Liu YT, Cheng YJ, Yen CY, Chang CC, Huang CK. Associations between emotional intelligence and doctor burnout, job satisfaction and patient satisfaction. *Med Educ*. 2011 Aug;45(8):835-42. 2. Pollak KI, Alexander SC, Tulskey JA, Lyna P, Coffman CJ, Dolor RJ, Gulbrandsen P, Ostbye T. Physician Empathy and Listening: Associations with Patient Satisfaction and Autonomy. *J Am Board Fam Med*. 2011 Nov;24(6):665-672. 3. Gerkin DG. Angry doctors! *Tenn Med*. 2011 Feb;104(2):7-8.

### **NR1-21**

#### **HUNTINGTON'S DISEASE AND THE EFFECT**

## OF DOPAMINE DYSREGULATION ON GAMBLING, DECISION MAKING AND RISK TAKING BEHAVIOR

*Chair: Salman Majeed M.D.; Author(s): Jonathan Barton, M.D., Sunil Verma, M.D., MRCPsych*

### Summary:

Huntington's disease is a neurodegenerative condition that involves a dysregulation of dopamine. This neurochemical is also implicated in gambling and risk taking behaviors. This case report discusses a 39 year old female patient with Huntington's disease who had a significant gambling problem and exhibited impaired decision making and dangerous risk taking behaviors. We will discuss the underlying dysregulation of dopamine as a causal factor which links this patient's multiple difficulties in a way that has not been emphasized previously in the literature.

## NR1-22 TRANSCULTURAL PSYCHIATRY AND INDIGENOUS PEOPLE: A CASE REPORT

*Chair: Sorin Nica M.D.*

### Summary:

Background: The Elmhurst Hospital Center Psychiatry Department provides culturally competent care to diverse populations. However, we face particular difficulties in the psychiatric assessment of indigenous inhabitants of remote regions. Such situations require an appreciation of complex interconnections between language, culture and behavior that may not be encompassed by traditional conceptions of immigrant acculturation. The present case of a member of a Mayan subculture illustrates these challenges. Method: Single case presentation Case presentation: B, a 43 year old Guatemalan male, with no known psychiatric or medical history, was initially admitted to Internal Medicine with alcohol intoxication. B was transferred to Psychiatry after ten days due to grossly disorganized and assaultive behaviors which persisted after treatment of alcohol withdrawal and which were not explained by a medical condition. Repeated psychiatric assessments conducted in Spanish, the official language of Guatemala, lead to the diagnosis of Alcohol dependence/Alcohol-induced persisting dementia. B remained disheveled, aggressive and appeared to exhibit disorganized speech. The MiniMental State Examination suggested extremely severe cognitive impairment (5/30), but was inconsistent with the observed level of instrumental functioning. After 4 months, we learned that B belonged to the Quiche branch of the Mayan culture and was not conversant in Spanish. He came from a remote village,

isolated from mainstream Guatemalan culture. A translator-facilitated phone interview in the Quiche language indicated that B was cognitively intact and not demented. He was referred for outpatient treatment but did not follow-up after discharge. Readmission two months later to Internal Medicine for alcohol intoxication resulted in a brief hospitalization that was not followed by transfer to Psychiatry. Discussion: Consideration of the characteristics of indigenous cultures can be critical for accurate psychiatric diagnosis and effective treatment. The relationship of indigenous people to the mainstream culture of their place of origin should be evaluated when assessing acculturation patterns.

## NR1-23 COMMITTING TO TREATMENT: THE USE OF "INVOLUNTARY" INPATIENT ADDICTION SERVICES FOR PATIENTS WITH GRAVE SUBSTANCE USE DISORDERS

*Chair: Arthur Williams M.D.; Author(s): Ryan McCormack M.D., Stephen Ross M.D.*

### SUMMARY:

Serving as the oldest public hospital in the United States, and as New York City's flagship public hospital, Bellevue Hospital Center proudly maintains its dedication to providing a safety net for vulnerable populations in America's largest and most diverse city. In addition to providing services and training as an academic urban, public, tertiary care and level one trauma center, Bellevue serves as the largest provider of inpatient addiction care in the United States and as a leader in the field for new innovations and technology to be disseminated throughout the public hospital network. Bellevue handles nearly 120,000 emergency patients and some 26,000 inpatients every year. The authors introduce a pilot program involving inpatient civil commitment for high-utilizer patients gravely disabled by substance use disorders (SUDs) at Bellevue Hospital in the setting of several patient deaths following hundreds of emergency room (ED) visits and brief yet expensive and ineffective hospitalizations. The pilot program grew from an interdisciplinary (emergency medicine, psychiatry, hospital administration and legal counsel, and the New York City Department of Homeless Services) initiative to better serve patients with multifaceted problems requiring extraordinarily complex treatment plans. Of 350,000 ED visits over a three-year span, a subset of 43 patients emerged as having more than ten visits a year for three consecutive years involving an alcohol-related diagnosis. These 43 patients, average age under 50, accrued over \$8.1 million in healthcare charges in those years despite a three-year

mortality rate of roughly 20%. A case series is presented of 12 (of the total 43) patients committed to inpatient treatment including a detailed case report of an early enrollee who was committed for inability to care for self-secondary to grave alcohol dependence. Data are presented tabulating use of ED, inpatient, outpatient, and housing services at 3- and 6-month time points both before and after the intervention of inpatient commitment. The authors discuss the use of involuntary inpatient commitment when appropriate as part of a comprehensive treatment plan to improve the standard of care for patients with grave SUDs and associated legal challenges and clinical realities.

### **NR1-24 IMPULSIVITY AND SUICIDALITY IN A WAR VETERAN**

*Chair: Andrea Brownridge M.D.*

#### **SUMMARY:**

PTSD is a normal response to a completely abnormal situation. Today's war veterans are suffering as they attempt to manage the multitude of PTSD symptoms and their sequelae after a return to everyday life. With the rising incidence of PTSD and the considerable amount of research done in an attempt to reduce the suffering of veterans, it remains a treatment challenge. A 35 year old Iraq combat veteran presented to the psychiatric emergency department, on referral from his outpatient psychiatrist for suicidal and homicidal ideations. The patient planned to kill himself following a child custody hearing involving his four year old son. At the hearing 5 days prior to admission, the patient impulsively fired his attorney for arriving late. He then demanded that the judge return from his chambers for the hearing, only to later imprudently storm out of the hearing. Enraged, he contemplated killing the judge, his attorney, and himself. The patient grew increasingly depressed upon learning that he was held in contempt of court and facing incarceration and a large fine. He planned to kill himself with his gun, but was stopped by his girlfriend. He was admitted for inpatient hospitalization because of worsening depression and suicidal thoughts in the setting of chronic PTSD. On admission, he endorsed depressed mood, hopelessness, anhedonia, decreased appetite, insomnia, and suicidal thoughts. He also reported irritability, impulsivity and occasional thoughts of harming others. He denied symptoms of mania and psychosis. He reported compliance with his medications which included citalopram, bupropion, alprazolam, amlodipine, and zolpidem. He denied any recent alcohol or drug use. Physical exam was unremarkable. The patient was calm, but guarded and hypervigilant with fair eye contact.

Speech was slow and soft. Mood was depressed with constricted affect. Thought process was linear. No delusions or perceptual disturbances were apparent. Suicidal ideations were present, without homicidal ideations. Insight and judgment were poor as was impulse control. In the hospital, his medications were resumed. Prazosin was added to target re-experiencing and hyperarousal symptoms. Supportive psychotherapy was beneficial in decreasing catastrophic thinking and in helping the patient develop a logical and flexible approach to addressing external stressors. An updated suicide safety plan was formulated. At discharge the patient had no suicidal or homicidal ideations, and his condition was fair. He was referred for intensive cognitive processing therapy. This case illustrates the complexity of PTSD and its disabling manifestations of depression, impulsivity, and suicidality. Combined pharmacotherapy and psychotherapy targeted toward affective instability and distorted thinking is integral in assisting veterans to reduce their suffering and restore their emotional coping capacity as they confront the challenges of everyday life.

### **NR1-25 ANXIETY DISORDER AND SCHIZENCEPHALY: A CONNECTION?**

*Chair: Neha Kansara M.D.; Author(s): Jeffrey A. Ali, M.D., M.Sc.*

#### **Summary:**

Rare neurodevelopmental disorders are often identified by the manifestation of neuropsychiatric symptoms. The case of a 38 year old patient with a history of congenital seizures without any known psychiatric contact who presented to a University Psychiatric Emergency Service and then to the University Adult Outpatient Psychiatric Clinic with symptoms consistent with an "Anxiety Disorder" is presented to illustrate this concept. The patient admitted to a history of having experienced both partial complex and generalized tonic clonic seizures and a single episode of an anxiety attack. A full psychiatric evaluation in the outpatient clinic was conducted; a complete neuropsychiatric interview, a mini neurologic examination and a detailed review of her past history, electroencephalographic (EEG) studies and neuroimaging studies were undertaken. The patient's response to a psychotropic agent prescribed in the emergency setting was also considered. A literature review was conducted and the paucity of reports of psychiatric complaints associated with schizencephaly recognized. This presentation will discuss these in the context of the current case. Keywords: Anxiety disorder, panic attack, schizencephaly, seizure.

**NR1-26****ASSESSING THE QUALITY OF MEDICAL DECISION MAKING CAPACITY CONSULTS AT AN ACADEMIC CENTER**

*Chair: Gaurav Jain M.D.; Author(s): Lokesh Shabani, M.D.; Kristina Dzara, Ph.D; Pravesh Basnet, M.D.; Mary E. Royce, ACNP-BC; and David S. Resch, M.D.*

**SUMMARY:**

**Background:** Patients are assumed to have medical decision making capacity (M.D.MC) unless proven otherwise. Many physicians lack formal training in M.D.MC evaluation. Appelbaum et al. (1988) proposed four criteria for determining whether a patient has M.D.MC: 1) understand the relevant information about proposed diagnostic tests or treatment; 2) appreciate their situation (including their underlying values and current medical situation); 3) use reason to make a decision; and 4) communicate their choice.; Authors sought to determine the comprehensiveness of M.D.MC consultation documentation (using Appelbaum criteria), by the psychiatry team in the medical and surgical inpatient facilities of an academic medical center. **Method:** All patients referred to psychiatry consultation for M.D.MC determination during a one-year retrospective period were included (N=51). The initial consultation and follow-up notes were reviewed.; Authors also recorded the reason for referral initiation and the final M.D.MC. The study was IRB approved. **Results:** The top three reasons for consultation were “leaving AMA” (25.5%; n=13), “placement after discharge” (21.6%, n=11), and “refusing medications” (15.7%, n=8). The majority of consultations resulted in the appropriate documentation for the ability to communicate a choice (92.2%; n=47), the ability to understand relevant information (88.2%; n=45), the ability to appreciate the situation and its consequences (88.2%; n=45), and the ability to reason about treatment options (78.4%; n=40). All four parameters were documented in 39 charts (76.5%). The consultation team agreed with the referring physician 48% of the time (n=24), although final M.D.MC was not documented in one chart. In patients with absence of M.D.MC (n=24), the majority did not have documentation of a health care proxy in the record (83.3%; n=20). **Discussion:** Quality of documentation was reasonably good. The ability to communicate choice was most often documented, while assessing the ability to reason about treatment options was often not documented. The results imply that physicians may stop short of assessing all four components before determining final M.D.MC. The assignment and documentation of health care proxy also needs improvement. Overall, the psychiatry consultation

team agreed with primary physician in about half of the referrals, suggesting that physicians may need additional training regarding assessment of M.D.MC.

**NR1-27****ANOREXIA NERVOSA AND FOLIE A DEUX: A CASE REPORT**

*Chair: Raman Baweja M.D.; Author(s): Aggarwal, Richa M.D.; Mab, Fauzia M.D.*

**SUMMARY:**

**Introduction/case:** Folie à deux is a rare delusional disorder shared by two people with close emotional ties. Anorexia Nervosa is a severe eating disorder characterized by intense fear of gaining weight, a refusal to maintain body weight above 85% of the expected weight for a given age and height, three consecutive missed periods and either refusal to admit the seriousness of the weight loss, undue influence of shape or weight on one’s self image, or a disturbed experience in one’s shape or weight (DSM-IV TR). We report the unique case of Anorexia Nervosa with Folie a Deux in which shared delusion was contributing to the psychopathology of Anorexia Nervosa. Here we present a case of 15-year-old girl who was transferred to the child and adolescent psychiatry unit for management of Anorexia Nervosa. She had shared paranoid delusion with her mother against her father. Her mother was primary person with these paranoid delusions and was inducing these delusions in the patient. Her shared delusion indirectly was contributing to her eating problem. Her psychiatric treatment included nutritional rehabilitation, monitoring her eating disorder behaviors, supportive therapy, individual and group therapy, and family therapy. Her delusional beliefs got weakened after separation from mother. **Discussion:** “Anorexia a deux” has been described for familial occurrence of anorexia nervosa in the literature. A clear mechanism for development of Anorexia nervosa in family is unknown. Most acceptable theories are genetic theory in twins and induction theories between family members. The progression of delusional symptoms between the family members is thought to reflect an attempt of a family to maintain cohesiveness in the presence of a perceived hostile environment. **Conclusion:** Clinicians should be aware about complex family dynamics in treating patient with Anorexia nervosa. Proper recognition of a rare disorder like folie a deux can result in successful treatment outcomes by separation of patients, behavioral treatment and psychopharmacological treatment.

**NR1-28****FALLS AMONGST PSYCHIATRIC INPATIENTS: A CASE CONTROL RETROSPECTIVE STUDY**

**IN A CENTER CITY PSYCHIATRIC- MEDICAL CARE UNIT**

*Chair: Deana Sabol D.O.; Author(s): Nivedita Mathur M.D., MRCPsych, Donald Kushon M.D., Gaurav Mathur M.D., MRCP, Arun Haridas M.D., MRCPsych, Renu Culas M.D., MRCPsych*

**SUMMARY:**

Background: Falls among inpatients have implications in terms of increased length of stay, costs and discharge plans in addition to adverse physical injury outcomes. Although there are studies to identify risk factors for falls there is a dearth of studies that focus on falls in psychiatric inpatient units. This study attempts to find risk factors associated with falls in psychiatric inpatients in an acute setting. Aims and Objectives: To compare the patients characteristics who sustained falls in inpatient setting (cases) with age-and-sex matched controls and to identify risk factors for falls in this understudied psychiatric population. Methods: We identified all cases (54) with documented falls between Jan 1, 2007 and Dec 31, 2009. Age-and sex matched controls (54) were randomly selected from all inpatients during the same time period who did not sustain a fall. Data regarding Psychiatric Diagnosis (Axis I & Axis II), Medical Diagnosis (Axis III), Psychotropic medications, Non-psychotropic medications, baseline vitals and EKG, Urine drug screen, labs, Morse Fall Scores at the time of admission, falls precautions instituted prior to the event, details of the actual fall event itself, and complications resulting from the fall were collected. Multivariate logistic regression was used to identify associations with faller status. Results: There were 72 falls in 54 patients from Jan 2007 through Dec 2009 out of which 24 were males and the mean age of cases was 45.6 yrs. The most common Axis I diagnosis was Substance dependence followed by Schizophrenia, Bipolar disorder and M.D.D. An average of 2.57 psychotropic medications were used per case and 2.2 per control ( $p=0.36$ ). The most commonly prescribed psychotropic medication was risperidone (18), followed by celexa (14), seroquel (10) and trazadone (10). 30 cases and 36 controls had positive UDS ( $p=0.63$ ). UDS was positive for benzodiazepines in 33 cases, cocaine in 28 cases, marijuana in 11 cases, opiates in 10 and barbiturates in 8 cases. Baseline BP and pulse was similar between cases and controls ( $p=0.07$  for SBP and 0.84 for DBP) ( $p=0.67$  for HR). The average Morse Fall Score was 38.1 for cases and 25.3 for controls ( $p=0.03$ ). Complications resulting from the fall were seen in 32 (59.3%) cases. Conclusions: The Morse Fall score is a useful predictor of the risk of falls in patients admitted to PMCU, and should be routinely utilized. Baseline vitals, EKG, UDS and number of medications (both psychotropic and non-psychotropic medications)

were not significantly different between cases and controls.

**NR1-29**  
**UNIQUE ASPECTS IN TREATING SOMATOFORM SPECTRUM DISORDERS BY COMBINED INTERNAL MEDICINE/ PSYCHIATRY PHYSICIANS**

*Chair: Sherrell Lam M.D.*

**SUMMARY:**

Somatoform disorders present a challenge to diagnose and treat, given the diversity of presentation and the resistance to standard treatments. Physicians can experience a negative countertransference towards somatizing patients, as they can be high utilizers of resources and progress can be minimal. Internists may focus on the physical aspects of illness and neglect the mental aspects; and patients may see referrals to psychiatry as a dismissal of physical symptoms. Physicians trained in both internal medicine and psychiatry may be in a unique position to care for these patients by limiting unnecessary procedures and providing a therapeutic framework to address underlying anxieties. Our case is of a 40 year old male soldier who had been suffering with chronic gastrointestinal, musculoskeletal and genitourinary complaints for two years. He had undergone thorough medical work-up and still did not have relief of his symptoms. Incidentally, he was referred to the Behavioral Health Clinic after endorsing anxiety symptoms through Deployment Health and there began treatment with an internal medicine/psychiatry resident. The patient was frustrated with the lack of attention he was receiving and concerned he had serious health problems. He was being seen in the ER 2-3 times per week—each time by a different provider and each time given a different diagnosis. As a result, the patient was accumulating new symptoms with each subsequent ER visit. Meanwhile, a therapeutic alliance was developing as the patient was seen weekly in the Behavioral Health Clinic and he began to feel as though a provider was truly listening. This relationship was used as a springboard to consolidate the patient's care to one primary provider, limit his interactions with too many specialists, and educate him about appropriate uses of the ER. He became accustomed to discussing his medical concerns at his psychiatry appointments, and also felt reassured that appropriate medical work-up would be performed if needed. With this support, the patient also began to develop insight into his need to escalate his symptoms in an attempt to get the attention of his providers. After nine months of treatment, the patient is no longer using the ER weekly and has a better outlook on the state

of his health. There is little data on evidence-based treatments for somatoform disorders. An interesting area to research further is whether dual specialty physicians' treatment of somatoform disorders results in better outcomes.

### NR1-30

#### Improvement of Severe Psychosis Immediately After Delivery in a Patient With Schizophrenia: a Case Report

*Chair: Natasha Dalseth M.D.; Author(s): Leorah M. Walsh, M.D.; Carolina Retamero, M.D.*

#### SUMMARY:

**Introduction:** The effect of pregnancy on the course of psychotic disorders has been extensively described in literature, with the predominant pattern of exacerbation of psychosis during the prepartum period, and further worsening during the postpartum period. We present an unusual case of a 23 year old woman with a prior diagnosis of Schizophrenia, who presented with delusional denial of pregnancy as well as predominant negative symptoms in the third trimester, and whose symptoms took an unexpected turn soon after labor and delivery which were remarkable for the unusually low level of pain. Within a day of delivery, she had complete resolution of delusions, and a rapid, dramatic reduction of negative symptoms. This improvement was sustained during the duration of her two week postpartum hospitalization. **Methods:** We completed a review of literature on PubMed using the following keywords: (1) psychosis and pregnancy, (2) psychosis and postpartum, (3) improvement/lessening/resolution/decrease of psychosis postpartum, (4) estrogen/oestrogen and psychosis, (5) FSH/LH/progesterone/oxytocin and psychosis, and (6) labor/delivery/childbirth and hypoalgesia and schizophrenia. This literature search was conducted to explore the link between physiological and psychodynamic changes of pregnancy and the course of psychotic illness, as well as the effect of various hormones on psychosis. **Results:** To our knowledge, there are no reports describing improvement or resolution of psychotic symptoms during the postpartum period. On the contrary, there are multiple reports describing worsening of psychosis postpartum. We believe that a possible cause for improvement of our patient's symptoms was the rapid, large amount of oxytocin released during delivery. This belief is partly based on reports from small clinical studies that have suggested that oxytocin may improve the negative symptoms of schizophrenia, increase prosocial behavior and overall social functioning. **Conclusion:** A greater number of case reports would be needed to further explore the possible link between natural release of

oxytocin during childbirth and its effect on psychotic symptoms during postpartum period. We suggest that this may be achieved through collaborative effort between psychiatrists and obstetricians, which would allow for a closer observation of women with psychotic illness during pregnancy, labor, delivery and postpartum period.

### NR1-31

#### IMPACT OF DEPRESSION ON SURVIVAL, REJECTION, AND HOSPITALIZATION RATES AFTER HEART TRANSPLANTATION

*Chair: Dara PuM.P.H.rey M.D.; Author(s): Ike Okwuosa, M.D., Kathleen Grady, Ph.D, APN, FAAN, Clyde Yancy, M.D., Edwin McGee, M.D. William Cotts, M.D.*

#### SUMMARY:

**Impact of Depression on Survival, Rejection, and Hospitalization rates after Heart Transplantation I.** Okwuosa, D. PuM.P.H.rey, K. Grady, C. Yancy, E. McGee, W. Cotts Background Depression occurs commonly in patients with chronic diseases. Clinical depression in heart failure has been associated with medication noncompliance and increased frequency of hospitalizations. Little is known about the effect of clinical depression after heart transplantation (HT). The purpose of this study was to evaluate the impact of depression on survival, cardiac rejection and hospitalization after HT. **Methods** We performed a single center retrospective review of 102 consecutive patients who underwent HT at Northwestern Memorial Hospital from June 2005 to October 2009. The diagnosis of depression was based on a review of pre-transplant mental health evaluation and attending physician documentation in the medical record. A Kaplan Meir survival curve was constructed, the difference between the curves was assessed with a log rank test. Post-transplant hospitalizations and biopsy proven cardiac rejection were assessed by review of fully captured medical record. **Results** Of 102 HT patients, 26 (26%) had depression. Depressed patients were similar demographically to non-depressed patients : Mean age at time of transplant = 57.6 years vs. 56.9 , p=0.79), white =81% vs. 75%, p=0.53, and male=65% vs. 76%, p=.23, respectively. Depressed and non-depressed patients were similar clinically, as well: bridge to transplant with a left ventricular assist device (46% vs. 45% p=0.92, and dilated cardiomyopathy as the etiology of heart failure (42% vs. 37% p=0.65), followed by ischemic cardiomyopathy (38% vs. 39% p=.92), respectively. There was no statistical difference in survival between groups at 5 years after HT (p=.94 ). All cause hospitalizations were higher in depressed versus non-depressed patients (4.3 vs. 2.6 p=0.05).

There were no significant differences in hospitalizations between the two groups for the following complications: cardiac (volume overload, arrhythmias, acute rejection) and infections. There was no significant difference in episodes of 2R and 3R rejection in depressed vs. non-depressed patients. Conclusion Depression is associated with increased resource utilization after HT, despite the lack of differences between depressed and non-depressed patients for morbidity and mortality. How treatment of depression impacts outcomes cannot be determined from our study, nor can it be determined how the presence of depression impacts longer term outcomes after HT. Additional study is warranted.

### NR1-32

#### 6 MONTH FOLLOW-UP OF RTMS EFFICACY IN TREATMENT RESISTANT MAJOR DEPRESSION: A CASE REPORT

*Chair: Onur Durmaz M.D.; Author(s): Mehmet Alpay Ates, M.D.*

##### Summary:

rTMS (repetitive Transcranial Magnetic Stimulation) is a novel treatment method shown to be effective in depression. Although underlying mechanisms of this treatment are not fully understood yet, effects on neuroplasticity, neuromodulation and cortical excitability are the most prominent hypotheses. Several studies have shown that rTMS have therapeutic benefits on major depression. Long-lasting effects of rTMS on depression is not clear. In this report a 44 year-old male diagnosed with unipolar major depression and under treatment of venlafaxine 375 mg/day and ziprasidone 40 mg/day for five months, received 15 sessions of rTMS(5 days per week) at %110 MT, 20 Hz, 1000 stimuli/day as add-on treatment due to insufficient medication response. MADRS performed at baseline at the end of the treatment and 1,3,6 months after course. MADRS scores were found to be 29,9,6,7 and 13. The patient showed significant improvement immediately after treatment course and maintained clinical improvement in 1,3 months while mild depressive symptoms are found in month 6 as confirmed by MADRS scores. This data shows that even though the relatively higher score of MADRS in 6th month, rTMS is a favorable therapeutic tool in depression with its long-lasting efficacy and benign side effect profile.

### NR1-33

#### SYMPTOM MIRRORING OF NECROTIZING FASCIITIS IN IDENTICAL TWIN BROTHERS WHILE DEPLOYED TO COMBAT ZONE

*Chair: David Hanrahan M.D.; Author(s): Harold J. Wain, Ph.D.*

##### SUMMARY:

Introduction: There are limitations to categorical classifications of mental disorders. This is especially true for describing phenomena that are distributed on a continuum and well-illustrated by our case of twin 20 year old soldiers who are medically evacuated out of combat zone for presentation of suspected necrotizing fasciitis. We review and present current available literature on best diagnostic and management approaches to maladaptive behaviors that lie outside the diagnostic classification systems we have in place today. Case: The patients are 20-year-old monozygotic brothers in the military who were both deployed to combat zone with twin A initially presenting with redness, bruising, and pain of left thigh that were concerning for necrotizing fasciitis resulting in urgent surgical exploration that showed only normal healthy tissue. However, this resulted in his medical evacuation out of the battlefield. Twin B presented with identical symptoms five days later of his right leg and similarly underwent surgical exploration revealing healthy tissue. Upon their arrival from the combat theater to our hospital, they were both found to be facing significant stressors and further review of electronic medical records showed a pattern of presentation with identical medical symptomatology in the past. Conclusion: This mirroring behavior was clearly maladaptive in these brothers however no particular diagnostic category fit the presentation. It is not unusual however for psychiatrists to face diagnostic dilemmas of clearly maladaptive behavior. Despite an unclear DSM-IV diagnosis, these patients still need empathetic care and attention. In the case of our soldiers, they continue to face significant barriers towards health. This is the first case to our knowledge of a somatoform spectrum-like disorder presenting in the form of suspected necrotizing fasciitis. Malingering however cannot be fully ruled out. Limited data is available that addresses the most optimal management approaches to such cases.

### NR1-34

#### LONG TERM FOLLOW UP OF A PATIENT WITH SCHIZOPHRENIA SUPERIMPOSED WITH MYASTHENIA GRAVIS

*Chair: Haebin Kim M.D.; Author(s): Seung-Yup Lee, M.D.; and Geon Ho Bahn, M.D., Ph.D.*

##### SUMMARY:

In a case of 46-year-old woman suffering from schizophrenia over 20 years, she had frequent episodes of dyspnea and confirmed as superimposed with myasthenia gravis(MG). Throughout seven year follow-up after diagnosed as MG, she has hospitalized

6 times because of respiratory symptoms, and neurologist and internist also engaged to treat her symptoms.; Authors experienced various conditions associated with untoward effects of medication for both myasthenia and schizophrenia. Therefore, authors reported considerations for the pharmacotherapy of schizophrenia with myasthenia gravis.

**NR1-35**  
**CONTINUITY OF CARE AFTER INPATIENT DISCHARGE OF PATIENTS WITH SCHIZOPHRENIA IN KOREA**

*Chair: Seungyup Lee M.D.; Author(s): Hae Bin Kim, M.D., Kyung Hoon Kim, Ph.D., Jong Woo Paik, M.D., Ph.D.*

**SUMMARY:**

**Objectives :** A failure to follow up with psychiatric outpatient care after leaving the hospital greatly increases the risk of nonadherence to prescribed medications, relapse and rehospitalization. Therefore, it is important to have a follow-up check on a regular basis, in order to have the Schizophrenia patients take the antipsychotics consistently. Using the Korean Health Insurance data, this study investigated the continuity of care after inpatient discharge of patients with schizophrenia. **Methods :** Data were extracted from information of Korean Health Insurance data. The study examined the rates of 30-, 180-day follow-up care for 55,879 National health insurance-enrolled patients with the diagnosis of Schizophrenia discharged from inpatient psychiatric facilities between January 1, 2007, and December 31, 2007. We analyzed status of follow-up visits and their types of health insurance coverage based on their age, sex, type of medical institution. **Results :** Depending on mental health policy environment, the entire body of patients (n=55,879) was divided into Health insurance(n=23,598) and Medical aid(n=32,281). Of the total 55,879 hospital discharges, 46.1% received schizophrenia-related outpatient visits in 30 days and 55.5% in 180 days following hospital discharge. According to the data about the health insurance types, the number of follow-up visits for patients with Health insurance reaches up to 63.8%(in 30days), 74.5%(in 180days); on the other hand, that for patients with Medical aid is only about 33.2%(in 30days), 41.5%(in 180days), which is almost as low as a half of follow-up visits for the former group. **Conclusion :** Overall rate of outpatient follow-up was low in all the patients after hospital discharge. Especially, the rate for the follow-up visits was considerably low for the patients with Medical aid. Lack of outpatient follow-up leading to increases in psychotic symptoms, the risk of relapse and rehospitalization ; Therefore, particular attention needs to be devoted to evaluate factors affecting failure

to attend outpatient follow-up after hospital discharge, especially for patients with Medical aid.

**NR1-36**  
**POST-TRAUMATIC LEFT TEMPORAL SEIZURE MANIFESTING AS BIZARRE BEHAVIOR AND SUICIDALITY IN A YOUNG SOLDIER**

*Chair: Adam Hunzeker M.D.*

**SUMMARY:**

**Introduction:** Behavioral and cognitive functioning changes in traumatic brain injury (TBI) patients have been well documented as early as Phineas Gage. Traditionally these behavioral and cognitive changes are difficult to treat as the potential pathophysiology ranges from mood disorders to organic brain injury. It is important to identify and treat contributing processes to maximize recovery in the vital 6-12 months after exposure. This is a case of a severe TBI patient found to have left temporal lobe seizure activity with drastic improvement of behavior and cognitive functioning after implementation and titration of lamotrigine. **Case:** The patient is a 26 year old male soldier with history of both combat related post-traumatic stress disorder (PTSD) and prior mild TBI who sustained significant head injuries following motor cycle accident. Our evaluation revealed severe TBI with rehabilitation complicated by the onset of bizarre behavior, suicidal ideations, and impaired cognitive functioning. Patient had complete work up including laboratory for altered mental status, head imaging and 24 hour EEG monitoring that revealed spike activity in the left temporal lobe. After implementation and titration of lamotrigine to 225mg twice daily, he demonstrated both decrease in disruptive behavior, resolution of his suicidal ideations, improvement of cognitive functioning based on Montreal Cognitive Assessment and neuro-cognitive testing. **Discussion:** The military population is particularly vulnerable population for development of TBI due to high risk activities both in combat theatre and at home. The behavioral sequelae from TBI are complex and often can include reaction to the trauma as well as organic injury to the brain. Hence, a thorough workup is done in order to treat reversible causes. In this case, it appears that the seizure activity in the left temporal lobe was at least one factor that explains his behavioral manifestation. This is supported by drastic improvement after treatment with lamotrigine and resolution of temporal spike activity on follow up EEG.

**NR1-37**  
**EFFECTS OF TRANSCRANIAL MAGNETIC STIMULATION IN THE TREATMENT OF**

**COCAINE DEPENDENCE**

*Chair: Philip Ribeiro M.D.; Author(s): Philip Leite Ribeiro, Debora Arnaut, Banca Bellini, Hellen Marra, Rodrigo Lancelote, Martin Myczkowski, Carlos Mansur, Danilo Baltieri, Marco A Marcolin*

**SUMMARY:**

Introduction: Cocaine Dependence is a serious worldwide issue. Data from the UNODC shows that in 2007 there were 16 million adult users in the world. Studies Suggests a reduction in cocaine craving with transcranial Magnetic stimulation (Polliti, 2008) We are conducting a clinical trial to study the effects of repeated Transcranial Magnetic Stimulation (rTMS) in the treatment of Cocaine Dependence. Material and Methods: In a Controlled randomized double blind study 20 patients will receive active rTMS and 20 patients will receive sham stimulation, all patients were diagnosed with SCID-P with cocaine dependence as the main disorder. The study is registered in Clinical Trials under NCT01259362 Procedure Each active Patient received a total of 25000Hz during a month in the left dorso lateral prefrontal cortex. Sham patients were treated with a sham coil. Cocaine urine analysis were performed once a week in the patients. Neuropsychological Evaluation and Scales Patients were tested with impulsiveness scale (BIS 11), Addiction Severity Index - 6 (ASI-6), Minnesota Cocaine Craving Scale, HAM A, HAM D and were submitted to a detailed neuropsychological evaluation (IGT, RAVLT, STROOP, TRAIL making A and B, Weschler Logical Memory, WEISS III). Statistical Analysis The statistical analysis of the data was obtained with SPSS 17. Until now 25 patients have completed the study. The statistical analysis of the data was obtained with SPSS 17. Results: The data collected suggest important reduction in cocaine craving in the active arm of the study, when compared to the sham patients. Other data updated to the latest patients will be presented in the poster as well as results from urine analysis database. References: UNODC, World Drug Report, <http://www.unodc/en/data-and-analysis/WDR-2010.html>, pg 67 Polliti et al. Daily Sessions of rTMS to left prefrontal cortex reduce cocaine craving, American Journal on Addic., 2008;Jul-AUG;17(4)345-6. Clinical Trials, <http://www.clinicaltrials.gov/ct2/show/NCT01259362?term=Transcranial+Magnetic+Stimulation+Cocaine&rank=1>

**NR1-38**

**BACLOFEN DEPENDENCE AND WITHDRAWAL DELIRIUM: A REVIEW OF NEUROPSYCHIATRIC PRESENTATIONS AND MANAGEMENT STRATEGIES WITH A CASE REPORT**

*Chair: Robul Amin M.D.*

**SUMMARY:**

Background: Despite many advances in the treatment of psychiatric disorders, there continues to be only limited number of available pharmacologic modalities for the treatment of substance dependence. In the past decade, baclofen has been of particular interest as a potential treatment for alcohol and other substance dependence disorders. However, the safety and efficacy profile of baclofen for this purpose is still not well-understood. Objectives: We first highlight this problem with a clinical case report of a patient with physiologic dependence and severe withdrawal from baclofen that was surreptitiously obtained and used at high doses in an attempt to self-treat alcohol dependence. We then review the available literature on neuropsychiatric symptoms induced by baclofen withdrawal and management strategies. Method: Articles were obtained through a systematic search of MEDLINE and from the bibliographies of relevant articles. Studies were considered relevant if the cases involved neuropsychiatric symptoms in the context of baclofen withdrawal. Results: Thirty-one publications of case reports and series were identified, yielding a database of 45 discrete withdrawal episodes. The most common neuropsychiatric symptom was visual hallucination (N=30, 66.6%). Treatment with re-institution of baclofen appears superior to alternative methods, with a mean time to resolution of 37.6 hours versus 292.4 hours, respectively. Conclusion: Early recognition of baclofen withdrawal is important given the potential for severe symptoms. Treatments with neuroleptic and benzodiazepine medications are minimally effective compared to baclofen. Therefore, reinstatement of baclofen is highly recommended to avoid prolonged withdrawal symptoms. Further well-designed studies are needed before baclofen can be recommended for the potential treatment of alcohol dependence.

**NR1-39**

**PROPHYLAXIS WITH ANTIPSYCHOTIC MEDICATION REDUCES THE RISK OF POST-OPERATIVE DELIRIUM IN ELDERLY PATIENTS: A META-ANALYSIS**

*Chair: Stock Veronika M.D.; Author(s): Polina Teslyar, M.D. Christopher Wilk, M.D. Ulas Camsari, M.D. Seth Himelhoch, M.D., M.P.H.*

**SUMMARY:**

Background: Delirium is a common occurrence in hospitalized elderly patients and can result in increased morbidity and mortality, prolonged hospitalization,

and a net increase in health care costs. Although there is a considerable evidence available for the treatment of delirium, the evidence supporting pharmacologic prevention of delirium in a high risk patient population is limited. This review aims to determine whether delirium in at risk patients can be prevented with antipsychotic prophylaxis. Methods: A systematic literature review of articles from January 1950 to November 2011 was conducted in Pubmed and PsychInfo databases. Only randomized controlled trials of typical or atypical antipsychotic medication used to prevent the onset of delirium were included for analysis. Key words used in the search were: “delirium”, “encephalopathy”, “ICU psychosis”, “prevention”, and “prophylaxis”. Studies had to include a validated method of assessing for delirium. Data analysis was performed using the metan command in STATA (StataCorp LP, College Station, Texas). Results: Four studies met our inclusion criteria for analysis. Medication administered included haloperidol (2 studies), risperidone (1 study), and olanzapine (1 study). All four studies examined elderly surgical patients (2 orthopedic, 1 cardiac, 1 gastrointestinal), spanning four different countries (USA, Japan, Netherlands, Thailand). Three of four studies showed a significant decrease in the relative risk of delirium. The overall treatment effect size was 0.52 (0.41-0.68) suggesting a significant protective effect of antipsychotic prophylaxis for delirium. Conclusion: Although there are few studies in the literature that have examined the impact of the prophylactic use of antipsychotic medications, this analysis suggests that either pre or peri-operative use of prophylactic antipsychotics may be an effective strategy to reduce the overall risk of post-operative delirium in high risk elderly patients.

#### NR1-40

#### A LIFE-THREATENING CASE OF ARIPIPRAZOLE-INDUCED DYSPHAGIA

*Chair: Muhammad Majeed M.D.; Author(s): Branden A. Youngman, D.O.; Aurangzeb Baber, M.D.; Jeffrey Bedrick, M.D.*

#### SUMMARY:

Dysphagia is a rare manifestation of EPS (Extra pyramidal symptoms), seen in patients taking antipsychotic medication. The mechanism involves spastic paralysis of voluntary muscles used in swallowing. To our knowledge this is the first ever reported case of dysphagia experienced in patient on low dose aripiprazole. A 43 year old female with past medical history of depression, anxiety and mitral valve prolapse, recently started on 1mg of aripiprazole and titrated up 10 mg to augment her anti-depressant medications

presented to the ER for evaluation of progressive dysphagia for the past 2 weeks. Her dysphagia had progressed to a point where she was not able to swallow her own saliva. A stat upper GI endoscopy performed in the ER for concern of foreign body, in the esophagus, showed no gross abnormality. She was admitted to general medical floor and made NPO. Psychiatry was consulted as the differential diagnosis included conversion disorder vs. medication side effect. Aripiprazole was held at this point. Her swallowing function failed to improve over the course of next 4 days both subjectively and through objective evaluation of speech pathologist. In the meanwhile her serum bicarbonate started to trend down to the point where she had to be transferred to ICU for non-gap acidosis and hypotension attributed to starvation ketosis. At this point neurology was consulted and patient was found to have Parkinson-like features on neuro exam including mask-like faces and cogwheel rigidity. She was started on diphenhydramine to treat the dystonic reaction. She was also started on IV bicarbonate infusion and naso-enteral tube feeds. Her acidosis resolved and she was transferred out of the unit. A video barium swallow showed moderated oral and severe pharyngeal impairment of swallowing function with aspiration risk. Over the course of next week after being transferred from ICU to general medical floor she felt that her swallowing function was getting better as she was able to swallow her own saliva. A repeat evaluation was done by speech pathologist showing significant improvement. Repeat video barium swallow also showed improvement from the prior study. She was started on a modified chopped diet and she did well. She was discharged home on diphenhydramine, off aripiprazole and on a modified chopped diet after two weeks of hospital stay. This case illustrates the possibility of extremely rare side effect of aripiprazole and clinicians must be aware of the possibility and consider early discontinuation of the medication if dysphagia develops. Patients taking aripiprazole should be educated about the side effect, which should be reported immediately.

#### NR1-41

#### CATATONIA: HOW MUCH LORAZEPAM IS TOO MUCH?

*Chair: John Gillean M.D.; Author(s): Renu Culas, M.D.; Andrea Papa-Molter, DO; Sunil Verma, M.D.*

#### SUMMARY:

The present research describes catatonia based on a review of the current psychiatric literature with a specific emphasis on diagnosis and treatment of the disorder using the lorazepam challenge and standing doses of lorazepam. A specific case is presented which outlines

the course of hospitalization and treatment of a patient with catatonia related to major depressive disorder with psychotic features. We aim to emphasize the importance of utilizing higher doses and more frequent dosing schedules of lorazepam in catatonic patients that do not initially respond to treatment.

**NR1-42****TWO CASES HIGHLIGHTING THE IMPORTANCE OF DIFFERENTIATING BETWEEN PRIMARY AND SECONDARY CAUSES OF DELUSIONAL PARASITOSIS**

*Chair: Mohammad Khan, M.B.B.S*

**SUMMARY:**

Message body The psychiatric literature describes the typical presentation of a primary delusional parasitosis as a middle-aged white woman with a monosymptomatic delusion of infestation with parasites despite no physical evidence of such an infestation. The present research compares two cases of delusional parasitosis, one a typical presentation and one an atypical presentation. The first case involves a middle-aged Hispanic female who was found to have a primary delusional parasitosis. The second case involves a young African-American male who was found to have a delusional parasitosis secondary to amphetamine abuse. We will highlight the importance of ruling out secondary causes of such a delusion, especially when an atypical presentation of the disorder is encountered, as often times treatment of the underlying cause will result in complete resolution of symptoms and may not warrant a trial with antipsychotic medication.

**NR1-43****RISK FACTOR ANALYSIS OF SYNDROME OF INAPPROPRIATE SECRETION OF ANTI DIURETIC HORMONE (SIADH) IN PSYCHIATRIC EMERGENCY ROOM (ER) POPULATION**

*Chair: Eswar Kumar Dayanandam M.D.; Author(s): Mohammad Asim Nisar M.D., Luis Betancourt M.D.*

**SUMMARY:**

Objectives: To determine the risk factors causing SIADH in the psychiatric ER population. Method- A case control study was done to evaluate the risk factors in patients with SIADH who visited the psychiatric ER from 2006-09. Case definition- Patients with sodium levels less than 133mg/dl, all the definable causes of hyponatremia were ruled out. Controls- Random selection of 130 controls from the patients who visited psychiatric ER from 2006-2009. Risk factors investigated

were age, gender, ethnicity, demographic variables, psychiatric diagnosis, psychotropic medications, medical diagnosis, medical medications based on the previous literature. Data was collected after reviewing the medical records. 57 patients had low sodium levels less than 133mg/dl. 20 patients were SIADH cases. Logistic regression analysis was used in determining the odds ratio significance in this population. . Results- Three factors elderly age, HIV and Sodium Valproic acid were implicated as the significant risk factors causing SIADH. Conclusions: Two factors age, HIV, are well known risk factors for SIADH. Sodium Valproic acid (VPA) has not been previously reported as a significant risk factor in the literature except few case reports. Further studies to be undertaken to confirm this finding. We are exploring the biological mechanisms for the relationship between VPA and SIADH.

**NR1-44****LAMOTRIGINE'S APPARENT EFFICACY IN TREATING IRRITABLE BOWEL SYNDROME IN ADDITION TO THE SYMPTOMS OF BIPOLAR AFFECTIVE DISORDER TYPE II- A CASE REPORT**

*Chair: Jonathan Barton M.D.*

**SUMMARY:**

This case report describes the story of a 43 year-old male suffering from both Bipolar Affective Disorder Type II and Irritable Bowel Syndrome. After several trials on different mood-stabilizers for the treatment of the patient's Bipolar Disorder, Lamotrigine was found to successfully alleviate the patient's mood symptoms. Of particular interest is that this patient also experienced dramatic resolution of their Irritable Bowel Syndrome. This case report examines various mechanisms by which Lamotrigine seems to have caused the resolution of the patient's Irritable Bowel Syndrome in addition to his Mood Symptoms.

**NR1-45****MANAGING CLOZAPINE SIDE EFFECTS: THREE CASE STUDIES**

*Chair: Pedro Bauza M.D.; Author(s): Nivedita Mathur, M.D.; Liudmila Lobach, M.D.; Sunil Verma, M.D.; Renu Culas, M.D.*

**SUMMARY:**

Clozapine is an atypical antipsychotic that is indicated for treatment resistant psychotic disorders not responsive to other antipsychotics. Its use is limited by its side effect profile. This report describes three patients with treatment resistant psychosis in whom

clozapine was effective but developed adverse effects to it. The management of these side effects allowed us to continue with clozapine treatment. KH is a 43 year old WF who was stable on clozapine for 10 years. She was treated with interferon for Hepatitis C infection and developed neutropenia. Clozapine treatment was stopped. She had a relapse of psychotic symptoms that required inpatient psychiatric care. Three antipsychotics were prescribed to no avail. She was given filgrastim and her WBC increased. Clozapine was restarted and has been in remission for two years. AM is a 40 year old WM, non-smoker, with a history of schizoaffective disorder. He had to stop lithium due to diabetes insipidus and had a psychotic episode. Conventional antipsychotic failed to control his symptoms. Clozapine was started and caused excessive sialorrhea. Clozapine levels were subtherapeutic i.e. 75ng/ml at 400mg daily dose. Fluvoxamine was started which increased clozapine levels without worsening of sialorrhea. RM is a 52 year old WM who developed postural hypotension while taking clozapine 500mg daily. Clozapine was reduced and psychosis recurred. Midodrine was added to help increase blood pressure. He eventually stabilized on clozapine, aripiprazole, citalopram, clonazepam, and midodrine. Thus Clozapine has proven to be effective in refractory psychosis but its side effect profile limits its use at times. This report describes three patients with treatment resistant psychosis in whom clozapine was effective but developed adverse effects to it and effective management of these side effects allowed us to continue with clozapine treatment and control of their symptoms.

**NR1-46**  
**EKG CHANGES IN ASYMPTOMATIC**  
**COCAINE USERS?: A CROSS SECTIONAL**  
**STUDY OF 269 IN-PATIENTS**

*Chair: Nivedita Mathur M.D.; Author(s): Don Kushon, M.D., Drexel University College of Medicine; Gurmu, Samson M.D.; Haridas, Arun M.D.; Mathur, Gaurav M.D.; Jobs, Michael BSN; Gebremeskel, Berhanu M.D M.P.H.; Boylan, Carol MSS LSW*

**SUMMARY:**

Background: To study the prevalence and type of EKG changes in asymptomatic intoxicated cocaine users admitted to a psychiatric inpatient unit. **HYPOTHESIS:** There would be significant EKG changes in cocaine intoxicated patients admitted to the psychiatric inpatient unit. **Methods:** We performed a retrospective chart review of all patients admitted to an inner city inpatient psychiatric unit affiliated with a general hospital over a 3 month period. Urine drug screen was used as a marker for recent cocaine use. Patients currently not using cocaine, as determined by a negative drug screen and

admitted during the study period served as controls. Baseline EKG on admission to the unit was obtained for both groups of patients (cocaine users and controls). The EKGs were interpreted by 2 physicians (one of whom was a cardiologist) who were blinded to the results of the UDS. The rates of abnormal EKG findings from both groups were compared. **Results:** The correlation between self-report of cocaine as compared to the results of UDS was .4485, with a p-value of <.0001, indicating that there is moderate correlation which is statistically significant. The odds ratio for the association between use of cocaine and abnormal ECG is .86 with 95% CI of (.35,2.83) which includes the null value of 1. The p-value is .7715 which indicates that given the data, there is no increased risk of abnormal ECG with use of cocaine. The majority of the patients were African American (75.46%), and males (64.29%). The mean age was 41, with SD of 11.8 and ranging between 16 and 71 years. **Conclusions:** Early EKG monitoring in asymptomatic cocaine intoxicated psychiatric inpatients may not distinguish risk for serious cardiovascular events. These findings support current clinical practice in emergency room settings where EKG monitoring is only mandatory in symptomatic cocaine users. **Source of Funding:** None

**NR1-47**  
**SYNTHETIC CANNABIS “SPICE”, MORE**  
**POTENT THAN NATURAL CANNABIS**  
**AND MAY HAVE INCREASED RISK FOR**  
**PSYCHOSIS?**

*Chair: Carlos Alverio-Pares M.D.; Author(s): Ashwin Reddy, M.D.; Elvin Hernandez, M.D., M.P.H.; John Renner, M.D..*

**SUMMARY:**

Background: Synthetic cannabis, sold since the early 2000's, was attributed to hundreds of ER visits in 2010. It is labeled as “herbal incense” and commercialized as a legal blend of natural herbs that produce cannabis-like psychoactive effects. Careful laboratory analysis revealed that it contains synthetic cannabinoid agonists which have very strong affinities to the CB1 and CB2 cannabinoid receptors. Natural cannabis contains THC but also has the compound cannabidiol which is known to have antipsychotic properties. “Spice” does not have an analogue for cannabidiol and therefore is suspected to have a higher risk of psychosis. **Methods:** A literature review of Medline from 2000 - 2011 was completed using the keywords synthetic cannabinoids, “spice”, psychosis, and cannabis. Blogs and internet pages where “Spice” users narrate their experiences were also reviewed. **Results:** Articles emphasize chemical properties, psychotic vulnerability and addictive properties of synthetic cannabis, and

hypothetical comparisons to natural cannabis. Due to its potent psychoactive components and lack of antipsychotic protective agents, various articles postulate the possibility of an increased risk for psychosis with “Spice” when compared to natural cannabis. Users report a “long lasting high” and psychotic symptoms like “seeing things, hearing voices, and extreme paranoia”. Conclusion: Synthetic Cannabis “Spice” contains synthetic cannabinoids such as CP-47497 and JWH-018 and may have an increased risk for psychosis due to its higher potency and lack of an antipsychotic compound such as cannabidiol that is found in natural cannabis. More formal studies are necessary to investigate the risk of psychosis from synthetic cannabis compared to natural cannabis.

**NR1-48**  
**TRAUMA AND DISSOCIATION IN**  
**SOCIAL PHOBIA: A COMPARATIVE AND**  
**CONTROLLED STUDY**

*Chair: Sermin Kesebir M.D.; Author(s): Sertac Guven, M.D., Esin Evren Kilicaslan, M.D., Elif Tatlidil Yaylaci, M.D.*

**SUMMARY:**

**Objective:** The objective of this study is to compare the trauma and dissociative symptom severity of social phobia between the cases diagnosed with generalised anxiety disorder and a healthy control group.  
**Method:** For this purpose, 42 patients diagnosed with Social Anxiety Disorder, 39 patients diagnosed with Generalized Anxiety Disorder and 41 healthy individuals according to the DSM-IV criteria were evaluated. Diagnostic interviews were made with the SCID-I, Liebowitz Social Anxiety Scale, DES and CTQ were applied to all individuals. **Results:** While the three groups were similar to each other in terms of gender, the average age and average years of education are lower in patients diagnosed with social phobia. History of physical illness and academic and social functioning scores were lower in the social phobia group. Rate of childhood trauma has been identified as 21.4% in the social phobic individuals. The mean DES score was calculated as  $19.7 \pm 5.4$ . The severity of dissociative symptoms in the healthy individuals was similar to the generalized anxiety disorder individuals and was lower than the social phobic individuals ( $p < 0.001$ ,  $F = 42.845$ ), ( $SP > GAD$ ,  $HI$ ). In terms of CTQ emotional abuse, physical abuse, sexual abuse, emotional neglect and physical neglect subscale scores:  $SP > GAD$ ,  $HI$ . There are strong correlations between the anxiety subscale of Liebowitz Social Anxiety Scale and CTQ emotional abuse, emotional neglect and the DES ( $r = 0.55, 0.70, 0.53$ ); and weak and moderate correlations between the physical and sexual abuse and physical neglect ( $r =$

$0.24, 0.22, 0.41$ ). Similar situation has also been shown between the avoidance subscale of Liebowitz Social Anxiety Scale and CTQ emotional abuse, physical abuse, sexual abuse, for emotional neglect, physical neglect, and DES ( $r = 0.71, 0.55, 0.24, 0.22, 0.41, 0.52$ ). Conclusion: Dissociative symptoms emerge severely in social phobia, this increases the anxiety and avoidance.

**NR1-49**  
**SLEEP STAGES AND BEHAVIORAL**  
**ABNORMALITIES IN CHILDREN AND**  
**ADOLESCENTS**

*Chair: Manana Lapidus M.D.; Author(s): M. Lapidus, M.D., G. Reeves, M.D., M. Ramagopal, M.D., J. Cabassa, M.D., M. Bollinger, DO, G. Nijjar M.D., B. Anthony, Ph.D., T. Achenbach, Ph.D., T. Postolache, M.D..*

**SUMMARY:**

**Objective.** Optimal sleep could be very important for the development of body and brain, emotional health, hormonal and immune function. Both REM and stages 3 and 4 sleep have been shown to contribute to the consolidation of complex, emotionally salient declarative memories. In this study we investigated associations of REM and slow wave sleep duration and externalizing and internalized behavior in children and adolescent  
**Methods:** A convenience sample of 95 children (15 boys and 8 girls with an age range of 2-3 year; 35 boys and 37 girls with an age range of 4-18 years) who came for screening for obstructive sleep apnea was used. We measured the duration of different stages of NREM sleep (N3 sleep representing the combined stages 3 and 4), REM sleep, total sleep time, hypoxemia parameters, amount of movement, and arousal index using polysomnography. Parents completed the age-appropriate version of the Child Behavior Checklist (CBCL; Achenbach, 1991) a standard method of assessing emotional and behavioral problems in children. Current analyses employed t-scores (mean = 50, standard deviation = 10) of the summary internalizing (i.e., anxious, depressed, withdrawn behaviors) as well as externalizing (i.e., aggressive, angry, non-compliance) behaviors and total problem scales. **Results:** We found a significant negative correlation between stage 4 sleep duration and parent report of externalizing problems in 2-3 year old children, and a trend towards a significant negative association between total slow wave sleep and externalizing problems. In 4- 16 year olds, there was a significant negative correlation between REM duration and externalizing problems. There was no association between externalizing behavior and total sleep time for either age group; the correlation appeared to be specific to REM sleep in school age children and stage 4 sleep in 2-3 year old children. **Conclusions.** Differences between

the associations of sleep stages and externalizing behavior in toddlers compared with older children suggests possible developmental differences in the association between sleep and behavior and consistent with the concept of an important role of sleep in normal child development.

**NR1-50**  
**COTARD SYNDROME IN A 65 YO HISPANIC MALE WITH MAJOR DEPRESSION**

*Chair: Nubia Lluberes M.D.*

**SUMMARY:**

This is a case study about a 65yo Hispanic male, married, retired, with history of Depression who presented to a psychiatric ward complaining about being dead. Patient vehemently stated that he knew he had died. His case has been a diagnosis challenge for 2 years after being discharged with improved condition. Other providers diagnosed him with Bipolar Disorder, Dementia and schizophrenia. He continues to have somatic delusions and delusion of being dead is recurrent. We have kept him out of the hospital and he is compliant with his medication but still a challenge since he has not achieved remission yet.

**NR1-51**  
**EARLY RESPONSE TO BRIGHT LIGHT AND OUTCOME AT SIX WEEKS**

*Chair: Monika Acharya; Author(s): Monika Acharya M.D. Gloria M. Reeves, M.D. Aamar Sleemi, M.D. Baharak Khabazghazvini, M.D. Dipika Vaswani, M.D. Manana Lapidus, M.D. Mubammand Tariq, M.D. Partam Manalal, M.D. Mary Johnson, Ph.D. Patricia Langenberg, Ph.D. Teodor T Postolache, M.D.*

**SUMMARY:**

**LACK OF PREDICTION BY THE FIRST HOUR OF LIGHT** Bright light therapy is a safe and effective method of treatment for Seasonal Affective Disorder (SAD). Sher et al (2001) reported that an early improvement after one session of bright light predicts response at 2 weeks. We now hypothesize that early improvement to the first hour of bright light rather than placebo red light would predict response at 6 weeks of treatment. Methods: Seventy-nine (24 men 55 women, average age 44 y) participants diagnosed by SCID, on no psychotropic medications and no prior exposure the phototherapy, were administered bright light vs. placebo light, in a cross-over fashion, in a random order. Depression scores were assessed with Structured Interview Guide for the Hamilton Depression Rating Scale, Seasonal Affective Disorders (SIGH-SAD),

Beck's Depression Inventory( BDI II) and the Profile of Mood States ( POMS-D) at three points; baseline, and after bright and red light. Treatment was continued using a manualized flexible dosage individually tailored to response and side effects. Changes in depression scores after one hour of red light and bright light were related to changes in depression scores at 6 weeks using multivariable linear regressions, and to response or remission status at 6 weeks using logistic regressions. No significant statistical associations were found between changes after 1 hour of bright or red light and outcome at 6 weeks ( $p>0.05$ ). It may be possible that using a flexible dosage dampened the predictive capability of the first session of light treatment

**NR1-52**  
**AN UNUSUAL CASE OF CPAP-INDUCED MANIA**

*Chair: Richa Aggarwal M.D.; Author(s): Saunders, E. M.D.; Barweja, R. M.D.; Singareddy, R. M.D.*

**SUMMARY:**

**Introduction/case:** Obstructive sleep apnea (OSA) affects 4-7 % of the general population. OSA patients have recurrent episodes of complete or partial cessations in breathing with associated oxygen desaturations and/or arousals. Bipolar disorder is a severely disabling mood disorder characterized by the presence of recurrent episodes of abnormally elevated energy levels, cognition and mood (DSM-IV TR). Here we present a case of a 51 year-old man, Mr. H, with stable, asymptomatic bipolar disorder, who developed a manic episode after he was started on CPAP for OSA for the first time. Mr. H's apnea/hypopnea index was high at 94.6, indicating very severe OSA. His SaO<sub>2</sub> was below 90% for 18.4% of the total sleep time in the laboratory. On CPAP, his apnea/hypopnea was eliminated, and his minimum oxygen saturation improved to 93% during REM and 94% during NREM sleep. After 3 weeks of CPAP treatment, Mr. H developed manic symptoms including euphoria with increased energy, physical aggression, motor hyperactivity, racing thoughts, pressured speech and visual hallucinations. He was treated pharmacologically and his manic symptoms resolved despite continued use of CPAP. **Discussion:** A clear mechanism for development of mania due to CPAP treatment of OSA is unknown. One hypothesis is the induction of affective symptoms due to sudden alterations in the concentration of gaseous elements in the blood, which in turn may affect the CNS. **Conclusion:** Clinicians should be vigilant for the development of manic episodes in bipolar patients who are treated with CPAP for their OSA, and should be aware of the possibility of development of a new mania in a patient with major

depressive disorder

**NR1-53**

**PSYCHO-EDUCATION IN BIPOLAR DISORDER: HOW MUCH DO OUR PATIENTS KNOW?**

*Chair: Mario Cristancho M.D.; Author(s): Alexander Hosey, Natalie Webb, Claudia F. Baldassano M.D.*

**SUMMARY:**

Background: Bipolar affective disorder is a chronic and recurrent condition associated with significant morbidity, reduced longevity, and disability. Multiple treatment modalities including psycho-education have been used in the treatment of this condition. Psycho-education including illness awareness, compliance enhancement, early identification, and lifestyle modification have proved to be of benefit in the treatment of patients with bipolar disorder. Benefits from psycho-education include decrease risk of relapse. Objective: In this study we attempt to assess the degree of illness related knowledge and psychoeducation of patients in an outpatient tertiary care bipolar disorder clinic at an academic medical center. Methods: A sample of 60 patients with Bipolar disorder is being studied. The sample is comprised of patients with Bipolar I and II disorder. Subjects are being recruited from the Bipolar Disorders Clinic at the University of Pennsylvania. We have conducted five minute interviews assessing knowledge of bipolar disorder. The interview consists of 5 questions adapted from the Barcelona Bipolar Disorders Psycho-education Program (Colom et al. 2003). Each item was scored on a scale of 0 to 2 with a possible total score of 10 on the interview. Participants were categorized as “not very knowledgeable”, “somewhat knowledgeable”, or “very knowledgeable.” Although research has shown that psycho-education is an effective tool for the prevention of bipolar relapse, we hypothesize that many patients treated in a tertiary care bipolar program lack knowledge about bipolar disorder. This is the first study to our knowledge that assesses patient’s own understanding of the disorder.

**NR1-54**

**SUICIDE ON FACEBOOK: SUICIDE ASSESSMENT USING ONLINE SOCIAL MEDIA**

*Chair: Amir Abuja M.D.; Author(s): Krystine Biesaga, M.D. R. Bryan Chambliss, M.D.*

**SUMMARY:**

Often in suicide assessment, an interviewing psychiatrist relies mostly on the patient’s oral history. In this case report, we explore the use of online social media to aid

in suicide assessment. We postulate that, with increased technology usage, social media should be an important form of collateral information, particularly in a safety assessment of suicide. With this patient, there was an impulsive suicide attempt without a diagnosable history of depression. With the patient’s consent, social media was used to reconstruct a picture of the suicide attempt and establish a clear timeline which we were unable to obtain from the patient due to his lack of insight. By obtaining the data from Facebook, a clearer diagnosis of depression was made. This information also helped us assist the patient in gaining more insight into the severity of his condition and helped in getting the patient to agree to a treatment plan. In the future, Facebook and other social media can be routinely utilized as part of a comprehensive safety assessment.

**NR1-55**

**“MY CHILD WON’T SPEAK”: TREATING SELECTIVE MUTISM IN CHILDREN AND ADOLESCENTS WITH ESCITALOPRAM, A CASE STUDY**

*Chair: Gaurav Kulkarni M.D.; Author(s): Aggarwal, A, M.D. Jahan, S, M.D.*

**SUMMARY:**

Patient is a 16 year old Caucasian female seen at The University of Missouri, Child and Adolescent outpatient clinic with a chief complaint: “She does not talk to anybody”. We were consulted by the primary care provider to help manage the selective mutism vs. social phobia. Parents reported she was talking and doing well until 4 years back when she had a next-door best friend left and they started to see a change in her. She stopped talking to everyone (except family members), even to her school teachers. Patient presented with non-verbal modes of communication like nodding her head and hand gestures, but with no spontaneous speech. She denied any depressive symptoms but nodded “Yes” when screened for anxiety especially around new situations or meeting new people. Denied any panic attacks, denied any Obsessive Compulsive Disorder or eating disorder symptoms, never been abused or victim of trauma, no Post Traumatic Stress Disorder symptoms. She nodded “No” to all other psychiatric disorders screening questionnaires. Patient was started on a low dose of Escitalopram 10mg once daily by mouth. This dose was later on titrated to 20 mg. Clonidine 0.05 mg by mouth, at bedtime, was added for sleep difficulties in the 7th month follow up visit (the patient has tried Benadryl and Melatonin in the past with no benefit). After almost a year of starting medications and therapy, the patient became spontaneously verbal with her doctors, with teachers and friends at school and with her therapist.

Patient later moved out of state with her family and was discharged from our clinic on Escitalopram 20 mg once daily and Clonidine 0.05 mg at bedtime. Differential diagnosis and other treatment recommendations for selective mutism are presented with emphasis on differentiating selective mutism from social phobia. On literature review, there are case reports on selective mutism, but the age of onset of selective mutism (in this case 12 years) and response to Escitalopram will further give new insight on assessing and managing older children and adolescents. Considering the dearth of data, continued reporting of cases may be useful in understanding the complexity of the clinical entity. Also, future research is warranted to bridge the gap between the impact of Clonidine on anxiety disorders and selective mutism. The authors have no disclosures of commercial support.

**NR1-56**  
**ANTIPSYCHOTIC DOSE ESCALATION PRIOR TO THE DEVELOPMENT OF NEUROLEPTIC MALIGNANT SYNDROME (NMS)**

*Chair: Julie Langan; Other Author(s): Dr Daniel Martin MBChB, BMSC (Hons) Dr Polash Shajahan MBChB, M.P.H.il, MRCP(UK,) FRCPsych*

**SUMMARY:**

Background: “Neuroleptic malignant syndrome” (NMS) which derives from the French “syndrome malin des neuroleptiques” was first described in 1960 by Delay and colleagues in association with haloperidol. It is a potentially fatal idiosyncratic reaction to antipsychotics. Pathophysiology remains enigmatic. Mortality rates may be as high as 55%<sup>2</sup>. Rapid alteration and escalation of anti-psychotic dose is thought to be an important risk factor. “Rapid escalation of dose” as a phenomenon has been difficult to define. Aims: To identify cases of NMS, review risk factors and focus on changes in antipsychotic dose in the 30 days prior to NMS onset. We also attempt to scientifically define “rapid escalation of antipsychotic dose.” Methodology: Retrospective analysis to identify NMS cases using DSM-IV criteria within NHS Lanarkshire, Scotland was undertaken. Once identified, demographics, risk factors for NMS and the episode were described by 2 independent psychiatrists. A 30 day antipsychotic dose trajectory prior to NMS onset was recorded. Cumulative antipsychotic dose was calculated using chlorpromazine equivalence to allow comparison and total cumulative dose of different anti-psychotics. In the UK the British National Formulary (BNF) contains information regarding maximum licensed doses of antipsychotic medication. Cumulative antipsychotic dose as a percentage of total maximum BNF dose was

also calculated. Dose trajectories were compared to inpatient and outpatient clozapine titration schedules. Results: 12 cases were identified. Sex distribution was equal. Average age was 47.8 years. The most common diagnosis was Schizophrenia (295){50%, (n=6)}, followed by Mood (Affective) Disorders (296){25% (n=3)}. 33.3% (n= 4) received parenteral antipsychotics within 30 days of NMS onset. Antipsychotic polypharmacy rates were high 41.7% (n=5). Individual 30 day dose trajectories prior to NMS onset were plotted and means obtained. Mean dose trajectory was compared to standard clozapine inpatient and outpatient titration regimens. NMS patients had higher total daily chlorpromazine dose and more rapid dose escalation, particularly in the 10 days prior to NMS onset, compared to individuals titrated on clozapine. Differences in cumulative dose and dose escalation using percentage maximum BNF were less marked. Discussion: It would appear that using higher doses and titrating anti-psychotics faster than standard clozapine titration schedules may be associated with the development of NMS. Converting antipsychotic medication received to a cumulative chlorpromazine equivalent and monitoring this over time may be useful in early detection and prevention of NMS. Chlorpromazine equivalence as a measure of total anti-psychotic dose received may better predict NMS compared to percentage BNF.

**NR1-57**  
**EMERGING STRATEGIES IN THE TREATMENT OF POSTSTROKE DEPRESSION AND PSYCHIATRIC DISTRESS IN PATIENTS**

*Chair: Vincent Capaldi M.D.; Author(s): Gary Wynn, M.D.*

**SUMMARY:**

Poststroke depression (PSD) is a common sequela of stroke associated with increased morbidity and mortality among stroke survivors. PSD has been associated with poorer rehabilitative outcomes, longer inpatient stays, inefficient use of medical resources, worsened cognitive decline, and increased suicidality. This poster reviews the definition and proposed etiology of PSD as well as current and emerging evidence-based prevention, screening, and treatment modalities. The timely use of prevention and treatment techniques including pharmacologic and nonpharmacologic methods may improve treatment outcomes and enhance the quality of life in stroke patients.

**NR1-58**  
**TINNITUS AND INSOMNIA: A SIGNIFICANT RELATIONSHIP WITH PSYCHOLOGICAL CONSEQUENCE**

*Chair: Kiran Majeed M.D.; Author(s): Prof. Gregory Asnis, M.D. Margaret Henderson, M.D. Manju Thomas, M.D. Clewert Sylvester, M.D.*

#### SUMMARY:

Objective: Tinnitus is a highly prevalent medical disorder occurring in approximately 15-20% of the population. Unfortunately, this condition can become chronic and severe leading to significant impairment in quality of life. Tinnitus has been reported to be associated with insomnia with rates ranging from 14-75%. It was our hypothesis that the presence of insomnia may be the cofactor that leads to compromised functioning in tinnitus patients. Insomnia by itself is well-known to lead to compromised daily functioning and predisposes people to develop anxiety and depressive disorders. Since most studies evaluating insomnia in tinnitus patients have relied on retrospective chart reviews or questionnaires asking a single question regarding sleep function, our project was to clarify some detailed aspects of sleep to more fully assess sleep problems and to evaluate other functions of daily-life such as energy and concentration. Method: We screened 72 prospective patients that were responding to an advertisement, recruiting for a tinnitus treatment study. Subjects were initially interviewed over the telephone using a structured questionnaire. The latter addressed issues of tinnitus (e.g., constant vs. intermittent), sleep functioning (total sleep time, sleep onset, awakenings, and awakening time as compared to prior to tinnitus), energy, concentration, etc. Results: The tinnitus sample (49 males and 23 females) had a mean age of 57.3 years (range 29-78 years). 70.8% of the sample endorsed some form of insomnia developing after the onset of their tinnitus; most had difficulties falling asleep (55.5%) or increased night awakenings (51.3%) whereas a minority (18%) of the insomniacs had early morning awakening. Approximately 60% had a DSM-IV-TR diagnosis of insomnia secondary to tinnitus(at least one sleep disturbance plus dysfunction in daytime functioning). Conclusion: Our data confirms that tinnitus is frequently co-morbid with insomnia as a symptom and as a diagnosis. Although prior studies have suggested this association, our study is the first to fully evaluate sleep disturbances identifying insomnia as a symptom as well as a diagnosis. Since insomnia is so highly prevalent; early identification and treatment of it should lead to better daytime functioning and tolerability of a patient to his/her tinnitus. Interestingly, insomnia was rarely treated in our sample.

#### **NR1-59 PSYCHOACTIVE BATH SALTS: A CASE SERIES**

*Chair: Benjamin Boche D.O.; Author(s): George Loeffler,*

*M.D., Ashley Penn, M.D.*

#### SUMMARY:

The recreational use of “Bath Salts” aka sympathomimetic “legal highs” are purchased at mini marts, smoke shops and online. Their use is becoming increasingly popular in the United States as evidenced by Poison Control contacts and Emergency Department visits. These products have not been tested in humans or animals and are not tested for during routine drug testing. These products are marketed under names such as Ivory Wave or Bolivian Bath and are sold in packets that contain synthetic cathinones, which are analogues of amphetamines. Individual synthetic cathinones vary in relative potency, but pharmacologically, these substances bind to monoamine transporters for dopamine, serotonin and norepinephrine, Intense feelings of euphoria, alertness, stimulation and sensory experience occur within 10-60 minutes of ingestion. Non desired effects of dependence, hallucinations, and paranoia have also been described as well. Deaths from behavioral conditions and medical conditions such as hyponatremia with encephalopathy and acute myocarditis have been reported. To our knowledge, we present the largest case series regarding the psychiatric effects of “bath salts” on patients admitted to a locked psychiatric ward. The sample consisted of seven otherwise healthy patients admitted to the Naval Medical Center San Diego inpatient psychiatry ward between February 2010 and July 2011. Patients had no prior history of psychosis and ranged in age between 21 and 29 years of age. The patient’s “bath salt” use was corroborated by the patient, work associates or friends. Symptoms observed included paranoia (7), agitation (7) requiring chemical sedation (2)/physical restraints (2), disorganized behavior (6), auditory hallucinations (5) and suicidal ideation (3). Syncope was observed in two patients and two patients had noticeable facial tics and tremors. 43% of these patients received low dose antipsychotic medication for mitigation of their symptoms. Psychotic symptoms resolved in the patients between 12 hours and three days. The average length of stay was between three and twenty-two days. The characteristic presentation is a preliminary period of agitation, disorganized behavior and confused paranoia, occasionally with unexplained syncope, tics, or tremors that manifests into persecutory delusions.

#### **NR1-60 RISK OF WITHDRAWAL DYSKINESIA IN CHILDREN**

*Chair: Garima Singh M.D.; Author(s): Pamella Campbell, M.D.*

**SUMMARY:**

**Objective:** Evaluation of the risk of Withdrawal Dyskinesia in children. **Method:** We present a case study of a 14 year old patient seen at the outpatient clinic for abnormal body movements for the past 3 weeks. He had a previous diagnosis of ADHD and Bipolar disorder type II and was on methylphenidate (MP) daily and divalproex at the time of visit. He was having abnormal body movements, including twitching of limbs, shrugging shoulders, grimacing, eye blinking, and hyper kinesis for 3 weeks. He was on aripiprazole 15-20mg for the last 5 years and various dosage of MP for the past 4-5 years, but 2 month ago aripiprazole was gradually decreased and discontinued in a period of three months. He was off MP during that period because of summer break at school. 3 weeks after the discontinuation, he developed some milder abnormal body movements like eye blinking, grimacing but was able to control them. The movements became worse once MP was restarted 3 week ago. The movements were so severe and frequent that he was unable to sit still and was unable to control them. He denied any history of recent infection, head trauma, seizures or tics. **Result:** The movements were exacerbated with the addition of stimulant medication in the treatment regimen and resolved with the addition of a small dose of atypical neuroleptic. **Conclusions:** Withdrawal Dyskinesia is not well studied in children and literature is very limited. In some individuals especially children even slow tapering of Antipsychotics can lead to abnormal body movements. Increase dopamine (by stimulants) can worsen these movements and interestingly the Movements usually resolve after restarting the antipsychotics mostly because of the sensitivity of the dopamine receptors. **Educational Objective:** 1. Long-term and high dosage use of antipsychotics should be avoided especially in children. 2. They need to be very slowly tapered and discontinued because of the risk of withdrawal dyskinesia Vs. tardive dyskinesia 3. Drug effects and their mechanism of action should be carefully studied and monitored. Our case highlights the role of psycho stimulants in the exacerbation of withdrawal dyskinesia.

**NR1-61**

**ASSOCIATION BETWEEN SHORT SEROTONIN TRANSPORTER GENE PROMOTER POLYMORPHISMS (5HTTLPR) AND HISTORY OF ABUSE ON BLOOD PRESSURE**

*Chair: Yingying Kumar B.S.; Author(s): Brooke Rosen, BS; Gen Shinozaki, M.D.; Simon Kung, M.D.*

**SUMMARY:**

**Background:** Serotonin transporter gene promoter

polymorphisms (5HTTLPR) have been shown to modulate transcription and expression of the serotonin transporter gene (SLC6A4)1. Variants of 5HTTLPR in combination with stressful life events have been associated with a likelihood of future depressive episodes2. However, it is unknown whether this interaction has an effect on objective physiological measures that may be affected by emotional distress or stress. **Objective:** To determine the relationship of 5HTTLPR genotype and history of abuse on resting heart rate (HR), blood pressure (BP), and body mass index (BMI). **Method:** Retrospective chart review of 252 Caucasian patients admitted to the mood disorder unit at St. Mary's Hospital, Rochester, Minnesota from 2010-2011. Inclusion required 5HTTLPR genotyping and record of HR, BP, and BMI within 12 hours of admission. History of abuse (sexual, physical, or emotional) was obtained from clinical records. Short/short (S/S) and short/long (S/L) polymorphisms were grouped together in analysis. Student T-test was used to examine the impact of abuse history on HR, BP, and BMI in each genotypic subgroup. **Results:** Of 252 (62.7% female, mean age = 41.3) subjects, 122 (48.8%) reported a history of any type of abuse and 83 had the long/long (L/L) polymorphism. Patients with the S/S or S/L polymorphism and a history of abuse showed significantly lower resting systolic blood pressure (mean of 120.43mmHg vs. 125.43mmHg, p=0.0058) and diastolic blood pressure (74.96mmHg vs. 78.39mmHg, p=0.0070). Patients with the L/L polymorphism and a history of abuse did not show any significant differences in blood pressure from those with the polymorphism and no history of abuse. No significant relationship was found between history of abuse and HR or BMI in either of the genotypic subgroups. **Conclusion:** There exists evidence for a gene by environment interaction of 5HTTLPR and history of abuse on resting blood pressure among acutely hospitalized psychiatric patients.

**NR1-62**

**TOXOPLASMA GONDII AND SUICIDE BEHAVIOR**

*Chair: Yuanfen Zhang M.D.; Author(s): Lil Träskman-Bendz M.D. Ph.D., Shorena Janelidze Ph.D., Patricia Langenberg Ph.D., Ahmed Saleh Ph.D., Niel Constantine Ph.D., Olaoluwa Okusaga M.D., Cecilie Bay-Richter Ph.D., Lena Brundin M.D. Ph.D., Teodor T. Postolache M.D.*

**SUMMARY:**

**Introduction:** *Toxoplasma gondii* (*T. gondii*) has been associated with suicide behavior (Arling et al. 2009; Yagmur et al. 2010; Ling et al. 2011; Okusaga et al. 2011). In this study, we would: 1) replicate the

association in a group from a different geographical setting; 2) investigate a possible association of *T. gondii* and the Suicide Assessment Scale self-rating version (SUAS-S), which has been indicated in predicting suicide completion. Methods: 54 patients with suicide attempt and 30 health controls were recruited in Lund University, Sweden. IgG antibodies to *T. gondii*, cytomegalovirus (CMV) and herpes simplex virus type 1 (HSV-1) were measured. Log-transformation was used for *T. gondii* IgG titer to reduce skewness. We used multivariable logistic regression to investigate the association between *T. gondii* seropositivity or serointensity and suicide attempt history. Multivariable linear regression was applied to exam the linkage between *T. gondii* seropositivity or serointensity and SUAS-S. Covariates in both models included sex, age and BMI. Results: Consistent with previous studies, *T. gondii* seropositivity (odds ratio = 7.12, 95% CI 1.66 to 30.6,  $P = 0.008$ ) and serointensity (odds ratio = 2.01, 95% CI 1.09 to 3.71,  $P = 0.03$ ) were significantly associated with suicide attempt history. The association of *T. gondii* seropositivity and SUAS-S was only observed in the whole sample (Odds ratio 7.12, 95% CI 1.66 to 30.6,  $P = 0.026$ ), but not in attempters only. The association of *T. gondii* serointensity and SUAS-S was not significant. No association of antibodies to CMV or HSV-1 and seropositivity or serointensity was found. Conclusion: The current findings are consistent with previous report showing an association of *T. gondii* antibodies and suicide attempt history. This association is specific to *T. gondii* infection, but not CMV or HSV-1. If replicated in future studies, our results could help develop new treatment approaches for *T. gondii* infection especially in patients with increased suicide risk.

#### NR1-63

### KAVA INTOXICATION: ACUTE MOVEMENT DISORDERS IN PATIENT WITH KAVA ADDICTION

*Chair: Liudmila Lobach M.D.; Author(s): Bryan Chambliss, M.D.*

#### SUMMARY:

Background: Kava (*Piper Methysticum*) is a psycho-active drink widely used among people of the South Pacific nations to relax and as ice-breaker in marital and other social ceremonies. In the US it is used primarily for sleep and anxiolysis. Once poorly known outside the Pacific, Kava -herbal psychotropic- is now being promoted as a safe health product and readily available in the US. Case Description: The present report describes the effects of acute Kava intoxication with heavy chronic consumption with a discussion of

the pharmacology and clinical manifestation of Kava toxicity. This patient used large amounts of Kava daily and developed classic dermatological, hematological, CNS and GI side effects. During a few overdoses of drinking 1-2 months' supply of Kava, he developed acute dystonia and choreoathetosis. Patient also was treated with conventional medications. Conclusions: Symptoms presented in this case, including dystonia and choreoathetosis, could be attributed to two major Kava mechanism of action: 1. Pharmacodynamic: Effect on dopamine level is dose-dependent: Kava decreases DA in recommended doses and increases DA level in significantly large doses what might correspond to the euphoric action of Kava and, as in this case, paranoia and ataxia. Potentiation of CABA-A similarly to benzodiazepines could contribute to potential addictive effect of Kava. Due to augmentation of sedative effects kava use with alcohol and benzodiazepines should be avoided. 2. Pharmacokinetic: As indicated by recent study, Kava has a high potential for causing drug interactions through inhibition of CYP450 enzymes. This suggests potentiation of extra pyramidal symptoms in present report as Kava significantly inhibits CYP 2D6 and 3A4 involved in Risperidone metabolism. Clinical relevance: Since Kava use is gaining popularity (estimated sale is \$17 million in the USA a year), the need for awareness of effects are highlighted. Adverse reactions apparently due to a conventional medicine might be due to a herbal medicine or interaction between herbal medicine and conventional drug, particularly when a health professional is unaware of the extent of a patient's self-medication with alternative therapies. Physicians should be aware of Kava's common and toxic side effects, Kava/drugs interactions and laboratory manifestations of Kava abuse to be able establish correct diagnosis and provide effective treatment with ongoing laboratory monitoring.

#### NR1-64

### THE EFFECT OF TREATMENT ON SOCIAL FUNCTIONING AMONG COCAINE DEPENDENT INDIVIDUALS

*Chair: Elia Valladares Juarez M.D.; Author(s): Elia M Valladares Juarez M.D.; Xin-Qun. Wang, MS; Bankole A. Johnson M.D.; Nassima Ait-Daoud, M.D..*

#### SUMMARY:

Introduction: Cocaine dependency affects 2.5 million people in the United States and has an estimated lifetime use of 1-3% in developed countries. Even though medical complications of cocaine usage have been well studied, there is limited data on its impact on social functioning. It is well established that substance abuse, in general, negatively correlates to level of social

functioning. The Social Functioning Questionnaire (SFQ) is a robust and well validated 8-item scale that has been used to evaluate social functioning in people with a variety of mental health problems ranging from BPD, M.D.D, anxiety, neurotic disorders and alcohol abuse. The score range from 0 to 24, with a score > 10 indicating poor social functioning. Studies validating the SFQ have found a mean score of 4.6 in the general population. Objectives: This study compares the social functioning level of cocaine dependent individuals to that of the general population using the SFQ. Additionally, we assess whether treatment for cocaine dependence will help improve social functioning and whether medication further improves social functioning. Another objective is to evaluate if improvement in social functioning is related to a reduction in cocaine use. METHOD A total of 142 cocaine dependent male and female individuals were enrolled in a randomized controlled clinical trial comparing the effect of topiramate up to 300 mg/day with placebo at reducing cocaine use and craving. All participants received weekly cognitive behavioral therapy for 12 weeks. For the purpose of this presentation, we focused primarily on the “therapeutic intervention” in general (i.e. being in a trial and receiving some kind of treatment) and secondary on topiramate’s effects on SFQ. The SFQ score was administered at various points during treatment (at intake, and every other week). The test was designed to be self-administered. Results: Overall mean SFQ at intake is 8.06 ( $\pm 3.15$ ). Overall mean SFQ score (mean  $\pm$  SD) at mid-point of study is 6.57 ( $\pm 3.55$ ) and 6.16 ( $\pm 3.79$ ) at the end of the study. The estimated mean difference from baseline to end of the study is -1.86 (95% CI: -3.33 to -0.39,  $p=0.014$ ) for the placebo group and -1.05 (95% CI: -1.99 to -0.11,  $p = 0.030$ ). There was a treatment main effect ( $F=3.89$ ,  $p=0.052$ ), and treatment and time interaction effect ( $F=3.81$ ,  $p=0.056$ ). Conclusion: Cocaine dependent individuals have higher SFQ scores compared to the general population however they did not have a score greater than 10 at any point during the study. This suggests that at least in our population cocaine dependent individuals have a fairly good level of social functioning compared to a population with mental disorder, but performing below an optimal level compared to the general population. Despite having SFQ scores lower than 10, our “therapeutic intervention” appeared to have had a positive effect on social functioning in these patients.

#### NR1-65

### COLLABORATIVE MODELS OF CARE FOR MEDICAL INPATIENTS WITH PSYCHIATRIC DISORDERS: A SYSTEMATIC REVIEW

*Chair: Maria Hussain M.B.B.S; Author(s): Dallas Seitz*

*M.D., FRCPC*

#### SUMMARY:

Purpose: Psychiatric disorders are common among medical inpatients and psychiatric illness is associated with adverse medical outcomes. Collaborative models of care (CMC) involving mental health providers and other health care professionals have been demonstrated to improve medical and mental health outcomes in primary care settings. However, the effects of CMC on the outcomes of medical inpatients with psychiatric disorders (MIPD) are not known. The purpose of this project is to examine the evidence for CMC for MIPD. Methods: We searched MEDLINE, EMBASE and Google scholar for relevant articles using key words and medical subject headings. We included all English language publications that evaluated effects of CMC for MIPD when compared to usual care or another model of psychiatric care. We included both randomized controlled trials and other quasi-experimental studies. We defined CMC as models of care which integrated medical and psychiatric practitioners in the same care team. We excluded studies that only examined consultation or liaison models of psychiatric care. We extracted data on the effects of CMC on psychiatric outcomes, medical outcomes, and health service utilization where this information was reported. Included studies were described qualitatively and summarized in tables. Results: A total of 855 unique citations were identified and 38 articles retrieved and reviewed in detail for eligibility. After review, three studies met inclusion criteria. All studies had methodological limitations placing them at potential risk of bias. The three studies were different in terms of study design, patient populations, and reported outcomes. In one study, the global improvement in psychiatric symptoms for the patients who received care in a CMC was significantly better than those admitted to an internal medicine ward. Two studies found that length of stay (LOS) was reduced with CMC while another study found the LOS was increased in the CMC when compared to usual care. One study reported an improvement in functional outcomes and decreased likelihood of placement at one year associated with CMC. There was limited information on the effects of CMC on medical outcomes or post-discharge health service utilization. Conclusions: Currently, there are few studies of the effects of CMC for MIPD. Based on the existing studies and evidence from other healthcare settings, CMC show some promise in improving psychiatric outcomes for this vulnerable population. There is a paucity of research on this topic and more studies examining health and economic outcomes are required.

**NR1-66**  
**AN ANALYSIS OF SOMATIC SYMPTOMS**  
**OCCURRING DURING THERAPY FOR**  
**POSTTRAUMATIC STRESS DISORDER**

*Chair: Robert Lloyd M.D.*

**SUMMARY:**

Currently, there is a higher prevalence of posttraumatic stress disorder (PTSD) in service members returning from recent conflicts. Additionally, there is a high rate of comorbidity of mild traumatic brain injury and other medical illnesses in this population. Members identified with PTSD are educated about their illness and encouraged to undergo an evidence-based psychotherapy as a first-line option. During psychotherapy, patients will often confront memories, beliefs, and strong emotions related to the trauma. While the trauma is being approached or processed, it is not uncommon for individuals to experience somatic symptoms that are either new or represent an exacerbation of preexisting illness. We look to describe common somatic presentations during therapy that are either of new origin or worsening conditions. Moreover, we consider the importance of collaborating with other specialities to avoid aggressive treatments of certain symptoms.

**NR1-67**  
**A DIAGNOSIS DILEMMA**

*Chair: Florentina Luiza Popescu M.D.*

**SUMMARY:**

**Aims & Objectives:** a debate of differential diagnosis and possible presentations of anorexia nervosa, autistic spectrum disorder, simple schizophrenia, obsessional slowness, catatonia in an adolescent patient. **Methods:** study case, close and thorough observation and monitor of the patient while an inpatient on a CAMHS ward, being involved a multidisciplinary team and literature search. **Description of symptoms and management plan.** **Results:** a multiple and very rare psychopathology in adolescents. **Conclusions:** only four similar cases have been described in the literature. The case is based on a study case of a 14 year old patient from a CAMHS ward. The patient has a 5 year history of deterioration of mental state, initially presenting with anorexic symptoms, which gradually developed into a full picture of obsessive – compulsive disorder, simple schizophrenia with right sided body neglect, catatonia, psychomotor retardation, bizarre behaviour (walking in circle, smearing of faeces). The patient was closely monitored and assessed by psychologists, speech and language therapists, neurologists, endocrinologists. The catatonic

symptoms had a very good response to Lorazepam, but unfortunately on discharge patient had residual obsessional slowness and obsessive compulsive disorder like symptoms, which gives a dilemma to the diagnosis and treatment.

**NR1-68**  
**CHANGES IN THE ICNDS BETWEEN TWO**  
**VISITS IN 762 YOUTH WITH EPILEPSY**

*Chair: Diana Lorenzo M.D.; Author(s): Prakash Kotagal M.D., Sarah Matthys, Robert Buttler, and Tatiana Falcone M.D..*

**SUMMARY:**

**Objective:** To evaluate changes in the Impact Childhood Neurological Disability Scale (ICNDS) and Liverpool Seizure Severity Scale (LSSS) between two consecutive visits in 762 youth with epilepsy. **Methods:** Patients were identified from an outpatient pediatric epilepsy clinic, patient data was self-entered in an electronic database, prior to their epilepsy appointment. The Knowledge Program was created with the goal to measure the patient overall outcome and quality of life over time. Patients were between 0 to 18 years of age, and with ICD-9 diagnosed coded for epilepsy. Subject completed the ICNDS and LSSS survey questionnaire which assessed general well-being and quality of life (QoL). Responses to QoL were coded Likert scales from 1= worst and 6= best QoL. The ICNDS was analyzed by 4 subscales; Behavior and inattention, cognition, physical/neurological disability and epilepsy. **Results:** Two of the 4 subscales of the ICNDS; Inattentiveness (p value=0.0004) and cognition (p value=0.0415) had a statistically significant impact on the QoL, especially for those subjects with scores 2,3,4 during the first visit. Patients hours of activities improved when the ICNDS subscales, on physical/ neurological disability score ( p value= 0.0471), epilepsy (p value =0.0001) and oyhe neurological disability score ( p value= 0.0471)improved for visit one to two. **Conclusions:** The 4 subscales of the ICNDS had an impact on the quality of life in youth with epilepsy. Early intervention focusing on the number of seizures as well as the different psychosocial and physical domains ( attention, cognition, social interaction, school performance)is the key to improve the quality of life in youth with epilepsy.

**NR1-69**  
**FITNESS TO STAND TRIAL: AN ATTEMPT**  
**AT EDUCATING AN INPATIENT FORENSIC**  
**PATIENT POPULATION THROUGH AUDIO/**  
**VISUAL AIDS AND MEASURING TIME TO**  
**ACHIEVE FITNESS**

*Chair: Peter Szymczak M.D.; Author(s): Varinderjit Parmar, M.D., Dr. Tariq Hassan, MBBS, MRCPsych*

#### SUMMARY:

**Background:** When a person is charged for a crime they are at first presumed to be mentally competent to mount a defense or 'fit to stand trial'. In Ontario, like many other jurisdictions, a judge orders an assessment as to whether a person is fit to stand trial. This assessment is ordered if there are 'reasonable grounds' to believe that an assessment is warranted based on possible mental illness. This assessment takes place in a Provincial Forensic Psychiatric Inpatient facility for a 30-day assessment. To our knowledge there have not been any studies, which measure the outcome of providing Forensic Psychiatry inpatients educational aids (audio/visual) regarding the issue of fitness to stand trial. **Purpose:** This study will look at whether providing patients with education regarding fitness to stand trial will improve their understanding when using a standardized measure regarding fitness to stand trial. **Methods:** Approximately 20 inpatients of the Forensic Psychiatry Inpatient unit at Providence Care in Kingston, Ontario will be approached for participation in this study. On day 7 after admission to our ward we administered the "Nussbaum-Metfors Fitness Questionnaire" as a baseline. The patients were then shown a video that was to educate the patients about the judicial system in general. The "Nussbaum-Metfors Fitness Questionnaire" was then administered immediately after the video session and then subsequently on days 14 and 21 of admission. **Conclusion:** In providing education through audio/visual means we were able to improve the understanding for patients to become fit to stand trial. This is an attempt to explore the outcomes and effectiveness of providing education through audio/video to Forensic Psychiatry Inpatients. This will, in turn, provide valuable information for future research through eliciting whether such an intervention may eventually be used to reduce the duration of inpatient stay by Forensic patients sent for such assessments.

#### **NR1-70**

#### **BUILDING A TEAM INVOLVED IN PREVENTION AND TREATMENT OF PRIMARY POLYDIPSIA IN A PSYCHIATRIC OUTPATIENT/INPATIENT POPULATION: A PILOT STUDY**

*Chair: Peter Szymczak M.D.; Author(s): Varinderjit Parmar, M.D., Richard Millson, M.D., Roumen Milev, M.D., Ph.D., Emily Hawken, Ewa Talikowska-Szymczak, M.D., Dianne Groll, Ph.D., Felicia Iftene, M.D., Ph.D.*

#### SUMMARY:

**Educational Objectives** At the conclusion of this session, the participant will be able to: 1. Recognize Primary Polydipsia; 2. Be involved as an active part in a professional network; 3. Make a therapeutic intervention, appropriate for his/her educational level. **Abstract Background:** The disturbances of water homeostasis among psychiatric patients have been widely recognized, particularly the condition whereby patients consume excessive quantities of liquid, which is termed "polydipsia." Long-term effects of excessive fluid consumption may include bladder dilatation, potentially leading to hydronephrosis and renal failure, hypocalcaemia, congestive heart failure, gastrointestinal dilatation and hypotonicity, hypothermia, and osteopenia with an increased incidence of fractures. Seen in both episodic and chronic polydipsia, water intoxication can be a reoccurring condition, which carries with it a substantial risk of morbidity and mortality. In a previous study we found that there is a lack of information on this topic, not only regarding the patients, but also the caregivers' professionals involved in their care. **Purpose:** This study we try to increase the awareness of the professionals on this topic and actively involve them in the prevention /therapeutic process. **Methods:** Approximately 100 mental Health Professionals and Volunteers will be approached to participate in 5 types of small groups workshops (5-10 participants/group) on the topic of Primary Polydipsia in psychiatric population (Community Outreach Teams -COT; Provincial Psychiatric Hospital -Providence Care, Kingston Ontario. The groups will include: case managers, nurse, social workers, psychologists recreational, case managers, occupational therapists, spiritual care; family doctors and nurse practitioners; medical residency program; home operators. Initial and final evaluation of their knowledge, will be done by using a questionnaire with 10 questions (7 multiple choice and 3 open questions) related to this topic. The open questions will offer us the opportunity to have ideas related to how to build a possible network, where each professional has his place and is able to perform his specific role. A brochure with the materials collected (guidelines) will be publishing in the future. The change in knowledge were measured pre-post intervention using t-tests **Results.** An increase awareness of the professionals on this topic was demonstrated, as well as an active involvement in building a network, finding the best intervention strategies and realize a guideline of intervention at each level. **Conclusion:** Results from this study help us to understand whether more needs to be done in the direction of actively involve the medical staff and volunteers in a well-coordinated assistance of the psychiatric patients who associated Primary Polydipsia.

NR1-71

**A PRACTICAL APPROACH TO PSYCHIATRIST'S ROLES AND RESPONSIBILITIES WHEN ASSESSING PATIENT'S CAPACITY TO DRIVE***Chair: Dimitri Markov M.D.***SUMMARY:**

Sleep deprivation, shift work, primary sleep disorders, sleep disturbance associated with medical and psychiatric illness or psychopharmacologic interventions cause excessive daytime sleepiness. Dementia affects memory, judgment, visual, spatial and motor skills. Psychiatrists are increasingly faced with patients whose driving ability may be impaired either by dementia or excessive daytime sleepiness. Drowsy driving imposes fatality rate and injury severity similar to that of alcohol-related crashes. Patients with dementia are three to five times more likely to be involved in a motor vehicle accident than age matched controls. This poster will offer a practical framework to approach questions related to a patient's capacity to drive in the setting of dementia, substance use disorders and excessive daytime sleepiness. Attention will be given to both the legal foundations and considerations related to assessments of capacity to operate a motor vehicle and a practical clinical approach to managing questions of driving capacity.

**SATURDAY MAY 05, 2012****MS-RES Competition Poster Session****Competition Poster Session 2****COMMUNITY SERVICE, CURRICULUM DEVELOPMENT AND EDUCATIONAL, PSYCHOSOCIAL AND/OR BIOMEDICAL RESEARCH**

NR2-01

**PSYCHIATRIC DISORDERS IN HOMELESS YOUTH: A REVIEW OF THE CURRENT LITERATURE AND AREAS FOR FUTURE RESEARCH***Chair: Nicole Kozloff M.D.; Author(s): Amy Cheung, M.D.***SUMMARY:**

**Objective:** To review the current literature on homeless youth with respect to their rates of psychiatric disorders, the relationship between psychiatric illness and homelessness, factors influencing their service utilization and the evidence for population-specific interventions.  
**Method:** MEDLINE was searched from January

2001-December 2011 for peer-reviewed articles using terms related to psychiatric disorders, homelessness, and youth, yielding 410 results. From these, articles reporting specifically on the epidemiology of mental disorders (M.D.s) and substance use disorders (SUDs), their relationship with homelessness, and mental health treatment and service use among homeless youth were downloaded and read in detail and reference lists of included articles were hand-searched. Fifty-nine articles presenting primary data were identified. Results: Rates of psychiatric disorders among homeless youth range from 28% to 89% in community samples and up to 97% in treatment settings. Comorbidity is high, with up to 93% of youth with a SUD meeting criteria for a M.D.. Homeless youth have high rates of trauma, both in childhood and once living on the street, and rates of suicidal ideation range from 35% to 66%. Homeless youth are likely to have had a psychiatric diagnosis prior to becoming homeless, and the burden of mental illness worsens without adequate housing. Reported rates of mental health and addiction service use vary widely depending on diagnosis and how recently utilization was considered; this review found rates ranging from 24% to over 90%. Service use is associated generally with higher burden of symptoms and perceived need. In qualitative research, accessibility and positive impression of care providers are consistently cited as facilitators of service use. There is limited literature on prevention and screening of psychiatric disorders in this population. While there is a growing body of research on treatment strategies including behavioural therapy and motivational enhancement therapy, studies have not demonstrated conclusive evidence. Conclusions: Despite the significant burden of mental illness in homeless youth, few strategies for prevention, screening, and treatment of psychiatric disorders have been adequately researched. There is a need for RCTs to establish effective interventions for this vulnerable population to reduce the chronic burden of homelessness and mental illness.

NR2-02

**GENERAL PRACTITIONER'S SATISFACTION WITH THE IMPLEMENTATION OF A C-L PSYCHIATRY SERVICE IN ULSM, PORTUGAL***Author(s): Cassilda Costa, M.D. Fátima Ferreira, M.D. Rosa Quelhas Ferreira, M.D.***SUMMARY:**

**Introduction:** Matosinhos Local Health Unit (ULSM) in Portugal has a model of organization consisting on the articulation between the general hospital and the center of community care (ACES Matosinhos) joining four community health care centers (CHCC).

Since 2009, around 50% of the clinical activity of the Psychiatry Service was done in the CHCC, through the interaction with general practitioners (GPs) and general psychiatry outpatient clinics. Traditionally, the GPs' referral to and communication with psychiatrists was made through electronic or written methods. In ULSM, digital clinical records are shared by these two specialties, allowing a better communication of clinical information. Clinical case discussion is an established practice offering important advantages such as the possibility of maintaining the patient's care in the GPs' clinic. Aims: The authors aim with this presentation to describe the functioning model of the ULSM Psychiatry Service and reflect on it and on its results, particularly evaluating the satisfaction of GPs with the implementation of the model. Methods: In January 2011 satisfaction questionnaires were sent to all the GPs of CHCC in an enclosed letter. Participation was voluntary; the questionnaires were self-rated and returned through mail, preserving confidentiality. The topics evaluated the frequency of referrals to psychiatry, satisfaction with the criteria for those referrals, with the administrative procedures, with the psychiatric and psychology staff, qualities and deficiencies of the model, suggestions of change and general satisfaction with the model. Results: 100 questionnaires were sent to all the GPs in the CHCC. Analysis included 59 questionnaires using SPSS. The participation varied in each CHCC, from 19 to 29%. The majority of the GPs referred patients once or twice a month. 28 considered the work of the psychiatrists "very good", 38 said the model was "appropriate" and 43 of the 59 considered that the patients benefited from the close articulation between GPs and psychiatrists. Conclusions: Acceptance of this model isn't always consensual to all parties involved. Implementation of these services requires knowledge of the needs of the general population and doctors and should ideally be done gradually, taking into account the need of adjustments according to the monitoring of satisfaction. From our results it's clear that GPs considered that the articulation and discussion of the cases between these two specialties was beneficial for the patients.

#### NR2-03

### **TIME TO HAND OVER THE KEYS: THE PSYCHIATRIST'S ROLE AND RESPONSIBILITIES WHEN ASSESSING A PATIENT'S CAPACITY TO DRIVE**

*Chair: Christine Marchionni M.D.; Author(s): Dimitri Markov, M.D., David Axelrod, M.D., Keira Chism, M.D., Craig Carroll, DO, Elisabeth Kunkel, M.D.*

#### SUMMARY:

Sleep deprivation, shift work, primary sleep disorders, sleep disturbance associated with medical and psychiatric illness, and/or psychopharmacologic interventions cause excessive daytime sleepiness. Epilepsy as well as its treatments can impact the ability of a driver to function a motor vehicle. Substances of abuse impair the driver's judgment and information processing speeds. Dementia affects memory, judgment, visual, spatial and motor skills. Psychiatrists are increasingly faced with patients whose driving ability may be impaired either by dementia or excessive daytime sleepiness. Drowsy driving is associated with fatality rates and injury severity that is similar to that of alcohol-related crashes. Patients with dementia are 3 to 5 times more likely to be involved in a motor vehicle accident than age-matched controls. Epilepsy is one of the most frequently implicated medical causes for MVA. This poster will offer a practical framework to approach questions related to a patient's capacity to drive in the setting of dementia, epilepsy, substance abuse and excessive daytime sleepiness. Attention will be given to both the legal foundations and how to assess capacity to operate a motor vehicle. We will offer a practical clinical approach to managing questions of driving capacity.

#### NR2-04

### **SUICIDAL MASS MURDER**

*Chair: John Liebert M.D.*

#### SUMMARY:

Suicidal Mass Murderers is based on a detailed study of the Virginia Tech massacre of 2007. Other perpetrators will be cited and compared to this detailed study of Cho Seung-Hui's progressive mental deterioration with red flags signaling the potential disasters they caused. Cases will be discussed within clinically organized format as follows: ? Known to be seriously mentally ill. 1. Jerad Loughner, perpetrator of the Tucson Shootings; 2. Seal Beach Mass Murderer, Scott Dekraai; 3. Fort Bragg murderer, Aaron Bassler; 4. Anders Breivik, perpetrator of the Oslo Government Building and Utoya Island Massacre; 5. Cho Seung-hui's highly visible Schizophrenic deterioration, prelude to Virginia Tech Killings; 6. Steven Kazmierczak, perpetrator of suicidal mass murder at Northern Illinois U; 7. Robert Hawkins, perpetrator of Omaha's Westlake Mall suicidal mass murder; 8. Rodrick Dantzler, perpetrator of Grand Rapids suicidal mass murder; 9. Robert Stewart, perpetrator of Carthage, NC nursing home mass murder; 10. Ross T. Ashley, Virginia Tech 2011; 11. Terry Thompson, perpetrator of the bizarre zoological mass murder attempt via intended wild animal attacks on an entire community, followed by suicide in Zanesville, Ohio. ? Personality Changes as premonitory signs of

imminent catastrophic dangerousness: 1. George Sodini, Revisiting Internet postings of suicidal mass murder at a Pittsburgh gym; 2. Shareef Allman, The Cupertino Quarry Suicidal Mass Murderer; 3. Terry Sedlacek, Infected with Lymes Disease, "The Diagnostic Great Pretender", for which most patients die without a diagnosis, fired into his church and killed his pastor in Illinois; 4. Major Nidal Hasan, The Fort Hood Shooter; 5. Underwear Bomber, Umar Farouk Abdulmutallab, ? Military Post-combat Killings and Suicides will be discussed: 1. David Stewart, Army Medic, perpetrator of suicidal mass murder after 2 combat deployments; 2. Leonard John Eglund A soldier suspected of killing four people was found dead of an apparently self-inflicted gunshot wound in after a daylong manhunt during which he fired at and injured officers, authorities said. ? "Going Postal": Fact or Reality: 1. The Montgomery Alabama Case ? The Anthrax Attacks of 2011; could one skilled bacteriologist inside DOD have committed attacks? 1. Was Mirage Man, Bruce Ivins, the worst suicidal mass murderer in US history?.; 2. Revisiting the case of Flight 93 hijackers. Case Closed but not Cleared: 3. Critique of FBI Anthrax Investigation by National Academy of Science ? Domestic Violence, Substance Abuse and the Workplace in Mass Murders with Suicidal Intent 1. Robert Stewart at Carthage, NC Nursing Home and Scott DeKraai, Seal Beach Case 2. David Stewart, Fort Lewis Army Medic and Anders Breivik of Oslo Disaster 3. Shareef Allman, the Cupertino Quarry Case, Robert Stewart, NC Nursing Home Case & Seal Beach Killings: The

## NR2-05

### PSYCHOTHERAPEUTIC APPROACH OF PRIMARY POLYDIPSIA IN PSYCHIATRIC OUTPATIENT POPULATION: A PILOT STUDY

*Chair: Varinderjit Parmar M.D.; Author(s): Peter Szymczak, M.D., Richard Millson, M.D., Roumen Milev, M.D., Ph.D., Emily Hawken, Ewa Talikowska-Szymczak, M.D., Dianne Groll, Ph.D., Felicia Iftene, M.D., Ph.D.*

#### SUMMARY:

Queen's University, Department of Psychiatry, Kingston, Ontario, Canada Key Words: Schizophrenia, Polydipsia, Group Psychotherapy Intervention. Educational Objectives At the conclusion of this session, the participant will be able to: 1. Recognize a patient with Primary Polydipsia; 2. Determine perceptions of outpatients using SIWI (self-induced water intoxication) in relation to reasons for drinking excessive fluids, symptoms patients experience and behavioural patterns associated with SIWI; 3. Make an educational group intervention for clients with Primary Polydipsia, in an outpatient setting. Abstract

Background: Primary Polydipsia is commonly associated with chronic psychiatric illness, and has been found to be prevalent in over 20% of long-term inpatients with schizophrenia. We studied the occurrence of excessive drinking behaviors in non-hospitalized patients. The incidence of Polydipsia among our study population was 15.1% (115 subjects were included in the initial clinical assessment). We determine perceptions of outpatients using SIWI (self-induced water intoxication) in relation to reasons for drinking excessive fluids, symptoms patients experience and behavioural patterns associated with SIWI. We showed that these patients are not fully aware of the severity of and possible complications from their problem. Purpose: Primary Polydipsia, seen (at least partially) as a form of addiction, might benefit from psychotherapeutic intervention used to treat substance abuse. Methods: A number of outpatients (14) from the Community Outreach Teams (COT) in Kingston, Ontario were approached for participation in this study. Patients (or their designated proxy) provided informed consent. Data collection at the initial evaluation of these patients included chart review, daily weight measurements, structured interviews, and urine collection. We randomly assigned one member from each of the seven pairs (14 clients) to the psychotherapy treatment group. They received two 60-minute sessions of psycho- educational group therapy for 2 months, followed by one/week for a month. The weight measurements (2/day, 3 days consecutively) and the structured interview were applied monthly for 4 months (including the last month without psychotherapy). The control group received "placebo psychotherapy" - non-directive group therapy, approaching daily possible problems but not "touching" their water seeking behavior. The two groups were compared using t-tests and correlation coefficients. Results: A decrease of the water seeking behavior in the study group was demonstrated, as well as a change in their attitude related to self-induced water intoxication. The results of an educational program in an inpatient setting done in 1993 showed that the effect of Psychotherapy quickly dissipated in the follow-up period (one month). We have much better results and maintenance, perhaps because our clients are more stable. Conclusion: Results from

### NR2-06 OUTCOMES OF 17 YEARS OF A STRUCTURED REHABILITATION PROGRAM IN A HALF-WAY HOUSE

*Chair: Pablo Gabay M.D.; Author(s): Fernández Bruno, Mónica D, M.D. Ortega, M. Occupational Therapist*

#### Summary:

We present the outcomes of 17 years of a structured rehabilitation program that has been offered to

chronic psychiatric patients referred to a specialist half-way house in Buenos Aires, the ultimate goal of which is social reintegration, or at least some degree of rehabilitation. Even in the largest cities and despite the approval of the new mental health legislation, the overall state of psychiatric rehabilitation services in Argentina remains unsatisfactory. However, there are many rehabilitation programs that have been running in Buenos Aires and other parts of the country, some of which for as long as 40 years. Adopting the premise that rehabilitation tools must be culturally sensitive and adjusted to local needs, the outcomes of our program show that it can successfully prevent relapses and re-hospitalizations. The program can also enhance the remaining skills of chronically ill individuals, strengthen family bonds, and effectively promote the reintegration of people with severe mental illness (SMI) into the community, thereby decreasing health and social costs to society. The success of the program is associated with the detailed assessment of candidates, clearly defined therapeutic boundaries, adequate pharmacological treatment, and 'experience-based learning' in a structured and homely environment.

#### NR2-07

### PROFESSIONALISM IN SOCIAL NETWORKING

*Chair: Almari Ginory D.O.; Author(s): Laura Michelle Mayol Sabatier, M.D. Spencer Eth, M.D.*

#### SUMMARY:

Objective: Facebook is the leading social networking website founded in 2004 with over 500 million users, including 51% of all Americans over the age of 12(1,2). Prior studies have shown an increasing number of medical housestaff accessing the site. A study conducted at Rouen University Hospital in France of residents in several specialties found that 73% of residents had Facebook profiles and 6% had friend requests from patients, which four of the residents accepted(3). A study at the University of Florida revealed that 65.5% of multi-specialty residents having a Facebook profile had public settings(4). While Facebook can be used to foster camaraderie, it can also create difficulties in the doctor-patient relationship, especially when boundaries are crossed. The authors previously studied Facebook use among psychiatry residents subscribed to the APA resident listserv (5). This research explored the prevalence of such boundary crossings and offers recommendations for training through a survey conducted of the entire housestaff at Jackson Memorial Hospital/University of Miami(JMH/UM), a large tertiary care urban teaching hospital complex affiliated with a VA. Methods: An anonymous voluntary

survey regarding Facebook use was emailed to residents at JMH/UM in May and June 2011 followed by two reminders sent one week apart. The survey consisted of 5-20 questions that took between 5-10 minutes to complete. Study was approved by the University of Miami IRB. Results: Of the 206 respondents, 85.4%(176) had current Facebook profiles, and of those with a profile 50% (88) previously posted work related comments and 10.8 % (19) posted about a specific patient. 16.5% (29) received friend requests from patients with 51.7% (15) accepting the request. In addition 6.3% (11) would automatically accept friend requests from patients. Of the 206 respondents, only 12.1% (25) received any education or training material from their program regarding professional and ethical uses of Facebook. Conclusions: There is a substantial utilization of Facebook among multi-specialty residents. Residents are routinely confronted with difficult ethical decisions and are subject to boundary violations. Guidelines have been recommended by the American Medical Association, which include separation of personal and private information online, maintaining privacy standards on online interactions, and reporting of inappropriate content(6). In February 2011, the American Association for Directors of Psychiatric Residency Training developed a task force which completed a curriculum on professionalism and the internet(7). In addition, the British Medical Association specifically recommends that physicians refuse friend requests from patients(8). Specific guidance regarding social media websites and the potential for ethical difficulties should be offered to trainees in order to prevent such boundary violations. Residency curricula should be updated to provide such education to its residents.

#### NR2-08

### UTILIZATION OF THE PSYCHODYNAMIC DIAGNOSTIC MANUAL (PDM) IN PSYCHIATRY RESIDENCY TRAINING PROGRAMS: A CLINICAL REVIEW AND PROPOSAL

*Chair: Lauren Schwartz M.D.; Author(s): Arthur W. Rousseau, M.D., D.F.A.P.A*

#### SUMMARY:

Objectives: To identify the gap between the current Psychiatry Residency Review Committee (RRC) psychotherapy competency requirements and existing residency education in clinical application of psychotherapeutic theories. Methods: PubMed was used to search the Medline database. Retrieved articles were reviewed to identify trends in psychotherapy in residency training and in psychiatric practice. A second

search examined empirical evidence of treatment success when utilizing a systematic approach to assigning best-fit psychotherapy. 62 articles containing “psychodynamic psychotherapy” and “residency” were identified. Results: 13 of the retrieved articles directly supported our identified gap. Secondly, we found very little research on systematic selection of specific psychotherapy treatments. However, results of a 2010 study were promising, providing further support for our proposal. The results presented by Watzke et al. demonstrated an improvement in psychodynamic psychotherapy treatment outcome when utilizing Systematic Treatment Selection (STS). This supported our proposed need to promote the development of skill sets in those coming into the field of psychiatry that would allow for the provision of well-suited therapy, thus decreasing the number of psychotherapeutic failures. Our literature search identified a lack of clinical guidance and feelings of inadequacy in conducting psychotherapy among residents, despite the RRC’s 2001 educational changes. Based on this evidence and PDM task force data (2006), psychiatry (in training and in practice) risks taking a symptom-based, biological approach to mental health care, distancing psychiatry from psychotherapeutic treatment modalities. To encourage those new psychiatrists to cultivate and use psychotherapeutic skills in practice, residencies are challenged with providing adequate foundations in therapy. Current mandates are not yet providing this. Conclusion: As found in the current literature, there exists an educational gap between residents learning psychotherapeutic theories and feeling competent to utilize them in practice. This gap may be addressed by expanding resident exposure to an accepted clinical model assessing patients’ personality organizations and mental functioning through the PDM. This would enable residents to identify best-fit treatment approaches, increase their number of therapeutic successes and boost confidence in their ability to utilize psychotherapy as a viable treatment modality.

**NR2-09**  
**INTERNATIONAL MEDICAL GRADUATES**  
**IN PSYCHIATRY: UNDERSTANDING THEIR**  
**JOURNEY THROUGH THE INTERVIEW**  
**TRAIL**

*Chair: Lama Bazzi M.D.; Author(s): Carolina Jiminez M.D. Suprit Parida M.D. Sherif Ragab M.D. Stephen M. Goldfinger M.D.*

**SUMMARY:**

Objectives/Background: International Medical Graduates (IMGs) account for half the applicants to the national residency matching program (NRMP).

About 25% of physicians practicing in the United States are IMGs, contributing significantly to the US health care system. Moreover, IMGs provide care for many ethnic minorities, and work in areas underserved by primary care physicians. The process IMGs go through on the interview trail and the challenges they face in choosing a program have gone largely unaddressed. We aim to describe this journey through the eyes of IMGs, represented by the psychiatry residents of SUNY Downstate Medical Center. Methods: An anonymous electronic semi-structured survey was administered to IMG residents of SUNY Downstate psychiatry program. They answered questions about their experiences during the residency interview season. The data was compiled and analyzed qualitatively. Quantitative enumeration was used to identify recurring themes. Results: The most common themes depicted in the responses were: 1) concern of securing a position compelled candidates to apply to a large number of programs 2) financial constraints were cited as a limiting factor in attending interviews, arranging accommodations and traveling comfortably 3) anxiety during interviews was common at the beginning of the season, but dissipated as the interview season progressed 4) factors influencing the decision to accept an interview invitation included location, finances, number of interview invitations received, visa status and type of program. When it came to rank list orders for the match or considering pre-matches, the type of program (community vs. university) seemed to hold the greatest weight in the decisions made by residents. Conclusions/Discussion: IMG residency applicants consider many factors, including finances, number of interviews, location of programs, visa type sponsored, type of program and research opportunities in choosing programs. Although our sample size was small and limited to one program in psychiatry, it allows for some insight into the hurdles residents face while interviewing. By providing some insight into the obstacles residents face while interviewing, and a deeper understanding of their choices, we believe some of the systemic issues might be ameliorated. Considering the forming of guidelines or an online program tailored to IMGs in the application process could be useful.

**NR2-10**  
**‘BRIDGING THE GAP’: USING FREE**  
**INTERNET-BASED TOOLS FOR MULTI-SITE**  
**RESIDENT EDUCATION**

*Chair: Ujjwal Ramtekkar M.D.; Author(s): Parikshit Deshmukh, M.D. Gaurav Kulkarni, M.D.*

**SUMMARY:**

Use of internet software and file sharing systems for

sharing educational material is becoming common at educational institutions (1); however, the use of similar tools for multi-site collaborative learning in Psychiatry is rarely reported. We describe a pilot project to assess the feasibility of such a multi-site learning model. The teleconferences were conducted from August to October 2011 with a goal to review a major psychopharmacology textbook published by APA and study material for PRITE. The residents from three institutions (Children's Hospital Boston/Harvard medical school, MA; Case Western Reserve University Hospitals, OH; and University of Missouri at Columbia, MO) participated during the entire period. These conferences used a free internet based conference service (www.freeconference.com) for discussions and 'Dropbox' for file sharing. Each week, a topic was decided using a consensus method and the reading materials such as presentations and salient notes based on the APA textbook chapter, PubMed and Psychiatryonline were sent to the central shared folder on Dropbox prior to the discussion. These materials were reviewed simultaneously during the discussion via telephone conference on the pre-decided time. At the end of each session, the salient points during the discussion were added to the shared document. All the conferences were successfully completed without major technical or logistical issues. The participants expressed satisfaction about this collaborative method of independently researching the topics and sharing the information to create a comprehensive resource for clinically oriented learning. Use of similar innovative model of internet-based free resources can be feasible for educational activities such as curriculum development and core competency training at different institutions. A formalized protocol with more residents and institutions to replicate this model and measure its impact on medical knowledge of participants is in progress. Reference: 1. Vautrot VJ, Festin FE, Bauer MS. The feasibility and effectiveness of a pilot resident-organized and -led knowledge base review. *Acad Psychiatry*. 2010 Jul-Aug;34(4):258-62

#### NR2-11

### MESSAGE ON THE BOTTLE: IMPORTANCE OF TRANSFER OF CARE FROM FRONT LINE TEAMS TO TREATMENT TEAMS IN THE HOSPITAL

*Chair: Madhavi Nagalla M.D.*

#### SUMMARY:

Introduction: Transfer of care in emergency situations is a key component of patient care and at the same time the most vulnerable part. While this holds true at all levels of transfer of care, we will focus on the transfer

of care from frontline medical teams to treatment teams in the hospital. Accurate history taking is the first step and the most sensitive diagnostic tool in medicine. In emergency settings, when patients are unable or unwilling to provide adequate history, the incident scene can provide us with pivotal information to help us treat our patients appropriately. Our front line medical teams are therefore the main access to this crucial information. Unfortunately, information is too often missed because, in emergency situations, the scene survey and description are largely overlooked. The purpose of this poster is to examine the often weak link in obtaining and relaying important collateral information and to suggest simple, but effective ways to improve this element in transfer of care. Methods: We conducted a cross sectional review of the charts of patients who accidentally or intentionally overdosed and were brought to the emergency room by emergency medical services. We also reviewed pre hospital care reports in some states in the country through Google search and by talking to Emergency Medical Team chiefs in different counties. We conducted telephone interviews with Emergency Medical Team chiefs about the protocols followed at the incident scenes and how pre hospital care reports are completed. An overview of these cases and discussion will be provided with focus on one case where the appropriate treatment was delayed because the medical team was unaware of the medication that the patient had overdosed with. This delay was life threatening, yet easily avoidable. Discussion: While stabilizing the patient is the most important task of the frontline medical team, evaluation of the scene should not be given any less importance. The pre hospital care reports are mainly designed for physical assessment of the patient and these reports when filled out properly give a very good evaluation of the patient's condition on site. While this remains a priority, including scene description in the pre hospital care reports will reveal the cause of the emergency and lead to better treatment. Front line medical teams are taught to identify the substance that a patient is suspected to have ingested and if possible to bring the substance and its container to the hospital. Too often things that should be done "if possible" do not get done. Including this crucial step as part of the protocol would ensure that it is routinely done and result in better patient care.

#### NR2-12

### FELLOWSHIP IN LEADERSHIP AND MANAGEMENT DURING PSYCHIATRY RESIDENCY IN LONDON THROUGH A LIVE PROJECT: PAYMENT BY RESULTS IN MENTAL HEALTH

*Chair: Pratima Singh M.D.*

**SUMMARY:**

Darzi fellowship is a yearlong bespoke leadership and management fellowship sponsored by the London Deanery and the strategic health authority of London (NHS London) to encourage leadership development in the young generation of doctors. The fellowship consists if a yearlong project along with management modules delivered by a business school. Forty residents from all specialities are competitively selected to participate in the programme. Following is the description of the experience of the project undertaken by one of the two Darzi fellows in Mental Health in 2011. The main aim of the project was to embed the concept of PbR in the organisation through training and care package development in preparation for the new way of commissioning of mental health services that was coming in England. This required clinical engagement in all stages of the implementation plan. The objectives were to lead the development of the care packages that described the units of activity and interventions that will be provided by Oxleas in each PbR cluster when PbR was fully implemented in the future. This would be used as an opportunity to drive quality of care by introducing best practice standards into the care packages. Challenges: The main challenge of the project was to use and critique a completely new model of mental health commissioning while still maintaining engagement of clinicians on whom it depended. This was achieved by working closely with the national developments in the area, contributing to evolving knowledge and applying the learning to the local experience of PbR implementation. This experience was then shared with other organisations at various stages of their own implementation. Key learning outcomes: The major gain of this programme has been an increase in my belief in my own leadership capacity. I have learned new skills for working creatively and sensitively within groups to tackle difficult problems. I have come to appreciate that good leadership is not only about having the right attributes but a willingness and courage to apply it to your passion regardless of your position.

**NR2-13****DEPRESSION, AMYLOIDOSIS, AND STEM CELL TRANSPLANTATION: CURRENT FINDINGS AND FUTURE DIRECTIONS**

*Chair: Janet Shu M.D.; Author(s): David C. Seldin, M.D.*

**SUMMARY:**

Significant research has shown that there is a correlation between depression and increased risk of mortality in patients undergoing stem cell transplant (1, 2). In most of these studies, patients had a variety of blood

dyscrasias, including leukemia, multiple myeloma, and amyloidosis. Amyloidosis, a rare disease, affects multiple organ systems, and has poor prognosis if untreated (3). With limited public knowledge of the disease, amyloid patients may feel more isolated than other populations, and be uniquely at risk for depression affecting prognosis. There is limited literature on the link between depression and amyloidosis (4), although one study found that stem cell transplant improved quality of life for amyloid patients (5). This case report illustrates how a 60 year-old woman's depression may have increased her morbidity and mortality in the context of familial amyloidosis, and describes future directions in exploring the correlation between depression and amyloidosis, including an ongoing study retrospectively comparing the mortality rates of a cohort of depressed versus non-depressed amyloid patients receiving stem cell transplant (6). 1. Prieto JM et al. "Role of depression as a predictor of mortality among cancer patients after stem-cell transplantation." *J Clin Oncol* 2005, Sep 1; 23(25):6063-71. 2. Loberiza FR Jr et al. "Association of depressive syndrome and early deaths among patients after stem-cell transplantation for malignant diseases." *J Clin Oncol*, 2002 Apr 15; 20(8):2118-26. 3. Merlini G et al. "Amyloidosis: Pathogenesis and New Therapeutic Options." *J Clin Oncol* 2011, May 10; 29(14):1924-33 4. Wells DA and SR Lennon. "Major depression and amyloidosis." *Gen Hosp Psychiatry*. 1989 Nov; 11(6):425-6. 5. Seldin et al. "Improvement in quality of life of patients with AL amyloidosis treated with high-dose melphalan and autologous stem cell transplantation." *Blood* 2004, 104: 1888-1893 6. Shu and Seldin, ongoing research, unpublished.

**NR2-14****INTERNATIONAL MEDICAL GRADUATES IN PSYCHIATRY: SETTING OUT AND DECIDING TO APPLY TO US PROGRAMS**

*Chair: Renata Sanders M.D.; Author(s): Lada Alexeenko M.D. Richard Kinyamu M.D. Chainllie Young M.D. Amjad Hindi M.D. Nikhil Palekar M.D.*

**SUMMARY:**

Objective: International Medical Graduates (IMGs) comprise one quarter of psychiatrists practicing in the United States. However, their acculturation and adaptation issues are seldom studied. The aim of this survey was to investigate professional and personal experiences of IMGs prior to applying to psychiatry programs in the United States as well as the main reasons affecting that decision. We also aimed to investigate what were the steps involved in the planning of the application for residency and which factors influenced key decisional aspects. Methods:

IMGs residents of a university based psychiatry residency program were requested to participate in an electronic survey consisting of open-ended questions with standardized probes to further explore topics. The participants were requested to provide free-text comments focusing on their personal and professional background, motives for deciding to pursue a residency in America, and details of the planning of their application. Qualitative analysis was utilized. Emergent themes were charted and interpreted to comprise the findings. Results: 35 out of 41 IMG Psychiatry residents of the program participated in this survey, providing free text responses. The most common themes depicted in the responses were: 1) Significant academic/ professional achievements before applying to US residency programs; 2) Expectations of better quality of life and standards in psychiatric care in the United States; 3) "Idealized" view of life, residency and the practice of psychiatry in the United States as a motivator to pursue residency in this country; 4) Feeling discriminated for being an IMG during the application process to residency programs; 5) Contentment with their achievements and quality of life in this country despite disappointment with some aspects of the practice of psychiatry in the United States. Conclusions: The knowledge produced in this survey can contribute to a better understanding of the academic/ professional background of IMGs applying to psychiatry programs in the US, as well as eliciting the main motivating factors, expectations and disappointments during the application process. The authors suggest a need for a venue where prospective and current IMGs residents could discuss their experiences with residency program directors and faculty members, in order to promote an increase in social support and facilitate acculturation.

**NR2-15**  
**INTEGRATION OF MENTAL HEALTH AND PRIMARY CARE SERVICES IN A STUDENT-FACULTY COLLABORATIVE PRIMARY CARE CLINIC: AN APPROACH FOR PSYCHIATRY EDUCATION**

*Chair: Chuan-Mei Lee M.A.; Author(s): John Heintz, MA, Janine Knudsen, BA, Oriana Vesga Lopez, M.D., Lazaro Zayas, M.D., Mary Lyons Hunter, PsyD, Derri Shtasel, M.D., M.P.H., Marya J Cohen, M.D., M.P.H.*

**SUMMARY:**

The Crimson Care Collaborative (CCC) at Chelsea is a Harvard Medical School student-resident-faculty collaborative clinic located at the Massachusetts General Hospital (MGH) Chelsea community health center. The clinic features co-located, integrative mental health and primary care services and serves two main patient

populations: 1) recently incarcerated individuals and 2) patients who have been unable to establish routine primary care and are high utilizers of urgent care services. **OBJECTIVE:** To demonstrate a model of integrating mental health and primary care services as an innovative approach for psychiatric education. **METHODS:** The authors will describe the operational structure of the clinic. Medical student participants will be asked to describe how the co-location of psychiatric and primary care services informed their approach to patient care. **RESULTS:** The CCC Chelsea clinic offers several learning opportunities in psychiatry with an emphasis on interdisciplinary teamwork: 1) student participation in psychiatric patient care, 2) a case conference co-led by residents from psychiatry and internal medicine, 3) a student-led case-management system that helps patients navigate social service resources available in the community, and 4) student-initiated discussions between psychiatric and primary care teams. Descriptive results of medical students' recognition of the effect of co-located psychiatric care will be presented. **DISCUSSION:** A student-resident-faculty collaborative clinic provides a unique learning opportunity for exposure to psychiatry in the context of an interdisciplinary care model.

**NR2-16**  
**DESIGNING A RELIGION AND SPIRITUALITY CURRICULUM IN A PSYCHIATRY RESIDENCY PROGRAM; PART 1: IDENTIFYING THE KNOWLEDGE GAP**

*Chair: Harshad Patel M.D.; Author(s): J. Luke Engeriser, M.D.*

**SUMMARY:**

Introduction: Despite the importance of religion and spirituality in human culture, these topics have historically been neglected by psychiatry. The Accreditation Council for Graduate Medical Education currently includes in its psychiatric training requirement didactic instruction in the religious/spiritual factors which influence development, but formal training in addressing spiritual/religious issues in patients is not universal in psychiatric programs. Objective: To survey our current residents to discover their attitudes towards, level of comfort with, and knowledge of how to best address spiritual issues in psychiatric clinical care. The responses to these questions will help guide our design of a religion and spirituality curriculum in our residency program. Methods: A survey was developed to identify the knowledge gaps among residents in our residency program. In April 2011, residents were given the option of filling out the survey, and it was explained that this was entirely voluntary and anonymous and that the

responses would be utilized for both research purposes and to help us design a Religion and Spirituality curriculum. All 12 residents present at the meeting chose to fill out the survey. Discussion: All of our residents agreed or strongly agreed that it is appropriate to take a spiritual history, but only 50% indicated that they routinely take a religious history from their patients. Only 25% of residents felt that there was sufficient training in religion and spirituality in our residency program. The gap between the perceived importance of taking a religious and spiritual history and actual practice may reflect a lack of attention to this issue within our educational curriculum. The results of this study support the need to incorporate better training in Religion and Spirituality in our Residency Training Program. Based on the results of this survey, a formal seminar on religious and spiritual issues in psychiatry will be incorporated into our didactic curriculum in the 2011/2012 academic year.

**NR2-17**  
**USE OF “THE BRIDGE” TO AUGMENT**  
**THE SUICIDE CURRICULUM IN**  
**UNDERGRADUATE MEDICAL EDUCATION**

*Chair: Leorah Walsh M.D.; Author(s): Carolina Retamero, M.D Guillermo Otero-Perez, M.D.*

**SUMMARY:**

Objective— to describe the use of the documentary “The Bridge” to augment second year medical student education about suicide. Method-- 183 second year medical students at Temple University School of Medicine watched “The Bridge” as a part of the Neuroscience curriculum in understanding suicide. They completed a pre and post-movie survey regarding the understanding of suicide risk, reasons for suicide, prevention of suicide, and impact of suicide on surviving families. The percentage of answers in categories agree, strongly agree, disagree, and strongly disagree were calculated. The significance of results was calculated using paired t-tests. Students were also asked to comment on the movie. The comments were grouped according to themes, and the percentages of comments on each theme were calculated. Results— Most students were very receptive to the idea of using a movie to augment instruction on suicide, agreed that watching and discussing a film reinforced concepts learned in lecture. Most students felt that lectures alone were not sufficient to understand suicide, with a statistically significant increase in the percentage of students who felt lectures were not sufficient ( $t=3.34$   $p=0.001$ ). Students felt that after watching the movie, they had a better understanding of the risk factors for suicide (85%), understood the stigma faced by Survivors

of suicide (85%), and understood what the last days of a suicidal patient were like (90%). They believed that “The Bridge” should be shown to other people in the medical field (80.6%). Conclusions— “The Bridge” represents a useful method for instructing students and residents on suicide and has utility in medical education. It provided a unique window into the lives of people who have committed suicide and of survivors of the suicide that cannot be fully learned by lectures alone. It can and should be used regularly use alongside lectures for assisting in education about suicide.

**NR2-18**  
**RESIDENT LED MORNING REPORT:**  
**A MODEL FOR INTEGRATING CASE**  
**BASED LEARNING AND RESIDENT LED**  
**CURRICULUM**

*Chair: Michael Francis M.D.*

**SUMMARY:**

Competition for an individual’s time is increasingly fierce as those in residencies progress through their training. Between clinical duties, research time, administrative responsibilities, and juggling lives outside of work, keeping education as a core component of a resident’s daily scope can be difficult. In psychiatry, it has been suggested that residents spend approximately 1-2 hours daily teaching medical students, and often informally turn to one another for guidance on a variety of clinical matters. In light of the significant reliance on residents on educators, it is interesting that only an estimated 62% of psychiatry residency programs offer training in teaching skills. The idea of a resident led morning report was born out of the belief that there are few better ways to learn than to teach. Though it is by no means a training program in the discipline, the intent was to provide residents with an informal milieu in which they could participate in the educational process as teachers and students simultaneously. In its inception, morning report was set up with three particular goals in mind: 1) To create a collegial learning environment amongst residents and medical students where the free exchange of ideas and thoughts can occur regarding patient care without fear of embarrassment 2) To foster an increased appreciation for evidence based medicine as a way of clinical practice as well as for the role of residents as educators 3) To use morning report as a way to help residents and students define the ways that they look at and present their patients. The belief is that by creating a comfortable and collegial environment in which to utilize case based learning, residents will gain clinical knowledge as well as feel increasingly comfortable holding discussions and educating on various clinical topics. It is also believed that through

the presentation of patients by post-call residents that comfort with patient presentation will be improved.

**NR2-19  
IMPROVING CHILD AND ADOLESCENT  
FORENSIC PSYCHIATRY TRAINING:  
DEVELOPMENT OF A CAP FORENSIC TRACK**

*Chair: Peter Martin M.D.; Author(s): Michael Scharf, M.D. Richard Ciccone, M.D. Tim Beal, M.D., MBA Jonathan Raub, M.D., M.P.H.*

**SUMMARY:**

**Identifying a Need:** Currently, “Correctional Psychiatry” or at least court mandated treatment remains common in the practice of Child and Adolescent Psychiatry. For Child and Adolescent Psychiatry Training programs, ACGME requires teaching regarding juvenile justice system and family court, but provides few specifics and there is tremendous variation between programs both in clinical experiences and actual involvement with court. Similarly, Forensic Psychiatry training programs are expected to provide teaching regarding the juvenile justice system, but details and actual experiences vary considerably between programs.

**Development of a Subspecialty:** While historically there has been extensive overlap between CAP and Forensic Psychiatry, over time these two fields have developed in parallel from a training paradigm. With an increased interest in specialized training to help navigate these specialties, there was a realization that specific additional training may be desired. To help address these issues, through a close collaboration between the training directors for Child and Adolescent Psychiatry and Forensic Psychiatry at the University of Rochester, the development of a tract within the Forensic Psychiatry fellowship specifically designed for CAP who desire additional training in forensic psychiatry was created.

**Development of the Child and Adolescent Forensic Psychiatry Track:** A key portion of the development in this tract has been utilizing one of the guiding principles at the University of Rochester in which trainees are an active part of curriculum development. Within the year-long Forensic Fellowship, a previously trained CAP takes part in multiple unique experiences, including family court observations, providing treatment at a secure juvenile justice detention center, conducting evaluations for competency in juvenile offenders, custody and visitation evaluations, and observing CAP expert witness testimony. In addition, there is a didactic lecture series covering the following topic areas: Child Abuse, Custody, Termination of Parental Rights, Juvenile Justice, and Youth/School Violence. **Conclusions:** The overall response to the training experience has been exceedingly positive by everyone involved. In the future,

additional exposure to civil matters as well as increased integration of experiences with the Child and Adolescent Fellowship should solidify various aspects of the fellowship training experience.

**NR2-20  
SHORTER PSYCHIATRY CLERKSHIP LENGTH  
IS ASSOCIATED WITH LOWER NBME  
PSYCHIATRY SHELF EXAM PERFORMANCE**

*Chair: Cara Alexander M.D.; Author(s): John Michael Bostwick, M.D.*

**SUMMARY:**

**Objectives:** The goal of this study was to evaluate a recent medical school curriculum change at our institution three years ago: specifically shortening the Psychiatry core clerkship from 4 to 3 weeks and adding an optional 6 week core/elective combination rotation in lieu of the 3 week core. We aimed to determine whether clerkship length was associated with lower scores on the NBME Psychiatry shelf exam (PSE), a requirement of all third year medical students at our institution. **Methods:** We collected a convenience sample of 12 years of shelf exam scores from all Mayo Medical Students and determined the length of each student’s clerkship. Creating three groups (6 week core/elective (n=14), 4 week clerkship (n=478), and 3 week clerkship (n=24)), we determined the mean exam score for each group and compared the means across the 3 groups using a one-way ANOVA. **Results:** The mean shelf exam score for each group was: 81.5 [95% CI = 76.6-86.4] (6 weeks), 75.3 [95% CI = 74.4-76.1] (4 weeks), and 75.5 [95% CI = 73.0-77.9] (3 weeks). A t-test showed statistical significance between 6 vs. 4 weeks and 6 vs. 3 weeks, but not 4 vs. 3 weeks. **Conclusions:** Students completing three weeks in psychiatry had an average shelf score almost identical to those completing four weeks, but both three- and four-week clerkship groups had exam scores significantly lower than students who completed six weeks of psychiatry. We propose that differences between groups are the result of shorter clerkship lengths, but other factors including differences between student cohorts or differences between individual students may also be in play.

**NR2-21  
I PHONED IT IN: A NOVEL WAY OF  
ASSESSING CHANGE OF MENTAL STATUS  
IN A NON-RESPONSIVE PATIENT THROUGH  
FAMILY SMARTPHONE VIDEOS**

*Chair: Muhammad Majeed M.D.; Author(s): Branden A. Youngman, D.O.; R. Bryan Chambliss M.D.*

## SUMMARY:

The usefulness of family smart phone videos was serendipitously discovered on a routine consult for a change in mental status in a non-responsive 83 year old man with mild dementia who had received the typical “shotgun” workup for acute delirium. His family was very well educated and gave a clear picture of waxing and waning confusion for several weeks, which only confirmed that the patient was delirious. However, when a son pulled an iPhone from his pocket and asked the consult team if they would like to see what a “character” his father was before this acute illness, the picture was greatly clarified. The son showed videos of his father performing ad lib vaudeville routines of singing, joking and playing the harmonica. Each time the patient was confused, he could not tell a joke that made sense, and he transformed from a two-handed harmonica player to a one-handed harmonica player. The videos had been time-stamped, so a timeline and course of the illness was easy to construct. The videos acted as 6 months of “virtual house calls” and revealed a chronic and progressive right-sided lean and a lower than expected use of the right hand for gesturing and eating, which pointed strongly to a longstanding left-sided CVA with acute TIAs. This new technology acted as an old-fashioned descriptive history and “physical exam”. The family appreciated that the team was willing to “be a guest in their home” and see their father’s pre-morbid vivacity, humor and talent. The visual details of becoming a one-handed harmonica player whenever he was confused made it easy to explain to the family why the confusion was most likely due to TIAs. Within a few days, most specialties had requested to see the videos, and there was more discussion of the visual observations of the patient’s behavior than the visual imaging on his brain. This case clearly illustrates the usefulness of family smart-phone videos for constructing a visual history of the present illness when a traditional verbal HPI cannot be performed. They are especially useful to assess transient phenomenology, which is common in psychiatry. Only psychiatry had a neurological history, because only the CL service had seen the videos of the progressions of the patient’s CNS status; so psychiatry was called for neurological questions until the neurology service had seen the videos.

## NR2-23

### UNDERSTANDING PATTERNS OF INTER-PARTNER ABUSE IN MALE-MALE, MALE-FEMALE, AND FEMALE-FEMALE COUPLES

*Chair: Alexandru Gaman M.D.; Author(s): Alexandru Gaman M.D., Scot McAfee M.D., Theresa Jacob Ph.D., M.P.H.. Department of Psychiatry, Maimonides Medical*

*Center, Brooklyn, NY*

## SUMMARY:

Background: Domestic violence is a major problem in the United States and all over the world, and can lead to mental health conditions such as alcohol abuse and depressive disorders. It is implicated in 30% of female and 5% of male homicide deaths. Men express more violent patterns of domestic abuse (mostly physical and sexual) than women (verbal). Due to distinct gender structure, disparate internalization / externalization attitudes and diverse sociocultural context, male-male (MM), female-female (FF) and female-male (FM) couples present challenging differences in domestic violence and help-seeking behaviors. We hypothesize that there is significant difference in the patterns of inter-partner abuse in these 3 distinct types of relationships, in terms of aggression and violence experienced by victims and their help-seeking behaviors. Aims: 1. To compare the patterns of violence experienced by victims in MF, MM, or FF domestic relationships. 2. To determine the prevalent help-seeking behavior in the above groups. 3. To examine the incidence of mental health conditions in the victim population. Methods: English speaking males and females, older than 18yo, admitting to experience domestic violence in MM, FF, or MF relationships will be recruited, with 22 subjects/group (n=66). Subjects will be recruited from the general population via internet postings, ads in community specific bars, clubs or other places of interest, and using snowballing or discussion/ forum lists. Screening tool will be HITS questionnaire for domestic abuse. Patterns of violence will be evaluated in screened subjects using a questionnaire modified after Renzetti (1992). Help-seeking behaviors, enhancing factors and barriers will be assessed using Likert-type questionnaires. Data will be analyzed by various statistical tests using SPSS package. Results: This is an ongoing study with insufficient subject numbers recruited to-date. We envision that the methods and behaviors used in partner abuse differ in all three groups. While it is difficult to predict outcomes without adequate data, it seems possible that women involved in FF couples deal with more verbal abuse compared to women involved in MF couples. It is expected that men experience more barriers in reporting abuse than women, possibly due to societal culture. Homosexual men may probably report abuse more often than heterosexual men overall. However, men in MM relationships not reporting abuse, perhaps refrain from doing so because of financial dependence rather than cultural views in comparison to an MF male. Discussion: This study was undertaken with the long-term goal of proposing interventions to decrease domestic abuse and its disastrous outcomes. To our knowledge, this is

the first study that compares inter-partner abuse in the diverse domestic partner-relationships of today. Our data would provide a basis to identify subgroups, methods of abuse and behaviors at high risk for aggression in these relationships.

**NR2-24**  
**DISSOCIATED ASS ANTIBODY LEVEL**  
**AND OXIDATIVE STRESS PARAMETERS**  
**IN ALZHEIMER'S DISEASE- POPULATION**  
**BASED STUDY**

*Chair: Kasia Rothenberg M.D.; Author(s): Sandra L. Siedlak, Xiongwei Zhu*

**SUMMARY:**

In the growing population of aged individuals who are at risk of developing Alzheimer disease (AD) there is an urgent need for a sensitive, specific and preferably, non-invasive, diagnostic standard. Deposition of A $\beta$  is believed to be centrally involved in the pathogenesis of AD. In our previous study, using a technique for dissociating antibody-antigen complexes, we found significant differences in serum antibodies to A $\beta$  between AD and aged-matched control subjects. In this study samples were obtained as a part of population based study of the prevalence of AD (Poland-Lublin district – 2 182 191, inhabitants). Stratified sampling and random selection strategies were combined to obtain a representative population for screening (ages >55). From the screened population, 52 persons were diagnosed with AD (DSM IV and ICD 10 criteria) and the group of healthy, age and gender matched controls was selected. The two groups did not differ with respect to other chronic diseases. Sera collected from AD patients and age-matched controls were examined using the antibody-antigen dissociation methodology previously described (Gustaw et al 2008). The level of antibody against A $\beta$ 1-42 was detectable both in control and AD before and dissociation of A $\beta$  antibody (ELISA). Sigma Stat 3.0 was the tool of statistical analysis. Mann-Whitney test and Pearson Product Moment Correlation were used to compare and correlate outcome parameters respectively. Significant differences was noticed between AD and control patients before dissociation (median O.D. 0, 67 vs. 0.47 respectively  $p < 0.001$ ). After dissociation, however, the level of antibody assessed was greater than before dissociation (median O.D. 1.07 vs. 0.7 respectively  $p < 0.001$ ). Significantly the increase in A $\beta$ 1-42 auto-antibody levels in AD cases after dissociation was much greater than in controls (median difference 0.4 vs. 0,2  $p < 0.001$ ). Level of A $\beta$ 1-42 after dissociation correlated negatively with duration of the diseases and the age of AD patient (correlation coefficient: -0.7 and -0,5  $p < 0,05$ ). Level of antibody

didn't seem to decrease with age in the controls however. Level of A $\beta$ 1-42 after dissociation correlated negatively with the level of TAS (total antioxidative stress parameters) in AD patient (correlation coefficient: -0.65  $p < 0,05$ ). The above phenomenon noticed may indicate the dissociated A $\beta$ 1-42 antibody level to be of a diagnostic value in the beginning of the neurodegenerative process with A $\beta$ 1-42 deposition in AD.

**NR2-25**  
**HEALTH POLICY AND INTERVENTION**  
**STRATEGY ISSUES WITH CURRENT**  
**EPIDEMIOLOGY IN ALCOHOLIC**  
**POPULATION**

*Chair: Vatsalya Vatsalya M.D.; Author(s): Vijay A Ramchandani, Ph.D. Marion A Coe, BA Robert Karch, EdD*

**SUMMARY:**

Alcoholism causes 79,000 deaths annually in USA, with 5% population indulged in heavy drinking. We used outcome reports of the NIAAA National Epidemiologic Survey of Alcohol and Related Conditions data from 2001-2002 (wave I) and 2004-2005 (wave II) years to identify concerning areas and to design revisions in current health care planning. Major results in the wave II surveys demonstrated 77.54 $\pm$ 0.43 % of the population (75.20 $\pm$ 0.60 % males and 79.97 $\pm$ 0.56 % females) continued drinking during the interval and remained without Alcohol Use Disorder (AUD) diagnosis from the wave I drinking population. 5.36 $\pm$ 0.36 % developed alcohol abuse and 3.55 $\pm$ 0.17 % developed alcohol dependence. Only 13.55 $\pm$ 0.41 % of the drinking population remained without AUD and stopped drinking. In the abuse group data, 52.43 $\pm$ 1.56 % showed non-abstinent remission, 29.95 $\pm$ 1.43 % remained alcohol abuse and 14.01 $\pm$ 1.23 % developed alcohol dependence. 42.21 % of white male drinkers with alcohol dependence at wave I, remained alcohol dependent at wave II whereas 37.24 % went into partial remission. These evaluations suggest strategic need for timeline healthcare recommendations for the observed developments in gender and race/ethnicity, alcohol drinking subcategories; with a reinforced intervention and care management emphasis on targeted planning; implementation, monitoring and evaluation components. These strategies need three-tier planned restructuring focusing on community-wide, agency-wide and health service bodies. For community scale developments, PATCH (Planned Approach to Target Population and Community Health) model can be developed to introduce mobilizing the planning directives for target population, collecting and organizing data; and evaluations at agencies; choosing health goals, timelines

and focus on target groups; selecting and conducting interchangeable long and short-term interventions and follow-up evaluation for intervention developments. For agency level, we designed APEXPH (Assessment Protocols for Excellence in Public Health) model to create scope for organizational capacity assessment for newer drinking groups and self-assessment approaches for improvements in managing new targets; community process including formation of advisory committees to provide detailed plans; and completing the cycle by monitoring organizational processes to develop follow-up on the newly emerged target drinking groups. For former drinkers at wave I that showed relapse in wave II chiefly in the 18-24 age groups, MAPP (mobilizing with planned partnership) model can be used to include awareness, engagement, continued monitoring and diversification in support group framework for healthcare providers.

**NR2-26**  
**SUBSTANCE P & AFFECT INTENSITY; A NOVEL CORRELATION**

*Chair: Rakesh John M.D.; Author(s): Dr. Royce Lee, M.D., Dr. Emil F Coccaro, M.D., Michael J. Owens, Ph.D, Becky Kinkead, Ph.D, Dr. Charles B. Nemeroff, M.D., Ph.D*

**SUMMARY:**

Background: The neurotransmitter Substance P (SP) is highly expressed in brain regions that are involved in regulation of affective behavior. There is evidence of elevated CSF SP levels in psychiatric patients, especially in those with affective disorders, but the mechanistic link between SP function and psychopathology is not yet understood. No previous studies have examined Substance P levels in personality disorder and how they may be related to affective behavior. We hypothesized that cerebrospinal fluid (CSF) levels of SP would be positively correlated with a measure of affective intensity, the Affect Intensity Measure (AIM). Methods: Lumbar CSF for levels of SP was taken from 22 consenting adult subjects with and without DSM- IV personality disorders. Affect intensity was measured using the AIM scale. The primary analysis was conducted using the Pearson correlation model looking at the correlation between CSF SP levels & AIM. Results: CSF levels of SP were not related to the presence or absence of personality disorder, but were correlated inversely with AIM total score and specifically with the negative reactivity & positive reactivity subscales of AIM. Conclusions: This is the first report that examines a correlation between Substance P and Affect intensity. The finding of a negative correlation between SP and affect intensity adds to the understanding of the role of substance P in

affect regulation and also guides future research further examining this relationship.

**NR2-27**  
**NEUROBIOLOGICAL RELEVANCE OF SCHIZOPHRENIA-ASSOCIATED GENETIC POLYMORPHISMS: THE EFFECT OF SMARCA2 AND NIPA1 OVER-EXPRESSION ON NEURAL CELL SIGNALING**

*Chair: Frank Fetterolf B.S.; Author(s): Kelly A. Foster Ph.D.*

**SUMMARY:**

Genome-wide studies have implicated structural variations of DNA, such as copy number variations (CNVs), in conferring risk for schizophrenia. Two Particular genes, SMARCA2 and NIPA1, reside in implicated CNV loci and have a role in neurodevelopment. In order to elucidate the neurobiological relevance of these two CNVs, the effect of their over-expression on neuronal cell signaling dynamics was explored. Gene-containing plasmids were created and biolistically transfected into P7 rat hippocampal slice cultures. Standard whole-cell patch clamp recordings were made from CA1 pyramidal neurons. AMPA-Excitatory Post-Synaptic Currents (EPSC) and NM.D.A-EPSC recordings were collected from both control and transfected neurons. Neuron cultures over-expressing NIPA1 had decreased NM.D.A-EPSC compared to controls. SMARCA2 transfected neurons yielded inconclusive results. At present, these findings are heuristically unclear. Future directions of this research include: further data collection, testing for the resulting changes in long-term potentiation and the identification of other genes that interact with NIPA1.

**NR2-28**  
**THE UTILITY OF STELLATE GANGLION BLOCKS IN DUAL DIAGNOSIS: PTSD AND NEUROPATHIC PAIN**

*Chair: Robert Nastasi M.D.; Author(s): Kevin O'Connor M.D., Marvin Koss M.D., Dongliang Wang Ph.D., Donna Ann Thomas M.D., P. Sebastian Thomas M.D.*

**SUMMARY:**

Objective: Posttraumatic Stress Disorder (PTSD) and its co-morbid conditions, specifically neuropathic pain, are rapidly gaining interest. PTSD has been associated with chronic pain (10%). More specifically 15-30% of patients with neuropathic pain suffer from PTSD. We identify the medical hypothesis and the results of how the use of stellate ganglion block (SGB) as a therapeutic technique improves the function of patients with both

PTSD and neuropathic pain. Methods: A review of the literature using PUBMED, OVID MEDLINE searching for posttraumatic stress disorder, PTSD, complex region pain syndrome, CRPS, reflex sympathetic dystrophy, RSD, neuropathic pain, chronic pain, stellate ganglion block, and SGB was performed. Results: From a neurochemical perspective, norepinephrine (NE) and neurotrophic growth factor (NGF) levels are high in patients with chronic stress. Increases in NGF lead to retrograde transport from intracerebral sites to the stellate ganglion. Specifically, an increase in NGF at the stellate ganglion causes neuronal sprouting at end terminals. Neuronal sprouting are often referred to as “leaky” because there is an increase in NE release from these synaptic terminals. Increased levels of NE have been shown to be contributory factors to conditions such as hyperesthesia in neuropathic pain and PTSD. The use of SGB with local anesthetic is thought to reduce NGF, which leads to decreases in NE, and a reduction in symptoms. There have been two case reports and one case series (N2) documented. Both case reports involved patients who developed CRPS and PTSD following an assault. The patients were noted to have a reduction in pain scores and in PTSD symptoms. Lastly two combat veterans who developed PTSD without any co-morbid pain disorders received SGB. The veterans had marked improvement in their symptoms, as documented using the Post Traumatic Stress Disorder Checklist. Additionally, the veterans required less psychotropic medications to alleviate their symptoms. Conclusion: The use of stellate ganglion blocks appears at present to be a promising treatment for those who suffer from PTSD with or without neuropathic pain. Presently, a multi-center study is under IRB review to further investigate the feasibility and utility of SGB in patients with PTSD with or without neuropathic pain.

**NR2-29**  
**BIOMARKERS OF GLUTEN SENSITIVITY**  
**IN PATIENTS WITH SCHIZOPHRENIA: A**  
**META-ANALYSIS**

*Chair: Laura Lachance M.D.; Author(s): Dr. Kwame McKenzie, M.D.*

**SUMMARY:**

Background: An association between gluten sensitivity and schizophrenia has been present in the literature since the 1950s. Several studies have reported increased antibodies to gluten in patients with schizophrenia. However, there has been inconsistency with regards to which antibodies are elevated and at what rate compared to the general population. Methods: A literature review was performed to identify all original articles that

measured biomarkers of gluten sensitivity in patients with schizophrenia compared to a control group. Three databases were used: Ovid MEDLINE, Psych INFO, and Embase, dating back to 1946. Forward tracking and backward tracking of results was performed. Results of the literature searches were subjected to a meta-analysis. Results: 11 relevant original articles were identified. Three biomarkers of gluten sensitivity were found to be significantly elevated in patients with schizophrenia compared to controls. The pooled odd’s ratios and 95% confidence intervals for the aforementioned biomarkers were Anti-Gliadin IgG OR=2.03(1.43,2.88), Anti-Gliadin IgA OR=5.34(4.09,6.97), Anti-TTG2 IgA OR=6.83(3.28,14.22). Anti-EMA and Anti-deaminated gliadin were two biomarkers of gluten sensitivity found not to be associated with schizophrenia. Conclusions: Certain biomarkers of gluten sensitivity are elevated in patients with schizophrenia. However, the specific immune response to gluten in this population differs from that found in patients with celiac disease.

**NR2-30**  
**EXECUTIVE FUNCTION AND PREFRONTAL**  
**DOPAMINE UPTAKE IN A RODENT MODEL**  
**OF ADOLESCENT BULLYING**

*Chair: Andrew Novick B.S.; Author(s): Gina L. Forster, Ph.D., Leah Müller, James Hassell, B.S., Christina L. Roberts, Jamie S. Bushman, M.S., Michael J. Watt, Ph.D.*

**SUMMARY:**

Experience of bullying victimization during adolescence is associated with an increased incidence of mental illness both acutely and in adulthood. This may result from psychosocial stress-induced disruption of the maturation and reorganization that occurs in various neural systems of the adolescent brain, particularly within the prefrontal cortex dopamine (PFC DA) system. Optimal PFC DA activity is crucial for executive function, the complex cognitive processes underlying behavioral focus and flexibility. Interestingly, many of the mental illnesses associated with bullying are characterized by deficits in executive function, but it is unknown if this is a direct result of stress-induced insult to the adolescent PFC DA system. We have shown that adolescent rats exposed to social defeat stress, a model of human bullying, develop long term deficits in PFC DA activity. Accordingly, previously defeated rats were found to exhibit poor performance in two separate tasks of working memory, a component of executive function. To further investigate mechanisms by which adolescent social defeat produces changes to PFC DA, quantitative autoradiography was used to identify potential differences in markers of DA function. This revealed an upregulation of the DA transporter (DAT) in the

PFC of previously defeated rats. As DAT is responsible for clearance of DA from the neuronal synapse, upregulation of DAT following adolescent social defeat may lead to decreased DA availability within the PFC and subsequent deficits in working memory. In order to test this hypothesis, *in vivo* electrochemistry was used to establish if DAT-mediated DA clearance is enhanced following adolescent defeat. By identifying the mechanisms by which adolescent social defeat produces neurochemical and cognitive deficits, results of the present studies can be used to help guide targeted therapies that prevent and treat the consequences of adolescent bullying.

**NR2-31**  
**DO NEIGHBORHOOD CHARACTERISTICS PROMPT EARLIER CANNABIS USE IN PATIENTS DIAGNOSED WITH FIRST-EPISODE PSYCHOSIS?**

*Chair: Christopher Horne J.D.; Author(s): Michael T. Compton, M.D., M.P.H.*

**SUMMARY:**

Accumulating evidence suggests a complex link between psychotic disorders and cannabis misuse (Ramsay & Compton, 2011). In fact, premorbid cannabis use may be associated with an earlier age at onset of prodromal and psychotic symptoms. Given that cannabis use is a complex behavior driven by genetic, social, and environmental influences, the role of neighborhood is worth considering. Recent research indicates that neighborhood impacts various health conditions, ranging from obesity in older adults (Glass et al., 2006) to intimate partner violence (Li et al., 2010). Objective: We hypothesized that neighborhood socioeconomic and stability characteristics would contribute to ages at onset of premorbid cannabis use in first-episode patients. Method: We combined data from 2 consecutive first-episode samples (n=200) gathered in Atlanta, Georgia. Into this dataset, we imported U.S. Census Bureau census tract-level data and performed exploratory factor analysis on 17 census tract variables, which revealed 3 distinct neighborhood factors that describe local attributes of the first-episode patients' environmental surroundings. Specifically, the 3 factors were labeled disadvantaged neighborhood (e.g., percentage of families living below the poverty level), immigrant neighborhood (e.g., percentage foreign-born), and transitory neighborhood (e.g., percentage of renter-occupied units). Continuous scores on these three factors were trichotomized to generate tertiles that indicated high, medium, and low levels of socioeconomic disadvantage, immigrant population, and transitory population. Also taking into account the

effects of gender, we examined 3 dependent variables: age at first use of cannabis (n=143), age at beginning weekly use (n=106), and age at initiation of daily use (n=83). Using 2-way analyses of variance, we examined the role of the 3 neighborhood factors and gender (given its known relation to cannabis use initiation and escalation; Brook et al., 1999) in predicting these age-of-use variables. Results: Neither the extent of socioeconomic disadvantage nor transitory factor scores were predictive of age at initiation, weekly, or daily cannabis use. However, there were significant associations between the immigrant factor score and age at initiation (p=0.041), weekly (p=0.048), and daily (p=0.004) use of cannabis. Throughout, gender remained significant for age at onset of weekly and daily use of cannabis, though gender was not a significant predictor of age at initiation of cannabis use. Conclusion: Our hypothesis that neighborhood characteristics prompt earlier use of cannabis in first-episode psychosis was partially supported in terms of the significant relationship between age at initiation and age at onset of weekly and daily cannabis use and the aforementioned immigration score, though results may be limited by the relative homogeneity of the study sample. Gender appears to play a larger role in escalation of cannabis use.

**NR2-32**  
**THE BEAUTY QUEUE: HOW DO THE PHYSICAL TRAITS OF BODY SIZE AND SKIN COMPLEXION INTERSECT IN THE EDUCATED AFRICAN AMERICAN COMMUNITY?**

*Chair: Aminata Cisse B.A.; Author(s): Thomas Brouette, M.D.*

**SUMMARY:**

Persons of the African Diaspora vary greatly in phenotype. The remarkable spectra of physical differences, which have been heralded as the beauty of the race have also created much dissension among blacks. By co-opting the values of the dominant Western cultural ideology, defining an attractive woman in the African American community is often fraught with inconsistencies. In a previous study, heterosexual African American women pursuing their undergraduate degrees were asked how they perceived themselves in regards to skin complexion and body size, and how did these variables affect their ability to develop intimate relationships. The present study, which will comprise approximately 100 heterosexual college educated African American women from across the United States, will explore the same constructs of skin complexion and body size. Methods: Participants will complete a brief

survey. The subjects will be recruited through blogs and discussion boards that cater to young, educated, African American women. The surveys will be anonymous and the data will be calculated as aggregated data by regions in the United States. This study is the follow up to research that was conducted approximately four years ago. The present study seeks to assess if the results from the previous study have changed as subjects of the same cultural and academic demographic have matured, not only as individuals but in their personal relationships as well.

### NR2-33

#### **SLEEP AND BIPOLAR DISORDER: ASSOCIATION BETWEEN CLINICAL IMPROVEMENT AND SLEEP IN ACUTE MANIA**

*Chair: Barney Vaughan M.D.; Author(s): Stephanie Stolberg, M.D.; Francisco Linares, M.D.; Lisa J. Cohen, Ph.D.; Igor Galynker, M.D., Ph.D..*

#### **SUMMARY:**

**Introduction:** Although bipolar disorder can be considered a disorder of mood and arousal, it is mood that is targeted preferentially for treatment. It has been hypothesized that arousal (sleep) could be a better target symptom for treatment in acute mania. In this regard, we investigated the relationship between clinical symptoms, sleep pattern and length of stay for patients with acute mania. **Methods:** This is a retrospective chart review of patients who were discharged between 2005 and 2010 from an inpatient psychiatric hospital after a manic episode. Illness severity was measured three ways: by length of stay (LOS) and with 2 clinical scales, the Clinician Administered Rating Scale for Mania (CARS-M) and the Clinical Global Impression, which has one subscale for illness severity (CGI-S) and another for illness improvement (CGI-I). Charts were rated by 3 raters. Least difference criteria were used to achieve a consensus score for each item on the two scales. Data on sleep quantity (hours of sleep/night) were collected from nursing reports. In addition to illness severity, information on other clinical markers (e.g. p.r.n. requirements; seclusion and restraint requirement; medications prescribed) as well as demographic data were obtained. **Results:** In correlation analyses, treatment outcome measures (CGI, CARS-M and LOS) correlated with each other, but not with improvements in sleep. CGI was strongly correlated with Psychosis and general symptom scale scores ( $r=.71$ ,  $r=.72$ , respectively). Changes in sleep hours correlated with days to peak amount of sleep ( $r=.47$ ) and days to at least 7 hours of sleep ( $r=.63$ ). The length of hospital stay did not correlate with any symptom severity scales.

**Conclusions:** Retrospective chart review of a small sample of patients with bipolar mood disorder in an acute psychiatric unit showed no association between hours of sleep, as recorded by nursing staff and symptom severity scales' scores. Neither clinical symptoms nor sleep were associated with LOS. It appears that LOS is determined, at least in part, by non-clinical factors.

### NR2-34

#### **HEALTHCARE DECISION-MAKING AS A POTENTIAL SOURCE OF PSYCHOLOGICAL DISTRESS AMONG RELIGIOUS NONBELIEVERS**

*Chair: Samuel Weber M.D.; Author(s): Kenneth I. Pargament, Ph.D.; Mark E. Kunik, M.D., M.P.H.; James W. Lomax II, M. D.; Melinda A. Stanley, Ph.D.*

#### **SUMMARY:**

**OBJECTIVE:** As research into religion and health has received increased attention in recent years, greater numbers of studies have examined the link between religious belief and psychological well-being. Despite this increased attention, many such studies overlook the psychological health of nonbelievers (i.e. atheists and agnostics). In a recent review, we found that various forms of psychological distress are experienced by nonbelievers and that greater certainty in one's belief system is associated with greater psychological health. One primary source of distress for nonbelievers involves the negative perceptions of atheists and agnostics by others. Research has shown that medical appointments and decisions regarding healthcare can also be sources of psychological distress. This distress is especially pronounced in settings where poor communication and understanding are present. Religious nonbelievers are a minority group in the United States, and their preferences may be less well understood by healthcare professionals. This difference in worldview can result in distress for the nonbelieving patient. The objective of this study is to examine healthcare decision-making as a potential source of distress for nonbelievers. **METHOD:** A systematic literature review was conducted with PsycINFO using the following search terms: "atheis\*", "agnosti\*", "apostasy", "apostate", and "deconversion." The search was limited to articles published between January 1980 and April 2011. 4 articles were identified for inclusion in the present review. **RESULTS:** All four studies focused on healthcare decision-making among nonbelievers. Nonbelievers demonstrate a general avoidance of religious forms of treatment and support, preferring to rely on family and friends in times of crisis. Nonbelievers are also less likely to participate in Alcoholics Anonymous. Many atheists have clear preferences regarding end-of-life care, and

express concern that healthcare workers may attempt to proselytize them prior to death. Despite these differences, nonbelievers are no different from believers in their perceptions regarding the efficacy of secular treatments for depression, and nonbelievers who do participate in AA derive benefits comparable to believers. **CONCLUSIONS:** There is a growing interest in the relationship between religion and mental health. One limitation to the existing literature is the lack of attention to nonbelievers. We have identified healthcare decision-making as a potential source of psychological distress among religious nonbelievers, but further research is necessary to determine how healthcare providers can most effectively minimize distress among their nonbelieving patients.

### NR2-35

#### SHOULD WE ROUTINELY ASK ABOUT PROBLEMATIC COMPUTER AND INTERNET USE AS PART OF THE PSYCHIATRIC HISTORY?

*Chair: Himanshu Tyagi M.D.; Author(s): Ankush Vidyarthi MRCPsych*

#### SUMMARY:

Internet mediated communications have revolutionised the asynchronous forms of interpersonal communications. Changes in our preferred mode of communications are increasingly being reflected in the various societal systems e.g. education (Mark Prensky 2001), relationships (Tyagi 2008) and governments (Arab Spring 2011). Proposals to include pathological computer use in DSM V indicate that technology related problems are now being acknowledged by the mental health profession. This study was conducted to identify some of the arguments for and against these changes and to establish some patterns or name the categories for the arguments. **Method** Our study investigated attitudes of mental health professionals toward internet, and knowledge and understanding of internet related problems and internet related generational differences along with the specific primary question of the inclusion of the assessment of dysfunctional computer and internet use in psychiatric assessments. Data was collected via a survey amongst mental health professionals in USA, UK and India. Out of 1830 requests made, 379 responses were received (20.71% response rate) and 315 responses qualified for the final data analysis. Quantitative data was analysed by using SPSS software and qualitative thematic analysis was performed for free text answers. 72.7% of respondents were psychiatrists, with 41.6% of the total sample being that of those working as consultants with an average clinical experience of 11 years in psychiatry.

Results 45.1% (n=142) of respondents were in favour of including the assessment of computer and internet use as a routine question. 21.9% (n=69) were against and 33.0% (n=104) were undecided. A qualitative analysis of the free text answers for our primary question produced some interesting themes (included in poster). Professional working in children and adolescent services were most aware about the internet related problems. Significant background effects of demographic variables were also apparent: differences by age and clinical status were found. Some culture-specific characteristics of understanding internet related problems could be observed in our study.

### NR2-36

#### GENE EXPRESSION PATTERNS FROM BRAIN SAMPLES IN ALCOHOLICS

*Chair: Kamal Bhatia M.D.; Author(s): Ann M. Manzardo, Ph.D., Merlin G. Butler, M.D., Ph.D*

#### SUMMARY:

**Objective:** Current research in psychiatry is geared towards identification of biomarkers for specific biological targets affecting human behaviors including addiction. Alterations of gene expression in the brain may impact mood, behavior and psychopathology. The present study examines differences in the expression of genes from the alcoholic brain at the mRNA level using advanced microarray genetic technology. **Methods:** RNA samples were isolated from the frontal cortex (Brodmann area 9) of 8 alcoholics (7 males, 1 female, mean age 51 years) meeting criteria for alcohol dependence, and 8 age and gender matched controls. Samples were obtained from the New South Wales Tissue Resource Center (Sydney, Australia). The Human Exon 1.0 ST microarray (Affymetrix) was used to study exon and gene expression levels. This whole-genome array uses 1.4 million probe sets to interrogate approximately 28,869 well-annotated genes. Total RNA was isolated and hybridized to the microarrays using established protocols. **Results:** A total of 265 genes were significantly down-regulated in alcoholics ( $p < 0.05$ ), 15 genes by more than 2 fold compared to controls (range -1.06 to -2.42). Of these, aspartoacyclase (ASPA), cadherin-associated protein (CTNNA3), gliomedin (GLDN), and myelin oligodendrocyte glycoprotein (GOG) are involved in neuronal development, cellular adhesion and myelination in the brain and have been linked to neuropsychiatric illness, e.g. Canavan disease, multiple sclerosis, obsessive-compulsive disorder and Alzheimer disease. In addition, 283 genes were significantly up-regulated in alcoholics ( $p < 0.05$ ). Of these, 8 genes were up-regulated at  $> 1.5$  fold (range 1.05 to 2.06). These include 3 cellular transporters: cationic

transporter(SLC7A11); high affinity glial glutamate transporter(SCL1A3) previously linked to alcoholism; and zinc transporter (SLC39A12). Interestingly, glutathione S transferase (GSTM1) and serine/threonine kinase 17B (STK17 B) linked to oxidative stress and apoptosis were also up-regulated. Conclusions: Several genes critical for neuronal growth and development and implicated in neurodegenerative diseases were significantly down-regulated in the alcoholic brain. Several specific cellular transporters were up-regulated in addition to cellular mediators of oxidative stress response. The observed disturbances in gene expression have the potential to disrupt neuronal functioning and contribute to the manifestation of neuropsychiatric illness including addictive behaviors. Ref:(1)Atmaca M,Onalan E,Yildirim H,Yuce H,Koc M,Korkmaz S.Association of myelin oligodendrocyte glycoprotein gene & white matter volume in obsessive-compulsive disorder. *J Affect Disord.*2010 Aug;124:309-313(2) Hayes JD,Strange RC.Glutathione S-transferase polymorphisms & their biological consequences. *Pharm.*2000 Sep;61:154-166 (3)Flatscher-Bader T,van der Brug MP,Landis N,Hwang JW,Harrison E,Wilce PA.Comparative gene expression in brain regions of human alcoholics.*Genes Brain Behav.*2006;5:78-84.

**NR2-37**  
**EVALUATION OF THE PREVALENCE AND SEVERITY OF DEPRESSION IN PATIENTS WITH OBSESSIVE-COMPULSIVE DISORDER (OCD)**

*Chair: Rupal Patel M.D.; Author(s): Dr Himanshu Tyagi MRCPsych Dr Lynne Drummond MRCP MRCPsych*

**SUMMARY:**

Current research evidence suggests that comorbid depression with OCD leads to poorer treatment outcomes. As depression frequently accompanies OCD, it can be one of the most important factors in producing refractoriness for OCD treatment. Our study investigated all patients with a primary diagnosis of treatment refractory OCD who were accepted for outpatient treatment at a specialist OCD service in London between 1st January 2008 and 30th June 2010. We explored the relationship between OCD, depression and treatment outcomes. Standardised measures for assessment of the severity of OCD and depression were completed at assessment, mid-treatment, discharge and follow-up reviews up to 1 year after completion of treatment. Yale Brown Obsessive Compulsive Scale (Y-BOCS) was used to assess the severity of OCD. To assess the symptoms and severity of co-morbid depression, self-rated Beck Depression Inventory (BDI) and clinician rated Montgomery Asberg Depression

Rating Scale (MADRS) were used. PADUA inventory was used to assess the symptoms of OCD. Routinely collected social and demographic data were also used to understand the role of any additional factors in treatment outcomes. Preliminary results indicate that greater than two-thirds of treatment-refractory patients in our sample (n=158) were depressed. Differences in symptom severity and treatment response between depressed and non-depressed OCD patients were found and their statistical and clinical significance is being analysed.

**NR2-38**  
**A RETROSPECTIVE STUDY OF ORAL VERSUS LONG-ACTING INJECTABLE NALTREXONE FOR TREATMENT OF ALCOHOL DEPENDENCE IN PATIENTS AT THE RALPH H. JOHNSON VA**

*Chair: Todd Magro M.D.; Author(s): Thomas Lewis*

**SUMMARY:**

Both long-acting monthly injectable and daily oral naltrexone are FDA-approved for treatment of alcohol dependence. Injectable naltrexone is thought to improve compliance and have greater efficacy, but there are no trials comparing the two. This retrospective study compares 93 veterans who received either oral or long-acting injectable naltrexone for treatment of alcohol dependence at the Ralph H. Johnson VA. The computerized records of 45 veterans treated with long-acting injectable naltrexone and 48 treated with daily oral naltrexone were reviewed. We recorded demographic data and several other data points. We then analyzed the data to determine if differences existed in the oral and injectable groups in length of time of treatment with naltrexone or number of 30-day prescriptions filled by the patient. This study is limited by its retrospective nature but can provide insight into outcomes at a high-volume treatment site and also guide future research.

**NR2-39**  
**A NOVEL APPROACH TO INDIVIDUALIZED TREATMENT IN PSYCHIATRY: USE OF NEUROIMAGING TO PREDICT EFFICACY AND TOLERABILITY OF ECT TREATMENT FOR DEPRESSION**

*Chair: Manjola Ujkaj M.D.; Author(s): Donald A. Davidoff, Ph.D., J. Eric Jensen, Ph.D., Stephen J. Seiner, M.D., Scott E. Lukas, Ph.D.*

**SUMMARY:**

Introduction: Treatment-resistant depression (TRD)

represents an additional major problem to the depressive illness itself with an increase in utilization of medical and mental health services, pharmacotherapy use, total health care costs, personal suffering, and suicide risk. Electroconvulsive therapy (ECT) continues to be the most effective treatment for TRD, yet its use is limited by existing stigma, the potential for cognitive side effects and lack of knowledge about the neurobiological mechanism underlying ECT. Neurometabolite changes associated with ECT use have long been a major focus of research, but only recent advances in neuroimaging such as proton magnetic resonances spectroscopic imaging (1H-MRSI) have allowed for in vivo assessments, albeit with limited results. Objectives: This study aims at using in vivo 1H-MRSI to investigate the hippocampal metabolic and volume changes induced by ECT in TRD patients and its correlation with treatment efficacy and safety. A better understanding of the underlying neurobiological effects of ECT in TRD could lead to use of spectroscopy for the identification of brain biomarkers as predictors of ECT treatment outcome in routine clinical practice. In the larger context, use of these biomarkers could provide a helpful tool for an earlier identification of ECT responders, thus anticipating ECT treatment as per FDA guidelines, rather than delaying it despite repeated pharmacological failures. This means that more patients will achieve response and remission with less of the trial-and-error approach that currently accompanies ECT treatment. Design: We will compare 4Tesla 1H-MRSI hippocampal findings in 15 TRD patients receiving ECT and 15 age/gender matched healthy controls, age 30-65 year old, men and women. The first part of the project involves four visits and three scans at baseline (pre-ECT), at 12 weeks (after acute ECT) and 16 weeks (continuation ECT) for all subjects. In the second part of the project only TRD subjects will be followed-up at 6 and 12 months to assess for changes at the end of continuation ECT and to compare those who continue maintenance ECT versus those who do not. The 1H-MRSI will measure in vivo levels of GABA, glutamate, glutamine, N-acetyl aspartate (NAA), and anatomical volume in both hippocampi. In addition, psychiatric and cognitive ratings will assess for efficacy and tolerability of ECT in TRD. Analysis plan: Baseline differences in neurometabolites between TRD patients and controls, within-subject changes in TRD relative to controls, associations between baseline clinical and cognitive ratings and clinical and cognitive changes with metabolite changes in TRD at all time points. We hope that that these biomarkers will predict response/tolerability to acute ECT as well the need for use of prophylactic maintenance ECT on the long term.

NR2-40

## DEVELOPMENT AND VALIDATION OF A SOCIAL COGNITIVE THEORY-BASED MEASURE FOR INTENTION TO ADHERE TO HIV TREATMENT

*Chair: Andrea Nelsen M.D.; Author(s): Barbara W. Trautner, M.D., Ph.D. Nancy J. Petersen, Ph.D. Maria Rodriguez-Barradas, M.D. Sunita Gupta, M.D. Thomas P. Giordano, M.D., M.P.H. Aanand D. Naik, M.D.*

### SUMMARY:

An increasing number of recent studies have used behavioral science concepts to evaluate treatment adherence behaviors of patients with chronic illnesses. Validated models such as the Health Action Process Approach (HAPA) have been used to predict a wide variety of health-related behaviors and to identify motivational factors that can serve as targets for intervention. We present here the development and validation of a cognitive theory informed scale to measure patients' behavioral intention to adhere to HIV care. Adherence to HIV care is a concept that includes attendance at appointments and adherence to HAART regimens. These two components have each been shown to have an independent association with long-term health care outcomes. Survey items were chosen to reflect behavioral intention as defined by HAPA. Items reflecting self-reported HIV knowledge were also included after expert panel review. The survey was completed by 287 patients in both English and Spanish at two urban HIV clinics. Factor analysis resulted in the retention and validation of two separate domains, knowledge and intention, based on Scree plot analysis of Eigenvalues. Retention of questions with factor loadings greater than 0.4 yielded 4 questions related to knowledge and 10 questions related to intention. The survey was found to have good internal consistency for knowledge (Cronbach's alpha = .83) and for intention (Cronbach's alpha = .81) factors. In separate multivariate analysis, intention was associated with HIV viral suppression, or having an HIV viral load < 400 copies/mL, (odds ratio (OR) = 1.75, 95% confidence interval (CI) = 1.00 – 3.07). In a separate multivariate analysis, knowledge was also associated with HIV suppression (odds ratio (OR) = 1.55, 95% confidence interval (CI) = 1.09 – 2.12) with viral suppression of HIV. The resulting scale provides a useful instrument to measure treatment-seeking behavioral intention in patients with HIV.

## NR2-41 LONGITUDINAL STUDY OF SYMPTOM REMISSION IN OLDER ADULTS WITH SCHIZOPHRENIA: A 4.5 YEAR FOLLOW-UP STUDY

*Chair: Mudassar Iqbal M.D.; Author(s): Imran Khan, M.D., Mirnova Ceide, M.D., Carl Cohen, M.D.*

#### SUMMARY:

**Rationale:** Although prior studies found that approximately half of older community-dwelling adults with schizophrenia were in symptomatic remission, these findings have been based on cross-sectional data. This study describes changes in symptom remission rates and predictors of remission on 4.5 year follow-up. **Methods:** The study consisted of 250 persons with schizophrenia spectrum disorders aged 55 and over living in NYC who developed the disorder prior to age 45. Data on 104 follow-up interviews is presented here. Mean follow-up was 52 months (range: 12 to 116 months); mean age was 60.5 years +/- 5.2 years, 55% were male, and 55% were white. The Remission in Schizophrenia Working Group criteria (<4 on eight selected positive, negative, and general items of the PANSS) was used with an additional criteria of having no history of hospitalization within the previous year in order to qualify for remission status. **Results:** On follow-up, there was a non-significant decline in the percentages meeting our remission criteria (49% baseline; 40% follow-up). Twenty-five percent of subjects met remission criteria at both assessments, 35% did not meet remission criteria at either assessment, 25% went from meeting remission criteria at T1 to not meeting remission criteria at T2, and 16% went from not meeting remission criteria at T1 to meeting remission criteria at T2. In logistic regression, there were two significant baseline predictors of overall remission at T2: community integration and number of entitlements. **Conclusion:** The longitudinal data indicated that overall symptom outcome differs considerably from what was suggested by initial cross-sectional data, and suggests considerable flux in symptoms in later life. Only one-fourth of the subjects attained permanent remission and one-third never attained remission. The largest group fluctuated between outcome categories. Two social factors—community integration and number of entitlements— had significant impact on remission rates at follow-up. This indicates the clinical importance of building social supports and providing an economic safety net for older adults with schizophrenia.

#### NR2-42

### SEROTONIN TRANSPORTER GENE-LINKED POLYMORPHIC REGION(5HTTLPR) AND BODY MASS INDEX IN A PSYCHIATRIC POPULATION

*Chair: Brooke Rosen B.A.; Author(s): Gen Shinozaki, M.D.; Yingying Kumar, BS; James Rundell, M.D.; David Mrazek,*

*M.D.; Simon Kung, M.D.*

#### SUMMARY:

**Background** The role of the serotonin transporter-linked polymorphic region (5HTTLPR) of the serotonin transporter gene (SLC6A4) in numerous psychiatric illnesses has been studied extensively.<sup>1</sup> Additionally, serotonergic function regulates many central nervous system processes, including appetite and feeding behaviors. In particular, 5HTTLPR variation is found to be associated with body mass index (BMI) values and, correspondingly, with obesity risk among the general population.<sup>2,3</sup> Given the strong implication of 5HTTLPR in psychiatric disorders, we hypothesized that this polymorphism exerts differential effects on BMI among psychiatric patients. Therefore, we sought to test the relationship between BMI and 5HTTLPR genotype in a sample of psychiatric patient population. **Methods** A retrospective chart review identified 933 patients (716 inpatients and 217 outpatients) who received psychiatric care at Mayo Clinic between 2006 and 2011 and had 5HTTLPR genotype data. BMI data were obtained at the time of genotype testing, and associations between 5HTTLPR genotype and BMI and obesity (BMI > 30) were analyzed. **Results** A significant main effect of genotype on BMI was identified in females ( $F(2, 642) = 3.02, p = .049$ ), which was primarily driven by the finding that patients homozygous for the long allele (l/l) had significantly higher average BMIs than heterozygous (s/l) patients ( $29.07 \pm 0.53 \text{ kg/m}^2$  vs.  $27.52 \pm 0.44 \text{ kg/m}^2$ ;  $p = .024$ ). Additionally in the female group, the inpatients had a significantly higher average BMI than outpatients ( $28.64 \pm 0.35 \text{ kg/m}^2$  vs.  $27.13 \pm 0.64 \text{ kg/m}^2$ ) (two-sample  $t(283.07) = 2.24, p = .026$ ). We also found that, regardless of gender, age was significantly associated with BMI ( $F(1, 928) = 4.17, p = .041$ ). The genotype distributions (s/s, s/l, and l/l) did not differ as a function of gender, inpatient vs. outpatient status, or obese vs. non-obese patients. **Discussion** Our finding that homozygosity for the long allele of 5HTTLPR is associated with higher BMI in females contrasts with that of prior studies, in which the short allele of 5HTTLPR confers a greater risk of obesity.<sup>2,3</sup> However, our study differs critically from previous research in that we examined the association in a psychiatric population with different demographic characteristics than preceding studies. 1. Serretti A, Calati R, Mandelli L, De Ronchi D. Serotonin transporter gene variants and behavior: a comprehensive review. *Curr Drug Targets*. 2006 Dec;7(12):1659-69. 2. Fuemmeler BF, Agurs-Collins TD, McClernon FJ, et al. Genes implicated in serotonergic and dopaminergic functioning predict BMI categories. *Obesity (Silver Spring)* 2008;16:348-55. 3. Sookoian S, Gianotti TF, Gemma C, Burgueno A, Pirola CJ. Contribution of the

functional 5-HTTLPR variant of the SLC6A4 gene to obesity risk in male adults. *Obesity* (Silver Spring) 2008;16:488–91.

#### NR2-43

### IDENTIFICATION OF PERSONALITY DISORDER TRAITS AND TENDENCIES FOR BETTER CLINICAL DIRECTION TO TREATMENT

*Chair: Yakir Vaks M.D.; Author(s): Jenilee Generalla MSIV, Trang Son MSIV, Gulam Noorani M.D., Gayane Begoyan M.D.*

#### SUMMARY:

Background: Current assessment of personality disorders (PD) is clinically inefficient and time consuming. Thus, PDs remain under-diagnosed, and may subsequently influence the prognosis, prevention, and treatment of patients with comorbid Axis I disorders. AIM: To develop a clinically efficient screen usable with both the clinician's current categorical approach and DSM-V's projected direction towards a more dimensional approach to diagnosis of PD. In addition, utilizing the screen to demonstrate self-behavioral modification as a patient transits from a hospitalized inpatient (IP), to a continually treated outpatient (OP), to a fully remitted individual. Methods: Participants were selected from a non-random sample of both OP and IP units within our community hospital. The screening questionnaire was derived from, and meant to represent, specific trait criteria for each PD as outlined by the DSM-IV-TR. IP, OP, and control subjects were compared for having met at least one PD tendency, and further compared for having at least one PD tendency to have met sufficient criteria to provisionally diagnose Obsessive-Compulsive PD (OCPD), using one-way Analysis of Variance (ANOVA). Validity was preliminarily approached by a detailed examination of 3 OPs with clinical baseline diagnoses, SCID II interview, and our screen. Results: Upon examination of having met at least one PD tendency, IP (91%) > OP (74%) > control group (43%), and ANOVA analysis found to have significant differences at alpha level=0.05. Further assessment for OCPD tendencies found IP (46%) < OP (59%) < controls (76%), and ANOVA analysis found to have significant differences at alpha level 0.05. Upon examination of 3 OPs, general agreement to diagnosis was observed comparing assessments of established baseline clinical diagnosis, SCID II interview, and our screen. Conclusion: Our screening tool is proposed to assess a patient's personality functioning at the time of assessment. The decreasing trend of having met at least one PD tendency for a provisional diagnosis was observed between IP to OP to control groups. This

supports the flexibility and fluidity of PDs as a patient transits from IP to OP to full remission of symptoms. Furthermore, by adopting the defense mechanism of sublimation, we explain the transit of general PD tendencies as redirected towards OCPD tendencies, implying there is a higher level of social functioning with regards to OCPD in the general population. This self-adaptation to sublimate impulsive cognition to compulsive behaviors embedded within OCPD traits is compatible with DSM-V's projected dimensional approach. By identifying traits as either cognitive or behavioral in nature, and recognizing cognitive traits are more difficult to restructure than behavioral traits, future aims for CBT treatment may be tailored to yield an improved therapeutic alliance.

#### NR2-44

### IS IT ETHICAL NOT TO PRESCRIBE PLACEBO? THE PATIENT'S PERSPECTIVE ON THE USAGE OF PLACEBO FOR THE TREATMENT OF DEPRESSION: A COMPARATIVE STUDY

*Chair: Kfir Feffer M.D.; Author(s): Uri Nirzan M.D. Shmuel Fennig M.D. Gideon Beker MA*

#### SUMMARY:

Introduction: The current stands of the medical establishment exclude usage of placebo in the clinical setting on ethical grounds. No attempt has been made to clarify the viewpoint of the psychiatric patient regarding the matter. Objective: To compare the viewpoint of healthy subjects to that of patients who suffered from depressive episode. Aims: 1) Investigate the willingness of subjects in both groups to receive placebo for the treatment of depression, and 2) compare both groups' views regarding the ethical aspect of placebo usage (e.g. doctor-patient relationship, patient's autonomy, etc.). Method: We enrolled 81 patients and 107 healthy subjects. Patients were recruited from an out-patient clinic and were diagnosed, in the past or present, as suffering from a depressive episode. All subjects were briefed thoroughly about the efficacy, potential benefits and limitations of placebo in treating depression and then completed a self-report questionnaire. Results: 64% of the patients (N=50) expressed consent to use placebo in case they suffer again from depressive symptoms, compared to 79% (N=85) of healthy subjects (p>0.05). In both groups over 70% of the subjects do not perceive prescribing placebo as a deceit or as an act that diminishes the patients' autonomy (p<0.05). Conclusions: The majority of patients agreed to receive placebo medication as a first line treatment, and do not feel that it will negatively affect their sense of autonomy or doctor-patient relationship. These findings question

some of the ethical justification of excluding placebo from the clinical practice and call for further discussion in the subject.

**NR2-45**  
**THE RELATIONSHIP BETWEEN COGNITIVE DECLINE ELDERLY PEOPLE AND BLOOD METAL LEVELS: A SYSTEMATIC REVIEW**

*Chair: Lee Sangkyung M.D.; Author(s): Eun Song Woo, M.D., Yun Hwan Lee, M.D., Ph.D., Jun Hyun Park, M.D., Dong Woo Lee, M.D., Ph.D.*

**SUMMARY:**

Objective: There have been several previous studies that the pathology of Alzheimer's disease(AD) might be in part caused or exacerbated by metals. But inconsistent results are often seen in evaluation of levels of metals in Alzheimer's disease patient's blood and control group. So, we conducted a systematic review using a comprehensive search strategy to find out whether there is significant difference between cognitive decline elderly people and normal control group. Method Studies were searched in Pubmed, CINAHL and EMBASE with predefined words according to MeSH and purpose of this study. 996 studies were selected as primary screening, and two reviewers extracted relevant data independent of each other. 172 studies fulfilled the inclusion criteria. 32 studies about aluminum, copper, lead, mercury, cadmium finally selected. The Newcastle-Ottawa Scale (NOS) was used for assessing the quality of studies. To synthesize the results of this study, summarized table was made. Result In most studies, blood levels of mercury were high in cognitive decline group. But the majority study shows lead was not that different between cognitive decline group and control group. Measurements of other metal levels in whole blood, plasma, serum were inconsistent. However, there are not enough evidences to generalize with just number of studies since the studies have various degrees of validity. Conclusion There is lack of evidences, till now, to use blood levels of metals as diagnostic purpose or predicting prognosis. Further studies which are supplemented limitations of previous studies are needed. Key words: Alzheimer's disease, Cognitive decline, Metals, Systematic review

**NR2-46**  
**EEG AND POWER SPECTRAL DENSITY IN FIRST EPISODE MANIA: COMPARING WITH REMISSION**

*Chair: Sermin Kesebir M.D.; Author(s): Sertac Guven, M.D., Murat Demirev, Mustafa Bilici, M.D..*

**SUMMARY:**

Objective: The aim of this study is to investigate and compare the EEG findings and the power spectral density (PSD) of the manic state (before the treatment) and remission in first episode bipolar patients. Method: Patients diagnosed with bipolar disorder first episode mania according to the DSM-IV-TR (n= 50) were investigated. Patients were evaluated with SCID-I, SKIP-TURK and YMRS. The EEG records was performed. The (PSD) of the EEG signal provides information on the power per unit frequency of the EEG waves in the frequency range defined in decibel microvolts per Hz. Results: Abnormal EEG during manic state more frequent than the remission, at a rate of 20%. Abnormal EEG is more frequent in females (p= 0.001). According to regression analysis, childhood trauma has been identified as a predictor of the EEG abnormalities in first episode bipolar patients (OR: 10.8, CI 95% 1.8-4.9) . Peak power values detected in the FP2F4 and F7T3 were found to be higher in the mania than remission (p= 0.027 and 0.033). It was found that the EEG abnormality in 6 out of 10 patients with abnormal EEGs during the episode period improved during the remission abnormality of the EEG in 4 patients continued in remission. Peak power values detected in the T5O1 and T3T5 were found to be higher in the abnormal EEG than normal EEG in the remission (p= 0.019 and 0.04). Conclusion: In bipolar disorder EEG abnormality is present from the beginning of the disease onwards and is specific to each period of the illness.

**NR2-47**  
**ADVERSE PSYCHIATRIC EVENTS ASSOCIATED WITH LEVETIRACETAM: AN ANALYSIS**

*Chair: Olufemi Ogundeji M.D.; Author(s): Nivedita Mathur M.D., Atul Kalanuria M.D., and Sunil Verma M.D.*

**SUMMARY:**

Background: Levetiracetam (LEV), is an antiepileptic drug that is used for multiple types of seizure disorders in adults and children. It has been reported to cause behavioral disturbances, for which it has a warning from FDA. Objectives: This meta-analysis was undertaken to identify reported adverse psychiatric events associated with LEV. Design: MEDLINE search and review of bibliographies were performed to identify randomized controlled trials and other reports for adverse psychiatric events associated with LEV, using the key words psychosis, depression, agitation, and hostility. The studies analyzed were case reports, open-label studies, and randomized controlled trials. Only studies in which LEV was used to treat epilepsy and in which tolerability

was reported were selected. Result: 1457 studies on LEV was found of which 59 were selected for analysis, after the exclusion criteria were applied. These reports gave data on a total of 5812 patients (928 children and 4884 adults). Of the 59 reports, 9 were case reports; the others were randomized controlled trials, open-label studies, and retrospective chart reviews. Of the 9 case reports, 6 were reports of children aged 5-17 years. The case reports focused on unusual presentations of psychosis including catatonia secondary to LEV. Among the studies reporting adverse psychiatric events, 6 cases (0.65%) described psychosis in children and 26 cases (0.53%) described psychosis in adults. Depression was reported in 12 (1.3%) cases describing children and in 119 (2.43%) cases describing adults. The major difference was in the number of cases reporting agitation and hostility 160 (17.25%) in children compared to 216 (4.42%) in adults. Not all studies provided information on gender distribution, but when the information was reported, the trend shows a higher prevalence of adverse psychiatric events in males. Conclusions: The rates of psychiatric disorders in patients with epilepsy vary tremendously from 19% in population-based studies to 80% in neurosurgical patients who have epilepsy, with mood disorders being the most common psychiatric condition. The analysis suggests that the overall prevalence of adverse psychiatric events is 9.26%, with a much higher prevalence in children compared with adults (19.2% compared with 7.3%). It is important to recognize that LEV can increase behavioral disturbances in patients, particularly in children with a history of psychiatric illness.

**NR2-48**  
**LONG RANGE FRONTAL/POSTERIOR**  
**PHASE SYNCHRONIZATION DURING**  
**REMEMBERED PURSUIT TASK IS IMPAIRED**  
**IN SCHIZOPHRENIA**

*Chair: Nithin Krishna M.D.; Author(s): Elliot Hong, Hugh O'Neill, Eva Sanchez, and Gunvant K. Thaker*

**SUMMARY:**

Background: Smooth pursuit eye movement (SPEM) a unique neurophysiological measure. Motion of a target falls on the retina activating in the retinal ganglion cells that relays to the mediotemporal cortex (MT). Once the eye catches up with the target, matching its speed, the motion of the target image on the retina is near zero. To maintain accurate pursuit, the system now generates predictive eye velocity using an internal representation of the target velocity, considered to be derived from the efference copy of the motor command and/or a memory trace of the previous motion. Frontal eye fields (FEF) play a role in driving pursuit initiation and eye

acceleration. In addition, FEF is a likely source of the efference copy relayed to the medial superior temporal (MST) cortex where it is integrated with the visual sensory input to form a motion percept. Both motion perception and SPEM maintenance are abnormal in schizophrenia, which could be a consequence of poor functional connectivity between FEF and MT/MST regions. Hypothesis tested examining long-range phase synchronization between frontal and posterior Electroencephalography (EEG) electrodes. Methods: Schizophrenia (SCZ=21) and healthy control (HC=18) participants performed a remembered pursuit task; the same target velocity was presented in quick sequence within a single trial. EEG recorded and phase synchronization between frontal and posterior electrodes were examined. The task is described in detail in a study described by Avila et al 2006. Trials consisted of 3 identical, sinusoidal moving targets (peak speed of 35 deg/sec) presented 1-2 seconds apart, each preceded by a 25 msec, 72 db audio cue (500 Hz). Results: HC showed significantly more improvement in SPEM response to repeated target motion than SCZ. Frontal/posterior phase synchronization increased in HC during the 3rd compared to the 1st target presentation, but not in patients suggesting abnormal functional connectivity. Correlations between the functional connectivity and eye velocity measures suggested that this relationship was inhibitory in the presence of maladaptive anticipatory SPEM prior to target motion whereas there was a facilitatory effect after the onset of target motion. Higher synchronization predicted higher predictive pursuit and higher ratings of enduring psychosis and hallucinations. Conclusions: Poor communication between FEF and MT/MST regions contributes to abnormal SPEM in SCZ. There was an overall improvement in the smooth pursuit response on repeated presentation, however robust in healthy control subjects. Poor performance in SCZ could be due to poor functional connectivity between brain regions used for the pursuit response. SCZ group had normal activation in the frontal cortical region during initial motion processing. However, during the pursuit response to repeated target motion, patients show significantly poorer frontal/posterior functional connectivity than HC.

**NR2-49**  
**THE CHANGE OF METABOLIC PARAMETERS**  
**AND PANSS SCORE OF PATIENTS WITH**  
**SCHIZOPHRENIA 8 WEEKS AFTER**  
**SWITCHING TO PALIPERIDONE**

*Chair: Jeong Tae-Yeong M.D.; Author(s): Young-Min Choi, M.D., Ph.D., Bongseog Kim, M.D., Ph.D., Dong-Woo Lee, M.D., Ph.D., Min-Suk Gim, M.D., Ph.D.*

**SUMMARY:**

**Purpose :** The purpose of this study is to examine the change of metabolic parameters and PANSS score 8 weeks after the paliperidone medication in the patients who had regularly taken other atypical antipsychotic drug before switching to paliperidone. **Method :** The changes of body mass index, leptin, lipid level, fasting glucose, and PANSS score of the patients with schizophrenia switched from other atypical antipsychotic drug to paliperidone were measured. Then, we compared them with results from the patients who had been antipsychotic drug naive before taking paliperidone. **Results :** In the case of the group(9 people) who began taking paliperidone and had been antipsychotic drug naive, there was no significant change of metabolic parameters with the significant decrease of PANSS score in all the factors. Meanwhile, in the case of the group(13 people) who switched from other atypical antipsychotic drug to paliperidone, body weight, body mass index and fasting glucose significantly increased while PANSS scores in all the factors significantly decreased. By the comparison of two groups, there was no significant difference in the change of metabolic parameters and PANSS score before and after taking paliperidone. **Conclusion :** The paliperidone medication of patients with schizophrenia who didn't take antipsychotic drug or had difficulty in continuing to take other atypical antipsychotic drug will bring the improvement of psychopathic state for them. But, if they took other atypical antipsychotic drug before, they should be careful with the probability that weight gain or fasting glucose will raise in a short period of time in the case of switching to paliperidone. **Key Words :** paliperidone, metabolic parameter, PANSS, schizophrenia

**NR2-50****OPIOID'S INDUCED  
LEUCOENCEPHALOPATHY**

*Chair: Kasia Rothenberg M.D.; Author(s): Jeanne Lackamp, Joseph Locala*

**SUMMARY:**

Opioid's related toxic encephalopathy is described associated with, oxycodone methadone, and after heroin intoxication. It's character and dynamics however is not well explained. Imaging of such an encephalopathy is not well documented as well We describe the clinical and radiologic findings of a 34-year-old man with heroin overdose who developed multifocal leucoencephalopathy with nuclei caudati and putamina involvement as well as severe cerebellitis Brain MRI showed a non-vascular distribution of diffusion positive lesions in both

cerebellar hemispheres and putamina and nuclei caudati with preserved cerebral perfusion, suggesting an inflammatory process. The occurrence of this rare toxic encephalopathy may be related to distribution patterns of opioids' receptors subtypes, genetic susceptibility, sensitization, and other specific comorbidities.

**NR2-51****OUTCOMES OF 17 YEARS OF A STRUCTURED  
REHABILITATION PROGRAM IN A HALF-WAY  
HOUSE**

*Chair: Pablo Gabay M.D.; Author(s): Fernández Bruno, Mónica D., M.D. Ortega, M. Soledad, Occupational Therapist*

**SUMMARY:**

We present the outcomes of 17 years of a structured rehabilitation program that has been offered to chronic psychiatric patients referred to a specialist half-way house in Buenos Aires, the ultimate goal of which is social reintegration, or at least some degree of rehabilitation. Even in the largest cities and despite the approval of the new mental health legislation, the overall state of psychiatric rehabilitation services in Argentina remains unsatisfactory. However, there are many rehabilitation programs that have been running in Buenos Aires and other parts of the country, some of which for as long as 40 years. Adopting the premise that rehabilitation tools must be culturally sensitive and adjusted to local needs, the outcomes of our program show that it can successfully prevent relapses and re-hospitalizations. The program can also enhance the remaining skills of chronically ill individuals, strengthen family bonds, and effectively promote the reintegration of people with severe mental illness (SMI) into the community, thereby decreasing health and social costs to society. The success of the program is associated with the detailed assessment of candidates, clearly defined therapeutic boundaries, adequate pharmacological treatment, and 'experience-based learning' in a structured and homely environment.

**NR2-52****META-ANALYSIS OF EFFICACY OF  
MIRTAZAPINE AS AN ADJUNCTIVE  
TREATMENT FOR SCHIZOPHRENIA**

*Chair: Carolina Vidal M.D.; Author(s): Carla Reese, M.D., MS Seth Himelboch, M.D., M.P.H. Josh Chiapelli, M.D. Pamela Ramos, M.D.*

**SUMMARY:**

**Context:** Despite advances made in treating the positive symptoms of schizophrenia, negative symptoms remain

frequently untreated. Using adjunctive treatment in order to treat negative symptoms is an area of great clinical interest. Objective: To assess the efficacy of Mirtazapine as an adjunctive treatment of negative symptoms in patients with chronic schizophrenia. Data Sources: A systematic literature review of articles in English and Spanish was conducted in October 2010 by searching PubMed, the Cochrane Library, the Clinical Trial Registry of the NIH, and SIGLE (System for Grey Literature in Europe). Free text search terms for PubMed were “schizophrenia,” “psychosis” or “psychotic disorders” and “mirtazapine.” Publication date was not a limitation. Study Selection: Seven studies were identified where schizophrenia or schizoaffective disorder subjects received adjunctive treatment with Mirtazapine. One study was excluded as it did not use the PANSS scale as a measure. A total of four studies were included in the final meta-analysis after removing duplicates. The two authors independently screened all articles for eligibility. Results: The overall analysis showed an effect size of 1.113(-0.045-2.271), difference that was close to significance ( $p=0.059$ ). Data from the negative symptoms subscale of the PANSS from 149 subjects was used in a forest plot to illustrate the relative strength of treatment effects. Two studies showed statistically significant results. The variation in S.M.D. attributable to heterogeneity was 90.1%, indicating a high degree of heterogeneity. Data was stratified to minimize the degree of clinical heterogeneity, grouping the studies that added Mirtazapine to FGAs and the studies that added Mirtazapine to SGAs. After stratification, the I-squared continued to be high in both groups. Conclusions: Currently there is not sufficient data supporting a statistically significant effect on negative symptoms by adding Mirtazapine to first or second generation antipsychotics. Additional randomized controlled trials are needed to confirm this hypothesis.

### NR2-53 A COMPARISON OF INFLAMMATORY MARKERS IN DEPRESSED AND NON-DEPRESSED SMOKERS

*Chair: Sandra Nunes M.D.; Author(s): Juliana Brum Moraes*

#### SUMMARY:

Introduction: Both smoking and depression have been associated with increased inflammatory markers. As there are few studies on inflammatory markers that distinguish between depressed and non-depressed smokers, it is unclear if there is a cumulative impact of these mediators of inflammation. The aim of this study was to investigate inflammatory markers in tobacco smokers, and compare depressed and non-depressed

smokers. Methods: Smokers ( $n=155$ ) were recruited from the Cigarette Smoking Cessation Service, Londrina. Mental health status was assessed using the Diagnostic Interview for Research, in accordance with the International Classification of the Disorders- 10th (ICD-10). Demographic information was collected by self-report questionnaire, and the Fagerström Test for Nicotine Dependence (FTND) was administered. Blood specimens were simultaneously collected and measured for C - reactive protein (hs-CRP), tumor necrosis factor alpha (TNF- $\alpha$ ), and interleukin- 6 (IL-6). Results: Depressed smokers had significantly higher levels of hs-CRP ( $p=0.05$ ), IL-6 ( $p=0.039$ ), and TNF- $\alpha$  ( $p=0.021$ ) compared to non-depressed smokers. Depressed smokers were also significantly more likely than non-depressed smokers to have been hospitalized in the previous month ( $p<0.032$ ), to suffer from cardiovascular disease ( $p<0.001$ ) and lung disease ( $p<0.003$ ), and to have more work related disability ( $p=0.001$ ). Conclusion: These findings demonstrate that depressed smokers had higher hs-CRP, IL-6, and TNF- $\alpha$  levels than non-depressed smokers, and had worse physical health outcomes and, greater disability for work. This may have important implications in identifying shared risk pathways for depressive and somatic disorders.

### NR2-54 TOPOGRAPHY OF MOOD SYMPTOMS AND PERSONALITY TRAITS IN MOOD DISORDERS AND CLUSTER B PERSONALITY DISORDERS (PRELIMINARY RESULTS)

*Chair: Sergio Apfebaum M.D.; Author(s): Regalado P+, Herman L\*, Gagliosi P+. CASA de FAMILIA\* Fundación Foro para la Salud Mental*

#### SUMMARY:

Various lines of evidence have established a relationship between Bipolar Disorder and Borderline Personality Disorder. The present study compares mood spectrum and temperamental symptoms, personality traits and clinical characteristics among outpatients ( $n=63$ ) diagnosed with Depression (M.D.  $n=19$ ), Bipolar Disorder (BD  $n=12$ ), Cluster B Personality Disorders (PD-B  $n=15$ ) and comorbidity of BD and PD-B ( $n=17$ ). Diagnoses were evaluated with two semi-structured interviews (MINI and SCID-II) for axis I and axis II disorders respectively, according to DSM-IV standards. Symptoms were assessed with several diagnostic instruments (MOODS- SR, TEMPS-A y IPDE). Differences between groups were explored by conducting analysis of variance with post hoc analysis. Preliminary results show that people diagnosed with bipolar disorder had more manic-like symptoms than people with M.D.D ( $p=0.008$ ), but no significant

difference to people with PD-B ( $p=0,54$ ). Patients with comorbidity diagnosis (BD and PD-B) had higher score on MOODS-AF scale ( $p=0,011$ ), more manic symptoms ( $p = 0,014$ ), and a trend in Depression and Rhythmicity domains with respect to persons with M.D.D. Comorbidity patients scored higher than all other groups in cyclothymic temperament ( $p=0.015$ ). People diagnosed with comorbidity ( $p=0,001$ ) and those with PD-B ( $p= 0,003$ ) had significantly more irritable temperament traits, unlike those with BD alone. The presence of personality disorders contributed to lower scores in global assessment functioning (GAF-DSM IV) and were related to earlier age onset and to a higher number of hospitalizations. Finally, results revealed that comorbidity patients (BD and PD-B) manifest more manic symptoms, pathological personality traits, bipolarity characteristics and temperament traits than the other diagnostic groups. More is discussed on the implications of the preliminary results reported. Future considerations for this study are proposed.

#### NR2-55

### ADJUNCTIVE LISDEXAMFETAMINE DIMESYLATE WITH ANTIPSYCHOTICS: EFFECTS ON NEGATIVE SYMPTOMS OF SCHIZOPHRENIA AND SELF-REPORTED EXECUTIVE FUNCTION

*Chair: Henry Nasrallah M.D.; Author(s): Bryan Dirks, M.D.; Jean-Pierre Lindenmayer, M.D.; Courtney Kirsch, BS; Jianwong Wang, Ph.D.; Steven James, M.D.; Brian Scheckner, Phar M.D.; David P. Walling, Ph.D.; Robert Lasser, M.D.*

#### SUMMARY:

**Objective:** To examine effects on self-reported executive function (EF) of adjunctive lisdexamfetamine dimesylate (LDX), a d-amphetamine prodrug, for treatment of predominant negative symptoms of schizophrenia (NSS) in clinically stable adults on atypical antipsychotics. **Methods:** After 3-wk screening, outpatients with stable schizophrenia ( $=2y$ ) with predominant NSS (Scale for the Assessment of Negative Symptoms [SANS-18; items 1-6, 8-12, 14-16, 18-21] score  $=55$ , score  $=3$  on  $=2$  SANS Global items, Positive and Negative Syndrome Scale [PANSS] positive score  $<20$ ) maintained on antipsychotics ( $=12wk$ ) underwent 10-wk open-label (OL) LDX augmentation (20-70mg/d). Eligible participants (any SANS-18 improvement at wk 10) entered a 4-wk, double-blind, placebo-controlled randomized withdrawal (RW; wk 10-14). Efficacy measures included the SANS-18 (primary). EF was assessed with the Behavior Rating Inventory of Executive Function-Adult version (BRIEF-A). Safety evaluations included treatment-emergent adverse

events (TEAEs). Results: 92 adults received OL LDX; 69 entered RW (LDX,  $n=34$ ; placebo,  $n=35$ ); 13 discontinued during RW (LDX,  $n=7$ ; placebo,  $n=6$ ). At baseline (wk 0), mean (SD) SANS-18 score was 60.2 (4.36). Mean change (95% confidence interval [CI]), in SANS-18 (OL; wk 0-10) was -12.9 ([-15.0, -10.8]; primary endpoint,  $P<.0001$ ). Mean (SD) baseline BRIEF-A Global Executive Composite (GEC) T-score was 60.2 (14.33) and improved at wk 10 by mean change (95% CI) of -3.8 (-6.6, -1.1) ( $P=.0064$ ). Mean change (95% CI) during OL LDX was -3.0 (-5.7, -0.4) for BRIEF-A Behavioral Regulation Index (BRI) and -3.9 (-6.6, -1.2) for Metacognition Index (MI) T-scores ( $P=.0267$  and  $P=.0047$ , respectively). BRIEF-A domains of initiate, shift, self-monitor, plan/organize, working memory, and monitor tasks showed improvement ( $P=.0286$ ) while inhibit, emotional control, and organization of materials did not ( $P=.1611$ ). During RW, no meaningful differences were noted (LDX vs. placebo) in change from randomization baseline to endpoint in SANS-18 scores or BRIEF-A indices or domains. Post hoc analysis showed no meaningful correlation between change in SANS-25 (full SANS scale) total score and BRIEF-A GEC, MI, and BRI ( $r=-0.172$ ,  $-0.194$ , and  $-0.117$ , respectively;  $P=.0772$ ). In the OL phase, TEAEs were reported in 60.9% (56/92) of participants; serious TEAEs in 3.3% (3/92). In the RW phase, TEAEs were reported in 32.4% (11/34) and 20.0% (7/35) of participants taking LDX and placebo, respectively. Conclusion: OL LDX augmentation to stable antipsychotic therapy showed small but significant self-reported improvement in global EF scores as well as in particular domain scores including initiate, shift, and self-monitor. The improvement in certain executive cognitive functions appeared to parallel NSS improvement. This is consistent with the notion that frontal dopamine activity may affect both neurocognition and negative symptoms.

#### NR2-56

### CHANGES IN SYMPTOMS AND FUNCTION OF ADULT ADHD PATIENTS WITH OR WITHOUT CO-MORBID GENERALIZED ANXIETY

*Chair: Sylvia Mousa M.D.*

#### SUMMARY:

**OBJECTIVES:** The main objective is to examine and compare changes in functional impairments in adult ADHD patients with or without Generalized Anxiety Disorder (GAD), treated with stimulants or non-stimulants. **METHOD:** Consenting adult ADHD patients ( $n= 86$ ) participated in this open label naturalistic study. Of the total number ( $n = 64$ ,

75 %) had significant comorbid anxiety symptoms (HAM-A > 7), who failed to respond to 8 week trials of SSRIs, or SNRIs prior to the adjunctive treatment with ADDERALL XR, (MAS-XR) or atomoxetine. Among the GAD-ADHD MAS-XR treated patients, thirty three were switched in the first four weeks to the non-stimulant atomoxetine as an adjunctive to the SSRIs, and SNRIS, and all patients (n=22) without comorbid GAD continued on the MAS-XR as monotherapy. Therefore, there were three treatment groups; the GA-ADHD, MAX-XR treated (n=33, 38%), the GA-ADHD atomoxetine treated (n=31, 36%) and the ADHD, MAX-XR treated groups (n= 22, 26%). The primary outcome measure was the Clinical Global Impression severity subscale (CGI-S). Other scales included; the Sheehan's disability scale, the adult ADHD self report scale (ASRS-v1.1) symptom checklist, and Hamilton anxiety scale (HAM-A). The Canadian Attention Deficit / Hyperactivity Disorder Resource Alliance side effect Scale (CADDRA) was utilized to monitor patients' tolerance to the adjunctive treatment. Baseline measures prior to the treatment with (MAS-XR) and atomoxetine were compared to those at 4, 8, and at 12 weeks of treatment. Monitoring for pulse, blood pressure and weight changes was carried out at baseline and at endpoint. RESULTS: Completed this open label naturalistic study (n=83, 97%) patients. There was significant ( $p > .001$ ) and robust resolution of symptoms of all outcome measures, including the symptoms of anxiety. However there were notable significant differences between the three treated groups. On the primary efficacy measure (CGI) severity subscale the ADHD- MAS-XR treated group was significantly ( $p > .01$ ) more improved at 12 weeks than the GA-ADHD, MAS-XR, and the GA-ADHD, atomoxetine treated groups. The GA-ADHD, MAS-XR treated, and the ADHD MAS-XR treated groups were more improved ( $p < .01$ ) at 12 weeks than the GAD-ADHD atomoxetine treated group on the (ASRS-v1.1) symptom checklist. On the Sheehan's disability scale, the ADHD-MAX-XR treated group was more significantly ( $p < .01$ ) improved at end point than the two groups with GA co-morbidity. There were no significant differences in the total disability and the HAM-A scores between the GAD-MAS-XR treated, and the GA, atomoxetine treated groups. Patients tolerated both MAS-XR and atomoxetine well. Side effects at four weeks were transient and these seemed to disappear at week 12. Only three patients administered atomoxetine discontinued the treatments due to side effects. There were no significant changes in pulse, systolic or diastolic blood pressure, and decrease in weight over 12 weeks were not significant.

SUNDAY MAY 06, 2012

## New Research Young Investigator 1

### NR3-01

#### DEVELOPING THE NORTH DIVISION DEPARTMENT OF PSYCHIATRY AT MONTEFIORE MEDICAL CENTER, BRONX, NY: FROM ACQUISITION TO INTEGRATION

*Chair: Yener Balan M.D.; Author(s): Matthew Schneider, M.D.*

#### SUMMARY:

In 2008, the assets of Our Lady of Mercy Medical Center (OLM) in the Bronx, NY, were acquired and became the fourth hospital within Montefiore Medical Center (MMC) and renamed Montefiore Medical Center – North Division. At the time, this acquisition made MMC a 1,491 bed academic medical center, with over 16,000 associates serving two million people in the community. Every department in MMC merged with their North Division counterparts, to create a seamless delivery of care mirrored on all campuses. The department of psychiatry finalized its merger in the summer of 2011. Planning for the integration of the former OLM department of psychiatry began in 2008, and staff trained at the Moses Division of MMC was placed into leadership positions at that time. Of the 369 inpatient beds acquired from OLM, 43 of them are in the department of psychiatry: 33 of them are acute psychiatric inpatient beds, and 10 are medical stabilization (detoxification) beds. The department also includes a psychiatric consultation service that covers the hospital, including the emergency department, a child outpatient department and a high volume adult outpatient department that includes mental health (MH), Mental Illness and Chemical Addiction (MICA), and Chemical Dependency (CD). This poster discusses the strategies employed in analyzing and transforming an existing department and developing it to meet standards of care of a large academic center. Issues from the mundane to the complex are examined, including the challenges faced among existing staff adapting during the transition to a new administration. In addition to the psychological factors, the financial as well as political aspects involved in the process are discussed.

### NR3-02

#### CANNABIS-INDUCED ATRIAL FIBRILLATION IN A PATIENT WITH TRAUMATIC BRAIN INJURY

*Chair: Lauren Mikesell M.S.; Author(s): Adekola Alao, M.D., MRCPsych, FAPM*

**SUMMARY:**

Case report the patient is a 40-year-old Hispanic man with a history of Post-Traumatic Stress Disorder (PTSD) and Traumatic Brain injury (TBI), which he sustained from three military tours in Iraq and Afghanistan. The patient's PTSD symptoms are being treated with diazepam 5mg po bid as well as remeron 15mg po qhs. He presented to the emergency department complaining of nausea and vomiting that began after ingesting a brownie containing cannabis. His presenting symptoms included diarrhea, diffuse abdominal pain, and chest discomfort. In the course of his emergency department visit, he developed tachycardia in the 140-150s. An EKG revealed atrial fibrillation (AF) with rapid ventricular response, premature ventricular or aberrantly conducted complexes, and nonspecific ST segment and T-wave abnormalities. Urine toxicity was positive for benzodiazepines, cannabinoids, methadone, and opioids. He was administered diltiazem, which resolved his tachycardia and AF. The patient was admitted to the hospital with a diagnosis of AF and gastroenteritis secondary to cannabinoid use. Discussion In recent years, there have been a number of case reports demonstrating an association between marijuana smoking and onset of AF1. The exact mechanism by which marijuana may induce AF remains unclear. Hypotheses focus on the well-documented role of the autonomic nervous system (ANS) in the pathogenesis of AF. Low to moderate levels of delta-9-tetrahydrocannabinol (THC), the bioactive component of marijuana, increases heart rate, blood pressure, and plasma catecholamine levels2. Data suggests these effects are mediated by cannabinoid-1-receptor regulation of the ANS3. Stimulation of the adrenergic system is potentially proarrhythmic as it reduces action potential duration and favors automaticity, triggered activity, and re-entry. The increase in sympathetic tone following marijuana use may contribute to the development of AF, especially in patients with preexisting cardiovascular complications. Conclusion The presence of TBI in this patient may have made him more susceptible to cardiovascular complications. Furthermore, marijuana induces alterations in coronary vasculature that may contribute to the development of AF1. More research is necessary to elucidate the precise mechanism involved in marijuana-induced atrial fibrillation. References 1. Korantzopoulos P, Liu T, Li G, Goudevnos JA. Atrial fibrillation and marijuana smoking. *Int J Clin Pract* 2007; 62: 308-313. 2. Beaconsfield P, Ginsburg J, Rainsbury R. Marijuana smoking: cardiovascular effects in man and possible mechanisms. *N Engl J Med* 1972; 287: 209-12. 3. Huestis MA, Gorelick

DA, Heishman SJ, Preston KL, Nelson RA, Moolchan ET, Frank RA. Blockade of effects of smoked marijuana by the CB1-selective cannabinoid receptor antagonist SR141716. *Arch Gen Psych* 2001; 58: 322-8.

**NR3-03****DO PREMORBID ALCOHOL CHALLENGE RESPONSES PREDICT ALCOHOL DEPENDENCE BY AGE 40?**

*Chair: Syed Karim M.D.*

**SUMMARY:**

Objective: To examine whether premorbid responses to an alcohol challenge test predicted future alcohol dependence. Method: As part of a high risk, longitudinal study of the antecedents of male alcoholism, 75 boys between 19/20 years completed a two-hour alcohol challenge test in a controlled environment (0.5 g/kg of 95% absolute alcohol) as well as a series of interviews before any had developed a problem with alcohol. The challenge test included objective and subjective ratings of the effects of alcohol. At age 30 and/or 40, 65 of these subjects were re-studied with a series of structured interviews administered by a senior psychiatrist who also provided DSM-III-R diagnoses. Fifteen of the 65 (23%) had developed lifetime alcohol dependence. Results: Ratings by the subjects over the two-hour alcohol challenge test failed to predict alcohol dependence. Ratings by an observer suggested that later alcohol dependent subjects were more talkative at the beginning of the session and sleepier at the end compared to those who did not develop alcohol dependence, a direction opposite to that expected. Self-ratings of the degree of intoxication over time did not predict later alcoholic drinking. Subject's estimates of the amount of drinks needed to produce certain alcohol-related effects also did not predict alcohol dependence. Conclusion: Our findings were not consistent with the hypothesis that premorbid low levels of response to alcohol are associated with later alcohol dependence.

**NR3-04****CLOZAPINE AND LITHIUM COMBINATION LEADING TO LITHIUM TOXICITY: A CASE REPORT AND LITERATURE REVIEW**

*Chair: Naveen Yarasi M.D.*

**SUMMARY**

**INTRODUCTION** Combining neuroleptic drugs with lithium can offer a valuable therapeutic contribution to the treatment of schizophrenia and schizoaffective disorder despite the potentially increased risk of side effects. (Cohen and Cohen 1974). Literature shows

vast majority (75-90%) of patients receiving lithium monotherapy become intoxicated at some point during the course of therapy and that more than 50% of the patients on lithium treatment received at least one concomitant antipsychotic medication during the course of their treatment. The neurotoxic reaction between lithium and any antipsychotic drugs is a rare and mostly reversible event. Although adverse reactions with lithium and haldol predominate, other antipsychotic drugs has been implicated in increased lithium toxicity, including thioridazine, fluphenazine, chlorpromazine, clozapine, and risperidone. Several case reports described neurotoxic side effects in the course of combined clozapine and lithium treatment without an apparent effect on the pharmacokinetic disposition of lithium. However we report a case where lithium and clozapine combination have increased serum lithium levels resulting in neurotoxicity. **CASE PRESENTATION** Patient is a 23 year old female with Paranoid Schizophrenia, who was initially treated with lithium carbonate 900mg/day with a lithium level of 0.6mEq/liter. Clozapine was started at 25mg qhs after a trial of risperidone and aripiprazole and was gradually increased to 200mg by seven days. On day 8 of combined lithium and clozapine treatment, she developed tremor, nausea, vomiting, myoclonic jerks, shuffling, stumbling gait, confusion, drooling, perioral dyskinesia, and dysarthric speech. She also had muscle stiffness and some signs of cog wheeling & rigidity, which were resolved with a shot of benzotropine. Vital signs were normal except for tachycardia. Stat EKG showed sinus tachycardia. CBC and CMP were unremarkable. Lithium level was interestingly high at 1.5mEq/l. No other medication changes were made apart from addition of clozapine. No signs of dehydration were present. The neurologic symptoms completely resolved after the discontinuation of lithium. **DISCUSSION** Literature shows that some drugs, such as antidepressant and neuroleptic agents, increase lithium toxicity without changing renal clearance, presumably by increasing intracellular concentrations. But our patient interestingly had increased serum lithium level and the mechanism of which was unknown. Although the development of neurologic symptoms in our patient can be explained by the lithium toxicity, the possible explanation for increased serum lithium level could not be found As a conclusion since there is a possibility of a rare but serious interaction with lithium and clozapine, clinicians should be aware of the risk of concomitant administration of lithium and clozapine. So we suggest the need for close and regular clinical observations and serum concentration monitoring to avoid any unexpected complications.

**NR3-05****DRUG ADDICTION IN SICKLE CELL DISEASE**

*Chair: Adekola Alao M.D.; Author(s): Jennifer Selvarajah, M.D.*

**SUMMARY:**

Sickle Cell Disease (SCD) is a genetic disorder of the blood that most often affects people of African, Middle Eastern, Mediterranean, and Asian ancestry. In individuals homozygous for this trait, over 50% of the hemoglobin is hemoglobin S. Approximately one out of 600 African-Americans has SCD. This report will describe the case of a 27 year old African American who expressed suicidal ideation after his pain was not adequately controlled in the emergency room. While this behavior from patients should not be encouraged, patients with documented SCD in bone pain crisis should be adequately treated. In persons with SCD, hemoglobin S predominates. Unlike normal hemoglobin (hemoglobin A), hemoglobin S forms polymers when the oxygen supply is reduced in any way. The rapidity of polymerization depends on the concentration of hemoglobin S, which explains why heterozygous carriers are essentially asymptomatic. Affected erythrocytes are rigid, crescent (or sickle) shaped, and fragile; they are also more adhesive than normal. By blocking small blood vessels, these abnormal cells compromise blood supply to tissues and bones, leading to vaso-occlusive crises. There has been widespread speculation that patients with SCD may become drug dependent if their painful crisis is treated with narcotics. However, there has been no scientific evidence to support this assertion. Paradoxically, individuals suffering from sickle cell disease who are not adequately treated may develop an addiction to narcotics due to self-medication to treat their pain. Conclusion patients with documented SCD in bone pain crisis should be treated aggressively. It is better to error on the side of treatment than risk negligence and sub-standard care.

**NR3-06****TOBACCO ABUSE AND DEPENDENCE, THE INVISIBLE DIAGNOSES**

*Chair: Yakir Vaks M.D.*

**SUMMARY:**

Background: It has been well documented that psychiatric patients are more likely to be smokers than the general population. Smoking rates among psychiatric patients tend to be two to four times the rate for the general population. As a group, individuals with psychiatric disorders are estimated to account for 44 percent of the U.S. tobacco market. The detrimental effects on health associated with tobacco smoking are

also well documented. Cigarette smoking is the leading preventable cause of death and disability in the United States, with approximately 440,000 deaths each year, or one in five of all deaths, attributable to tobacco use. Given the complicated relationship between mental illness and smoking, integration of cessation efforts into psychiatric care is recommended. The American Psychiatric Association (APA) recommends that psychiatrist assess the smoking status of all patients, including readiness to quit, level of nicotine dependence, and previous quitting history. Despite this, there is a lack of research aimed at eliminating tobacco related health risks inherent in tobacco use in this population. My study examines the possibility that the documentation of actual diagnosis of tobacco abuse or dependence is one possible reason for this lack. Methods: The sample was drawn from an adult inpatient psychiatric service in a community psychiatric hospital in New Jersey. 500 unique patient charts of patients admitted from July 2009 to July 2010 were selected randomly for review. Exclusion criteria used included: no tobacco use history, age below 18 years old or over 65 years old. Of the 500 charts reviewed, 265 patients were identified as tobacco users between the ages of 18 years old and 65 years old and were included in the study. Data collected from the charts of non-tobacco using patients was used for demographic comparison. Results: 98% of people with recorded tobacco use did not have any mention of a tobacco related diagnosis on Axis I both on admission and on discharge. The percentage did not change despite the fact that 64% of these patients required pharmacological treatment of tobacco withdrawal symptoms while hospitalized. Conclusion: Many psychiatric patients remain addicted to tobacco smoking. In terms of lives saved, quality of life and cost efficacy, treating smoking is considered to be the most important activity a clinician can undertake. Despite the fact that this is well recognized, and the many guidelines requiring screening and appropriate treatment, it appears that the screening is either not done or not recorded as a formal diagnosis. Consequently the appropriate treatment is not initiated. It is evident that educating practicing physicians, as well as, physicians in training about the importance of formally diagnosing this important illness is still as necessary as it has been in the past. With increasing number of appropriately recorded diagnosis, appropriate treatment will follow.

### NR3-07

#### **CASE REPORT OF FACIAL TICS FOLLOWING SELF REPORTED PSYCHOACTIVE BATH SALT (PABS) INTOXICATION IN A HEALTHY 19 YEAR OLD MALE**

*Chair: Chai Wu M.D.; Author(s): Chai H. Wu, M.D., Alan*

*Mayfield, M.D.*

#### **SUMMARY:**

Psychoactive Bath Salt (PABS) use has been on the rise since first reported by Poison Control Center in 2010. Cathinone derivatives that act as sympathomimetics appear to be the primary psychoactive ingredient. Psychiatric symptoms reported include hallucinations, agitation, panic attacks, paranoid delusions, and suicidal ideation. Physiologic symptoms of tachycardia and hypertension are common. Neurologic symptoms such as seizures, headache, tinnitus, bruxism, hypertonia, tremors, hyperreflexia and myoclonus are less commonly reported. Facial tics resulting from PABS intoxication have not been reported and further support the unique actions of this designer drug on the CNS as described below. D is a 19 y/o male with history of alcohol abuse without comorbid medical issues. He initially presented to the ED for evaluation of suicidal ideation in the context of worsening depressive symptoms. He reported synthetic cannabinoid (Spice) use over the past three days and PABS use less than 24 hours from presentation. During mental status exam, he was noted to demonstrate right facial tics involving the right eye, cheek and mouth that did not impede his speech and which he remained oblivious to even upon direct questioning. The movements occurred once every three seconds at baseline and appeared to increase proportionally to his anxiety or agitation. D denied previous history of movement or tic disorder. D was admitted voluntarily for danger to self given continued suicidal ideation. He was mildly hypertensive and tachycardic but otherwise medically stable. There was no indication for medications or supportive care at time of admission. Upon evaluation by the primary team in the morning, his facial tics had resolved completely. Drug screen upon admission was positive for amphetamines. This is known to occur after PABS use. Confirmatory amphetamine testing was negative. Lab testing for mephedrone was negative. This is not uncommon given variance in cathinone derivatives and lack of cross reactivity. Calcium was normal at 9.7mg/dL. D was discharged to substance abuse rehab one week later. Follow up evaluations reveal no recurrence of facial tics. PABS use is on the rise with varying psychiatric and neurologic symptoms of intoxication reported. D's case is remarkable as it appears to be the first report of patient without prior history of movement disorder manifesting facial tics during period of intoxication that resolved completely 48 hours after use with no apparent lasting sequelae. It demonstrates dopaminergic effects of PABS and additional variable to consider when evaluating an agitated or psychotic patient with new onset tic disorder. This case serves to magnify the continuing evolution of PABS and designer drug use and need for expedient and

specific laboratory testing to identify the substance of intoxication given varying presentation and occasionally life threatening symptoms.

**NR3-08**  
**CURRICULUM TO TEACH EVIDENCE-BASED MEDICINE TO PSYCHIATRY RESIDENTS**

*Chair: Shab Jalees M.D.; Author(s): John Sutton, M.D.*

**SUMMARY:**

Overview/ Rationale: In spite of extensive evidence and agreement on effective mental health practices for persons with severe mental illness, research shows that routine mental health programs do not use evidence-based practices when treating the great majority of their clients with these illnesses (Gray 2001). Needs assessment: To assess the need of teaching EBM in our program in the department of psychiatry at NEOMED, the faculty members and the residents were asked to respond to the following open-ended questions via email: Do you think that our faculty is familiar with the philosophy and methodology of evidence-based medicine? Do you think we teach enough evidence-based medicine in our program? How much evidence-based medicine do you use in your practice? What concerns do you have about incorporating evidence-based practices in our department? The residents and the faculty both agreed that the faculty is only "somewhat" familiar with evidence-based medicine and that they do not use it much in their practice. After discussing the results of the survey with the chairman of the department, it was concluded that there is a need to teach evidence-based medicine both to the residents and to the faculty members. Goals: 1) Acquire competence in finding answers to clinical questions using evidence-based medicine 2) Apply the above to real patients 3) Appreciate the importance of evidence-based medicine and use it in day to day clinical practice 4) Identify factors that interfere with the application of the evidence-based-medicine model in everyday clinical practice 5) Understand the limitations of evidence-based medicine Objectives: Following completion of the course, the participants will be able to: Formulate a foreground question List the elements of a foreground question including the patient(s) or problem of interest; the intervention to be studied, or any comparison group; and the outcome anticipated Identify that an intervention of interest can include a treatment, a diagnostic test, a risk factor or a prognostic factor Search for answers Match the study design to the question Identify the hierarchy of evidence for studies of therapy or harm List some general reasons for not finding the answers 3) Appraise the evidence 4) Apply results to their patients Assess the outcome Whether a particular

treatment worked or whether a diagnostic test provided helpful information Evaluate the clinicians' performance in the EBM process Conclusion: Psychiatrists express some ambivalence toward EBM, wondering if it ignores the humanistic side of psychiatric practice (Blisker and Goldner 1999). The goal of this curriculum is to lessen the ambivalence and move faculty and residents toward better understanding of EBM and the roles of clinical judgment and patient preference, coming to realize that EBM and patient-centered care are complementary to each other.

**NR3-09**  
**MEDICAL STUDENT TOBACCO CESSATION CONSULT PROGRAM (MSTCCP): A QUALITY IMPROVEMENT PROJECT**

*Chair: Danielle Alexander M.S.; Author(s): Ingrid Allard, M.D. MSED, Karen Dylong*

**SUMMARY:**

Tobacco use is the leading cause of preventable morbidity and mortality in the United States. Fortunately, patients who receive tobacco cessation assistance from their clinicians are more likely to quit successfully. The Medical Student Tobacco Cessation Consult Program (MSTCCP) at Albany Medical College provides comprehensive tobacco cessation services to all inpatients at the Medical Center. Medical students undergo intensive training to meet this demand. This quality improvement research project aims to 1) Outline the requirements of the MSTCCP so that others may implement similar consult services at their institutions, 2) Summarize the results of student logs and reflection essays, 3) Assess the effectiveness of the program, 4) Identify areas for improvement.; Authors reviewed medical student log notes and anonymous personal reflection essays. Recurrent themes were identified and suggestions for program improvement were compiled. Didactic curriculum time, practical training time, and consult hours were also tabulated. Several themes were identified, including, 1) Students are satisfied with the program and feel the benefits extended beyond the scope of tobacco cessation facilitation curriculum, 2) One of the unique strengths of the MSTCCP is that it allows first and second year medical students, with often limited patient exposure, an opportunity to cultivate significant patient contact time through behavior modification counseling. Areas of improvement for the program include moving the didactic curriculum online and providing greater upfront transparency to students regarding time commitment. The program is a valuable addition to the medical school curriculum as well as hospital services. Greater student recruitment in the future will further expand the

benefits to more individuals.

### **NR3-10 PSYCHOACTIVE BATH SALTS: A CASE SERIES**

*Chair: Benjamin Boche D.O.; Author(s): George Loeffler, M.D., Asley Penn, M.D.*

#### **SUMMARY:**

The recreational use of “Bath Salts” aka sympathomimetic “legal highs” are purchased at mini marts, smoke shops and online. Their use is becoming increasingly popular in the United States as evidenced by Poison Control contacts and Emergency Department visits. These products have not been tested in humans or animals and are not tested for during routine drug testing. These products are marketed under names such as Ivory Wave or Bolivian Bath and are sold in packets that contain synthetic cathinones, which are analogues of amphetamines. Individual synthetic cathinones vary in relative potency, but pharmacologically, these substances bind to monoamine transporters for dopamine, serotonin and norepinephrine, Intense feelings of euphoria, alertness, stimulation and sensory experience occur within 10-60 minutes of ingestion. Non desired effects of dependence, hallucinations, and paranoia have also been described as well. Deaths from behavioral conditions and medical conditions such as hyponatremia with encephalopathy and acute myocarditis have been reported. To our knowledge, we present the largest case series regarding the psychiatric effects of “bath salts” on patients admitted to a locked psychiatric ward. The sample consisted of seven otherwise healthy patients admitted to the Naval Medical Center San Diego inpatient psychiatry ward between February 2010 and July 2011. Patients had no prior history of psychosis and ranged in age between 21 and 29 years of age. The patient’s “bath salt” use was corroborated by the patient, work associates or friends. Symptoms observed included paranoia (7), agitation (7) requiring chemical sedation (2)/physical restraints (2), disorganized behavior (6), auditory hallucinations (5) and suicidal ideation (3). Syncope was observed in two patients and two patients had noticeable facial tics and tremors. 43% of these patients received low dose antipsychotic medication for mitigation of their symptoms. Psychotic symptoms resolved in the patients between 12 hours and three days. The average length of stay was between three and twenty-two days. The characteristic presentation is a preliminary period of agitation, disorganized behavior and confused paranoia, occasionally with unexplained syncope, tics, or tremors that manifests into persecutory delusions.

### **NR3-11**

### **CLONIDINE TREATMENT OF NIGHTMARES AMONG PATIENTS WITH CO- MORBID PTSD AND TRAUMATIC BRAIN INJURY**

*Chair: Adekola Alao M.D.; Author(s): Syed Razi M.D., Jennifer Selvarajah M.D.*

#### **SUMMARY:**

Over 2 million US service members have now deployed and returned over 3 million times to the Iraq and Afghanistan conflicts. Mental health providers in the Departments of Defense and Veterans Affairs healthcare systems have consequently observed steep increases in mental health service use among these veterans. Dysregulation of the autonomic nervous system is thought to explain the physiological changes in patients with PTSD. PTSD is associated with enhanced noradrenergic activity and peripheral biomarkers of the sympathetic nervous system activity has demonstrated an increased 24h urinary or plasma catecholamines in PTSD patients. Case Report Mr. H is a 33 year old Iraq and Afghanistan wars active military soldier who was involved in several combat scenarios in which several lives were lost. He presented with symptoms of PTSD and TBI including nightmares, flashbacks, and exaggerated startle response as well as avoidant behavior. He was treated with cognitive processing therapy, citalopram 20mg po q daily and clonazepam 1mg po bid prn as well as prazosin 4 mp po qhs for the distressing nightmares. He was the treated with clonidine 0.1 mg po qhs which was gradually titrated up to 0.3mg. The patient’s nightmares symptoms resolved about 2 weeks after initiation of treatment. Discussion: Clonidine a centrally acting alpha-agonist agent used to treat hypertension stimulates alpha-adrenoreceptors in the brain stem. This action results in reduced sympathetic outflow from the central nervous system. We hypothesize that this central mechanism of action is why clonidine may be more effective in treating nightmares in PTSD. Conclusion: Clonidine should be considered as an alternative in the treatment of nightmares among patients with PTSD.

### **NR3-12 TYPES OF SOCIAL FEARS CAN INFORM ASSESSMENT OF SOCIAL PHOBIA SEVERITY**

*Chair: Erica Crome*

#### **SUMMARY:**

Revisions proposed for social anxiety disorder (social phobia) diagnostic criteria in the forthcoming fifth edition of the Diagnostic and Statistical Manual for Mental Disorders include a dimensional severity measure. This recognises social anxiety is more complex

than current “present”/“absent” conceptualisation. Whilst several supplementary severity measures have been proposed, creating a measure using information routinely collected in diagnostic assessment would reduce respondent burden and facilitate treatment implementation. The types of social situations feared may provide an innovative measure of social anxiety severity, with some evidence suggesting performance-based fears reflect less severe presentations of anxiety. Item response theory techniques facilitate the ranking of feared social situations along a continuum of social anxiety severity. This paper aims to establish whether the type of social situations feared can be used to create a dimensional measure of social anxiety severity. Methods: Data was derived from responses to structured diagnostic interviews conducted in four large scale epidemiological surveys of American and Australian populations. Item response theory models were used to estimate two parameters for each social situation feared. The first parameter, difficulty, provides an estimate of the point on an underlying social anxiety dimension people have a 50 percent chance to endorsing that item. The second, discrimination, parameter reflects how efficiently each item distinguishes between people with mild and severe social anxiety. Results: Distinct profiles of situations associated with mild, moderate and severe social anxiety was consistent over all four samples. Performance-based fears were spread along the severity spectrum, and not restricted to lower levels of social anxiety. Comparable social scenarios differed in rankings of discrimination across surveys. Conclusions: Support was found for using types of social situations feared to create a dimensional measure of social anxiety severity. Differences in the wording of screening items across measures may account for differences in the discrimination of items across samples. No support was found for performance-based social fears representing a less severe form of social anxiety. Creating an efficient and effective screener for social anxiety severity based on types of situations feared would enhance both research and treatment implementation.

### NR3-13 BRAIN-DERIVED NEUROTROPHIC FACTOR, POSTTRAUMATIC STRESS DISORDER AND MEMORY

*Chair: Sharain Suliman M.A.*

#### SUMMARY:

Introduction: Brain-Derived Neurotrophic Factor (BDNF) is a neurotrophin that helps to support the survival and encourage the growth and differentiation of neurons in both the central and peripheral nervous systems. BDNF has been associated with mood disorders

and with trauma exposure, but there is less information regarding its association with Posttraumatic Stress Disorder (PTSD). The first aim of this paper was thus, to compare BDNF levels in trauma-exposed adults with and without Acute Stress Disorder (ASD) within 2 weeks of the trauma (baseline visit) and PTSD 3 months later. As BDNF levels have also been associated with memory, the second aim of this paper was to correlate BDNF levels with memory. Methods: We collected blood samples from 37 participants who had been involved in a motor vehicle accident in the previous 2 weeks (59.5% male; mean age:  $33.35 \pm 11.54$  years). BDNF levels were determined using a standard ELISA protocol. We used clinical and self report measures to assess for ASD at the time of blood collection and PTSD 3 months later. Neuropsychological measures were used to assess for disturbances in auditory, visual and working memory at the baseline visit. Results: We did not find any significant differences in BDNF levels between those with and without ASD at the baseline visit, or in those with and without PTSD at the 3 month follow-up. Additionally, baseline BDNF levels and memory did not correlate. Conclusion: Our findings suggest that in our sample, alterations in BDNF level might be a marker of trauma exposure, rather than psychiatric diagnosis. These findings are, however, limited by the small sample size.

### NR3-14 FACTOR STRUCTURE OF THE BECK DEPRESSION INVENTORY IN ANXIETY DISORDER

*Chair: Chung Yeub Chung M.D.; Author(s): Yong Chon Park, M.D., Ph.D. Seong Jin Cho, M.D. Hyun Jin Jung, M.D.*

#### SUMMARY:

Objective : Depressive symptoms often coexist with other anxiety disorder symptoms. Furthermore, an anxiety disorder that is comorbid with a depressive disorder results in more severe symptoms and a poorer outcome prognosis. To understand the construct of depressive symptoms in anxiety disorder, this study investigated the factor structure of the Beck Depression Inventory among outpatients with anxiety disorders. Methods : All data were from psychiatric department outpatients at a university-affiliated hospital. We conducted a principal component analysis using data from 194 outpatients with DSM-IV anxiety disorders and calculated goodness-of-fit-indices. Results : Exploratory factor analysis revealed a four factor structure--Cognitive-affective symptoms (Factor 1), Somatic symptoms (Factor 2), Self-reproach (Factor 3), and Hypochondriasis/indecisiveness (Factor

4)--and a 57% total variance. This four-factor model demonstrated an acceptable level of model fit, and it fit better than did a three-factor solution from the literature on depressive disorder. Conclusion : This study's results suggest a difference in the construct of self-reported depressive symptoms in anxiety disorders. These findings also support a dimensional approach to studying anxiety and depression. Further studies may benefit from including comorbid depressive disorder and its influence on anxiety disorders.

### NR3-15

#### SALIVARY CORTISOL AS A PREDICTING FACTOR OF BURN PTSD

*Chair: Jin-Nab Kim M.D.; Author(s): Boung-Chul Lee, M.D., Ph.D. Ibn-Geun Choi, M.D., Ph.D. Jee-wook Kim, M.D. Guk-Hee Suh, M.D., Ph.D. Myung Hun Jung, M.D., Ph.D.*

#### SUMMARY:

Objective : HPA axis and its end product cortisol are two of our defensive mechanism to stress. There are controversies of cortisol level in PTSD patients compared with various control subjects. We measured salivary cortisol level and its diurnal variation and change around severe burn dressing stress to verify difference between the burn patients with and without PTSD. Method : From 33 male inpatients hospitalized to the burn ICU from February to September 2011, salivary cortisol was measured at 6:00 AM, just before burn dressing, two hours after burn dressing, and 7:00 PM. The measurements were done three times with the interval of two days each. The patients were tested for Clinician-Administered PTSD Scale (CAPS) to test the presence of PTSD and Hamilton Depression Rating Scale (HAM.D.) to control the coexisting depression. Results : In the PTSD group, basal salivary cortisol level was somewhat higher than the non-PTSD group. Unlike the non-PTSD group, in the PTSD group, the salivary cortisol level before burn dressing was lower than both the basal cortisol level and the cortisol level at two hours after burn dressing. The basal salivary cortisol level was significantly ( $F=10.9$ ,  $p= 0.006$ ) decreased during the period of 6AM and 7PM on the 4th day of the test only in the PTSD group. The salivary cortisol was significantly decreased after burn dressing in the non-PTSD group on the first day of test, in contrast to the PTSD group ( $F=5.66$ ,  $p=0.041$ ). Conclusion : We think normal salivary cortisol increase disappearance in PTSD group may explain defected stress response. These abnormal stress responses may predict the development of PTSD.

### NR3-16

#### CLONIDINE AND PTSD ; HYPOTHESIS FOR THE ETIOLOGY AND TREATMENT OF STUTTERING

*Chair: Jennifer Selvarajah M.D.; Author(s): Professor Adekola Alao M.D., MRCPsych, FAPM*

#### SUMMARY:

We observed 2 patients with a diagnosis of PTSD, who also presented with newly acquired stuttering following their combat exposure. It was noted that after the addition of clonidine for the treatment of nightmares, their stuttering symptoms resolved. We propose a hypothesis to the mechanism of action of clonidine in the treatment of acquired stuttering in PTSD. Research has already demonstrated that activation of the amygdala in patients with PTSD can explain the fear response seen. Similarly activation of the orbitofrontal cortex may explain re-experiencing phenomenon such as flashbacks. Studies have also demonstrated that there is a deactivation of Broca's area during the symptomatic state in PTSD . Lesions in Broca's area are known to produce a motor aphasia in which the patient understands but has difficulty speaking. This deactivation of Broca's area in PTSD can explain the symptoms of stuttering in which flow of speech is disrupted by involuntary repetitions, prolongations of sounds, syllables or words and involuntary hesitation or pausing in which the stutterer is unable to produce speech, but understands. In studying patients with stuttering, investigations have also revealed an activation of their right cortical motor area and deactivation in the left hemisphere and in addition successful treatment of stuttering eliminated compensatory brain activity and shifted activation back to the left hemisphere. Clonidine is a centrally acting alpha adrenergic receptor agonist which acts at noradrenergic autoreceptors and may be responsible for reducing the release of norepinephrine in the brain. Clonidine may prevent an increase in blood flow to the right cortical motor area and restore normal perfusion to the left hemisphere where Broca's area is located. This resulting restoration of normal relative perfusion to Broca's area may be the mechanism by normal speech fluency is restored and stuttering resolved. 1 Dougherty D, Rausch S. Psychiatric Neuroimaging research, contemporary strategies. 2 Bhatnagar S, Buckingham H. Neurogenic stuttering: its reticular modulation. Current Neuro Neurosci Rep. 2010 Nov; 10(6):491-8.

### NR3-17

#### XEPLEKOMANIA – A RARE VARIANT OF TRICHOTILLOMANIA

*Chair: Juliana Kalaf M.D.; Author(s): Leonardo F. Fontenelle, M.D., Ph.D., Heloisa Alves Brasil, M.D., Ph.D.*

and Antonio Leandro Nascimento, M.D., MSc

#### SUMMARY:

Introduction: Trichotillomania is the compulsive urge to pull out one's own hair leading to noticeable hair loss. This disorder is associated with significant distress and social or functional impairment. Although trichotillomania may be present in infants, the peak age of onset is 9 to 13. Hair pulling in patients with trichotillomania is usually preceded by feelings of rising tension and anxiety and succeeded by feelings of pleasure, relief or gratification. Trichotillomania is classified as an impulse control disorder by the DSM-IV and it is a part of the obsessive-compulsive spectrum. It is frequently associated with other disorders of this spectrum, as obsessive-compulsive disorder, skin picking and eating disorders. Objective: to describe the case of a 16-year old student who presented trichotillomania and a variant of this disorder, the habit of unknitting fabrics, which we describe as xeplemekomania (from the Greek Xepleko – to unknit and mania – an abnormal love for a specific object, place, or action). Case Report: We present the case of a 16-year old student who started psychiatric treatment at the age of five for restlessness and attention deficit. At the age of twelve, she started to pull hair from her head and eat it. She would also unknit pieces of clothes, playing with the fabric between her fingers for endless hours, until the textiles were completely unwoven and reduced to fibers. She would destroy her clothes and also bathing towels and bed sheets by unknitting. She described the sensation of unknitting fabrics as similar to what she felt pulling her hair. In spite of presenting areas of alopecia and also destroying her clothes, she could not stop this behavior, which persisted even when she was asleep. Meanwhile, she also presented hostile behavior towards adults and shoplifting. The patient was initially treated with fluoxetine (40mg/day) and cognitive-behavioral therapy with poor results. When fluoxetine dose was raised to 80mg/day and risperidone was added (1mg/day) the patient presented remission of the habits of pulling hair and unknitting fabrics and also of shoplifting. Discussion: Patients with trichotillomania have been described to present several variants of this habit (cutting the hair of dolls, eating raw rice or pasta in order to have the tactile sensation of eating hair bulbs) and the habit of unknitting fabrics has been described in 1969, but other reports of this habit have not been published so far. Further studies are needed to reveal the relations of this habit to trichotillomania and other obsessive-compulsive spectrum disorders and also to develop treatment approaches for this variant of trichotillomania.

#### NR3-18

#### EVALUATION OF THE PREVALENCE AND

#### SEVERITY OF DEPRESSION IN PATIENTS WITH OBSESSIVE-COMPULSIVE DISORDER (OCD)

Chair: Rupal Patel M.D.; Author(s): Dr Himanshu Tyagi MRCPsych Dr Lynne Drummond MRCP MRCPsych

#### SUMMARY:

Current research evidence suggests that comorbid depression with OCD leads to poorer treatment outcomes. As depression frequently accompanies OCD, it can be one of the most important factors in producing refractoriness for OCD treatment. Our study investigated all patients with a primary diagnosis of treatment refractory OCD who were accepted for outpatient treatment at a specialist OCD service in London between 1st January 2008 and 30th June 2010. We explored the relationship between OCD, depression and treatment outcomes. Standardised measures for assessment of the severity of OCD and depression were completed at assessment, mid-treatment, discharge and follow-up reviews up to 1 year after completion of treatment. Yale Brown Obsessive Compulsive Scale (Y-BOCS) was used to assess the severity of OCD. To assess the symptoms and severity of co-morbid depression, self-rated Beck Depression Inventory (BDI) and clinician rated Montgomery Asberg Depression Rating Scale (MADRS) were used. PADUA inventory was used to assess the symptoms of OCD. Routinely collected social and demographic data were also used to understand the role of any additional factors in treatment outcomes. Preliminary results indicate that greater than two-thirds of treatment-refractory patients in our sample (n=158) were depressed. Differences in symptom severity and treatment response between depressed and non-depressed OCD patients were found and their statistical and clinical significance is being analysed.

#### NR3-19

#### THE NEED FOR A PERINATAL SPECIFIC GENERALIZED ANXIETY SCALE

Chair: Jasmin Abizadeh B.A.; Author(s): Gillian Albert, B.Sc., Arjun Nanda, Shaila Misri, M.D.

#### SUMMARY:

Background: Perinatal anxiety disorders almost always accompany mood disorders. As a result of an under reporting of anxiety symptoms by patients, these illnesses are often under-diagnosed by clinicians. These comorbid psychiatric disorders have shown to be significantly associated with maternal morbidity and adverse neonatal and developmental outcomes. Existing validated measures of anxiety assess anxiety

as a global construct or specific anxiety disorders, with a few scales that have been validated in the perinatal population. No one scale assesses Generalized Anxiety Disorder (GAD) in the perinatal period, perpetuating the complexity in identifying this disorder during pregnancy and postpartum, as worry symptoms are often mistaken for normal worry of a new mother. Objective: To review anxiety disorders in the perinatal period, specifically GAD. To identify existing anxiety tools for anxiety symptoms, GAD and the perinatal period. To advocate for a perinatal-specific GAD scale. Methods: Several online databases were searched using a combination of search terms specific to GAD and the perinatal period. Additionally, a variety of literature specific to the perinatal period and GAD was reviewed to assess commonly used measures. Results: No perinatal-specific GAD scale was found. Several validated measures of anxiety include the State Trait Anxiety Inventory, Beck Anxiety Inventory, Hamilton Anxiety Measure, Goldberg Anxiety Scale and Penn State Worry Questionnaire (PSWQ). Some measures capture GAD specifically: Generalized Anxiety Disorder Inventory, Generalized Anxiety Disorder Severity Scale, Generalized Anxiety Disorder Questionnaire-IV, and the Generalized Anxiety Disorder Scale 7 (GAD-7). Although the Edinburgh Postnatal Depression Scale contains only two anxiety sub-questions, it is the most commonly used postnatal mental health questionnaire and has often been used as an anxiety screening instrument. The Pregnancy Anxiety Scale measures maternal anxiety during pregnancy, but has not been widely validated and is limited to retrospective answers non-specific to GAD. Clinicians often rely on DSM-IV structured interviews to capture perinatal GAD symptoms. Conclusion: Perinatal anxiety disorders are debilitating and need to be properly screened for in pregnancy and among new mothers. Specifically, GAD symptoms during the perinatal period can be difficult to differentiate from normal, nonpathological worries of a new mother. Thus, it is crucial to develop a scale specific to GAD in the perinatal period. A self-rated scale would allow new mothers to report symptoms that she may be uncomfortable speaking about out of fear of being deemed a “bad” mother.

**NR3-20**  
**MEMORY AND EXECUTIVE FUNCTIONS**  
**AFTER VAGUS NERVE STIMULATION FOR**  
**REFRACTORY DEPRESSION**

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**SUMMARY:**

Purpose of the study: Previous studies on vagus nerve stimulation (VNS) have reported mixed results for cognitive changes. Some studies described an enhancement of memory, positive effects on cognition, while others reported no significant cognitive changes, or even a negative effect on visual memory. The purpose of this study was to longitudinally assess the evolution of cognitive factors of patients treated with VNS for refractory depression. Method: We studied 13 patients (8 women) suffering from refractory depression and treated with VNS. Evaluations were done at 1 month, 3 months, 6 months post-stimulation and compared to the baseline obtained pre-operatively. Patients were assessed for memory [Rey Auditory Verbal Learning Test (RAVLT), Rey-Osterrieth Complex Figure Test (ROCF)], executive functions [Verbal Fluency, Stroop Task, and Symbol Digit Modalities Test, Trail Making Test], depressive symptoms [Hamilton Depression Rating Scale (HAM.D.), and anxiety (Hamilton Anxiety Scale (HAMA)]. Different versions of the cognitive tests were used for each testing session to prevent a possible learning effect. Repeated measures ANOVAs were used for statistical analysis with planned contrasts. Results: After 1 month (and at 3 and 6 months) of stimulation, we observed a significant and stable improvement in verbal memory (total words encoded) ( $F(4, 44) = 8.7, p < 0.01$ ) as well as in depression ( $F(4, 44) = 14.33, p < 0.01$ ) and anxiety ( $F(4, 40) = 9.046, p < 0.01$ ). After 3 months of stimulation, we observed a significant improvement in visual memory ( $F(4, 32) = 10.2, p < 0.01$ ), as well as verbal fluency ( $F(4, 44) = 3.369, p = 0.04$ ) and executive functions (color reading of Stroop task) ( $F(4, 44) = 3.3, p < 0.05$ ). No other cognitive measure showed significant changes. Conclusion: Our results demonstrate positive and stable impacts of VNS treatment on cognitive functions of patients with refractory depression as early as 1 month post-stimulation. Verbal memory seems to be a sensitive variable of early changes, while visual memory and executive functions tend to change later in the treatment. Our results may be explained by a number of factors, including a reduced variance due to one study site; biologically informed resistant depression criteria; longitudinal cognitive testing looking at possible long-term improvement of baseline results. Cognitive functions should be systematically evaluated in refractory depression and could be used as early predictors of VNS response.

**NR3-21**  
**EFFECTS OF ANTIPSYCHOTICS ON SODIUM**  
**CHANNELS: A CASE REPORT ON CYSTIC**  
**FIBROSIS**

*Chair: Ferhana Nadeem M.D.; Author(s): Mallik Patel BSc, Rumana Rabmani, BSc, Aditi Shah, BSc*

#### SUMMARY:

**Introduction:** Cystic fibrosis (CF) is a recessive multi-system genetic disease with an abnormal transport of chloride and sodium across epithelium, leading to viscous secretions in the lungs, pancreas, liver, and intestine. CF is caused by a mutation in the gene of proteins, cystic fibrosis transmembrane conductance regulator (CFTR). This channel is responsible for controlling the movement of halogens from inside to outside of the cell. Hence, chloride and thiocyanate are trapped inside the cells in the airway and in the skin. Chloride is negatively charged, this creates a difference in the electrical potential inside and outside the cell causing cations to cross into the cell. Sodium is the most common cation in the extracellular space and the combination of sodium and chloride creates the salt, which is lost in high amounts in the sweat of individuals with CF. **Objective:** Our goal is to determine effects of antipsychotics on sodium channel which adversely affect patients with electrolyte abnormalities, cystic fibrosis. **Method:** This is a case report of SB, 27y/o AAF with a diagnosis of Schizophrenia paranoid type continuous and history of Cystic Fibrosis as an infant transferred to BRMC from another healthcare system. Two weeks prior to this admission, the patient was non-compliant with her medications and was decompensating. She was not sleeping, nor eating and was internally preoccupied, talking to herself. She became increasingly paranoid that her family was after her and on the day of admission became combative, aggressive and physically assaultive to her family. After admission to the inpatient unit SB was started on Quetiapine 50mg orally, twice daily, which was increased gradually. She improved and was discharged. **Discussion:** Severe hyponatremia results in neurological symptoms – such as headache, muscle cramps, confusion, delirium and agitation – it mimics symptoms of psychotic illnesses, making it difficult to recognize hyponatremia as an adverse drug reaction. Some theories state that antipsychotics cause SIADH. Antipsychotics stimulate the release by acting as a non-osmolar stimulus and enhance the activity of ADH on the kidney. Atypical agents such as risperidone can induce excessive water intake and on aripiprazole.; Authors have suggested that antipsychotic-induced hyponatraemia may be serotonin-mediated through increased ADH release, augmentation of the effects of endogenous ADH on the kidney and lowering of the threshold for ADH release by influencing the osmostat. Even though the mechanism through which antipsychotic drugs causes disturbance in Na<sup>+</sup> concentration remains unclear, there have been numerous theories to explain the electrolyte imbalance.

Further studies need to be done to find relationship of the sodium channel with use of antipsychotics and exacerbation of symptoms that may worsen medical conditions. References: Manesse CK, DRUG SAF 2010 JUL1;33 :569-78 L.,CHIAPPETTA 2008 NOV-DEC; 19(82): 364-70

#### NR3-22

#### USE OF PALIPERIDONE IN A PATIENT WITH CYTOCHROME P450 DEFICIENCY

*Chair: Shilpa Sachdeva M.D.; Author(s): Thomas Schwartz, M.D.*

#### SUMMARY:

**Introduction:** Genetic screenings are now more commercially available regarding the cytochrome p450 metabolic enzymes whereby clinicians may be armed with information that will help predict which patients will develop more side effects on certain drugs. Alternatively, as our case will depict, patients sometimes arrive with this metabolic data in hand which then dictates future prescribing. **Case:** A 44 year old female patient with Major Depressive Disorder, Generalized Anxiety Disorder, Post Traumatic Stress Disorder and Borderline Personality Disorder presented to the inpatient unit with ideas of delusional intensity, obsessive rumination, thought disorganization, alternating depressed and elated mood, and inability to sleep. This was interpreted as a micropsychotic episode of Borderline Personality Disorder. There was no substance abuse or organic medical conditions to account for these symptoms. She had a history of clinical trials on many antipsychotic and antidepressant medications in the past and had developed severe side effects to small doses of these medications. Upon history and record review, she was found to have a genetic incapacity with low activity of p450 enzymes, CYP2D6 and CYP2C19. The patient insisted that we not use any medications that utilize these pathways. As far as medications that would not utilize her deficient pathways, she was started on hydroxyzine 25mg up to three times daily for anxiety and insomnia as needed and started paliperidone 3 mg/d for psychotic symptoms and mood lability. She was followed up as an outpatient with some degree of resolved symptoms and tolerated the low doses of these two medications fairly well with side effects of dizziness. After three months of treatment she developed an increase in total cholesterol from 260 to 354 and LDL cholesterol from 168 to 254. She developed headaches and restlessness. Prolactin level was also found to be high (43.74) without any symptoms. As she was no longer psychotic and her moods were controlled and she was actively engaged in psychotherapy, the paliperidone was discontinued

and as needed hydroxyzine continued. Discussion: This case shows that certain patients due have inability to metabolize psychotropics and that genetic testing is available to clinicians to guide in treatment decisions. This patient was given choices of certain medications to treat her symptoms that avoided her deficient pathways (paliperidone, lithium, desvenlafaxine, hydroxyzine, etc.) after the treating team analyzed available medications using psychopharmacology texts, FDA package inserts and drug company websites. This took substantial effort, but the result was a mutually acceptable drug regimen which the patient tolerated for some time. This case also shows paliperidone's usefulness and also that despite evaluating a drug's p450 profile, usual adverse effects may occur. A table regarding the SGA class of medications and their pharmacokinetic profiles is provided.

### NR3-23

#### A CASE OF DELAYED HYPONATREMIA WITH SERTRALINE THERAPY

*Chair: Shilpa Sachdeva M.D.; Author(s): Anurag K Singh, M.D.*

#### SUMMARY:

CASE A 68-year old female with history of depression and bronchial asthma presented to the hospital with a seven-day history of generalized weakness and an episode of pre-syncope. Her medications included sertraline 200 mg daily, albuterol inhaler and multivitamins. Her sertraline dose had been stable for the last five years. Physical examination revealed stable vital signs, no edema or focal neurological deficits. Her laboratory data revealed sodium of 120meq/L, blood urea nitrogen of 7mg/dl, serum creatinine of 0.6 and urine sodium of 126 meq/L. Her serum osmolality was 240 meq/kg and concurrent urine osmolality was 434 meq /Kg. Her serum sodium was found to be 132 meq/L two months ago. This was suggestive of SIADH and sertraline was discontinued. She was placed on water restriction with resulting improvement in serum sodium in next three days. She was started on Citalopram and her subsequent clinical follow-up showed no recurrence of hyponatremia DISCUSSION Depression is the second most common chronic condition encountered in outpatient medical practice after hypertension. Selective serotonin re-uptake inhibitors(SSRI) are the preferred treatment with Sertraline being the most commonly used antidepressant. Hyponatremia is a rare complication of sertraline therapy, seen typically between 5 and 120 days after initiation or dose change. But, as evident from our case, hyponatremia can develop even years after SSRIs are started. Risk factors for the development of hyponatremia include advanced

age, female gender, concomitant use of diuretics, recent history of pneumonia, dose, low body weight, and low baseline serum sodium concentration (<138 mEq/L). Mechanism of hyponatremia with sertraline is multifactorial but the most studied mechanism involves increased release of ADH through serotonin receptors. Presenting symptoms commonly include confusion and fatigue but focal neurological symptoms can also develop with severe hyponatremia. In addition to a low serum sodium concentration, serum osmolality is low and urine osmolality and sodium are inappropriately high. Sertraline induced SIADH often improves with fluid restriction and discontinuation of the agent but symptomatic severe hyponatremia might need aggressive diuresis or electrolyte replacement with hypertonic saline. CONCLUSION Physicians prescribing Sertraline should be aware of the possibility of delayed development of hyponatremia. Routine monitoring of electrolytes might benefit those who have additional risk factors but all patients should be educated about the signs and symptoms of hyponatremia

### NR3-24

#### EMOTION PROCESSING IN YOUNG WOMEN WITH BORDERLINE PERSONALITY DISORDER: A FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY

*Chair: Lori LaRiviere M.D.; Author(s): Lori L. LaRiviere, M.D.; Kathryn R. Cullen, M.D.; Nathalie Vizueta, M.D.; Kathleen Thomas, Ph.D., S. Charles Schulz, M.D.*

#### SUMMARY:

Objective: A core feature of BPD is affect dysregulation. Previous work has suggested elevated amygdala activity in response to fear in BPD. Reactivity to positive emotion stimuli has been understudied. One way to tease apart the reason for elevated amygdala activity is to examine neural activity using both overt and covert stimuli. (Covert stimuli elicit emotional reactions via automatic pathways, bypassing the frontal regulation elicited with overt stimuli.) The goal of this study was to explore how neural activity patterns in BPD compared with those of healthy subjects when viewing fear, happy and neutral expressions, using both overt and covert paradigms. Method: 12 young, unmedicated women with BPD with limited co-morbidity and 12 age-matched healthy women were studied. Structural and functional images were acquired using a 3T Siemens Trio scanner. Five separate functional MRI scans (5 minutes each) were collected, utilizing a passive face viewing task utilizing a block design: overt fear versus neutral, masked fear versus neutral, overt happy versus neutral, masked happy versus neutral, and all neutral. The FMRIB software package was used to conduct data

pre-processing and analyses. Statistical analyses were performed using a general linear model (GLM) with predictors for emotion condition. First-level analyses were conducted for each individual using FEAT (FSL) in which each emotion was identified as a predictor against the fixation baseline. Results of these analyses were then entered into group-level analyses using FLAME (FSL). To correct for multiple comparisons, contrasts were performed using a random effects analysis, using Gaussian random field theory with a corrected p-value of 0.05 and a z-stat threshold 2.3, (relaxed to 2.0 to explore differences in the masked happy condition). Results: For all scans, group comparisons revealed areas in which the BPD had greater activation associated with emotion processing than the control group; the reverse comparisons revealed no significant findings. Group differences included right frontal pole/paracingulate, bilateral thalamus and right parietal cortex (overt fear); right hippocampus and bilateral lingual gyrus (masked fear); anterior cingulate/bilateral frontal cortex and right occipital lobe (overt happy); bilateral caudate and posterior cingulate (masked happy). Discussion/Significance: These results demonstrate increased activation in women with BPD vs. controls in response to both fear and happy stimuli. However, we observed that these group differences occurred in different regions depending on whether the stimuli were overt versus covert. In contrast to prior studies, none of the regions differentiating groups included the amygdale. Since our sample were unmedicated and had limited comorbidity, these findings may be more specific to emotion circuitry abnormalities in BPD.

### NR3-25 SELF-CIRCUMCISION IN A TEENAGER: A CASE REPORT

*Chair: Lauren Mikesell M.S.; Author(s): Marcus DeCarvalho, M.D. Adekola Alao, M.D., MRCPsych, FAPM*

#### SUMMARY:

Case Report A 17-year-old male presented to the emergency for profuse penile bleeding due to attempted self-circumcision. He had requested the procedure previously because his girlfriend wanted him to be circumcised, but was refused as it was deemed medically unnecessary. Using ideas from websites describing self-circumcision, he cut his foreskin with scissors after self-anesthetizing with vodka. The urology team decided to complete the circumcision pending psychiatric clearance. The patient reported a past psychiatric history of anxiety but denied symptoms of depression, mania, or psychosis. Mental Status Exam revealed an anxious Caucasian male who appeared his stated age, made good eye contact, and had good

hygiene. His speech was normal and he described his mood as "embarrassed." Thought process was logical and goal-oriented. Thought content was negative suicidal or homicidal ideation, or delusions. There was no cognitive abnormality and his perception was negative for auditory or visual hallucinations or illusions. Insight and judgment were impaired. The patient was cleared for completion of circumcision, and outpatient psychiatric follow-up was scheduled. Discussion Genital self-mutilators typically divide into five subtypes: psychotic with delusions regarding their genitalia, dissociative identity disorder, severe personality disorder, self-sexual reassignment, and reflections of religious/cultural beliefs(1). Previously, we described female genital self-mutilation(2). Although most reported cases of female genital mutilation involve self-induced abortions or insertion of a foreign body, one report describes a female who masturbated with scissors(3). It has also been suggested that female habitual self-mutilators may have a higher incidence of genital self-mutilation(4). Conclusion To our knowledge, a case of a teenager mutilating himself to impress his girlfriend has not been reported. With increasing availability of internet resources, practitioners should be prepared to provide information and assist with patient decisions regarding circumcision. Dismissing requests for circumcision without discussing with the patient may lead to self-mutilation. Information about the potential advantages disadvantages of circumcision should be made easily available to the public. This will afford individuals the ability to make intelligent discussions with their providers. References 1. Favazza AR: Bodies Under Siege: Self-Mutilation and Body Modification in Culture and Psychiatry, 2nd ed. Baltimore, John Hopkins University Press, 1996 2. Alao AO, Yolles JC, Armenta W. Genital sekf mutilation. Psychiatr Serv. 1999 Oct;50(10):1362-3 3. Favazza AR: Masturbation or mutilation? Medical Aspects of Human Sexuality 25:45-46, May 1991 4. Favazza AR, Conterio K: Female habitual self-mutilators. Acta Psychiatrica Scandinavica 79:283-289, 1989

### NR3-26 QUALITY OF LIFE IN YOUTH WITH EPILEPSY: THE ROLE OF INATTENTION A 1500 PATIENT STUDY

*Chair: Sarah Matthys B.S.; Author(s): Tatiana Falcone, M.D. Prakash Kotagal, M.D. Robert S Butler, MS Diana Lorenzo, M.D.*

#### SUMMARY:

Epilepsy is a chronic, life-altering disease with episodic, recurring, and unpredictable symptoms. It is associated with increased risk for a number of psychosocial

problems, yet treatment has focused primarily on seizure control. The following study was designed to examine the relationship between quality of life ratings and the following domains: inattentiveness, ability to think and remember, neurologic and physical limitations, and epilepsy, for children with epilepsy. Subject data was obtained from the Knowledge Project© Database at Cleveland Clinic Foundation. The Knowledge Project is a program created by the CCF Neurologic Institute to assess patient outcomes for neurologic conditions. Data was obtained for patients 0-18 years with a diagnosis of any form of epilepsy or infantile spasms seen between Jan 2009-June 2011 in the Cleveland Clinic Pediatric Epilepsy Outpatient Service (n=1531). We analyzed scores from the Impact of Childhood Neurologic Disease Scale, Liverpool Seizure Severity Scale, and patient reported hours of activity and number of friends using mixed models regression methods. The individual ICNDS subscales for a single visit were examined for significant differences with respect to individual patient Quality of Life rating, controlling for age and sex. Pairwise comparisons of least square mean differences between QOL ratings were made using the Tukey-Kramer adjustment for multiple means comparisons. To compare differences between individual ICNDS subscales within a QOL rating, a Bland-Altman test of agreement was used. The impact of inattention, neurological/physical limitations, ability to think and epilepsy each significantly associated with reduced quality of life ratings, adjusted p-value <0.05. Bland-Altman analysis of the differences in ICNDS scores for Attentiveness, Other Neurological, and Thinking against the ICNDS score for Epilepsy indicated a significant bias between the ICNDS scores of Attentiveness and Other Neurological when contrasted with the ICNDS score for Epilepsy. Seizure severity and seizure frequency associated with reduced quality of life,  $p < 0.005$ . Increasing number of friends ( $p < 0.0005$ ) and hours of activity were positively associated with quality of life ratings ( $p < 0.005$ ). Psychosocial factors such as the ability to focus attention are significantly associated with reduced quality of life. Children with epilepsy have increased risk for ADHD and behavioral problems. It is evident from this study that illness-associated symptoms of seizure frequency and severity are not the only symptoms associated with decreased quality of life. Providers focus on treatment of the epilepsy with the goal of being seizure free improves quality of life. Yet, attaining this goal will not address the other issues, such as behavior and cognition, which also impact QOL. Broadening treatment by addressing psychosocial factors and co-morbid conditions may help improve quality of life for children with epilepsy.

NR3-27

### A 15-YEAR-OLD PATIENT WITH AN ATYPICAL NEUROPSYCHIATRIC PRESENTATION OF LYME DISEASE (OCD)

*Chair: Carolina Mercader D.O.; Author(s): Amel Badr, M.D*

#### SUMMARY:

Intro : Lyme disease is a multi-systemic illness that can cause neurologic and psychiatric symptoms. We present a case of Lyme Disease in a 15-year-old female who manifests behavioral disturbance and symptoms of Obsessive Compulsive Disorder. Case: This is a case presentation of a 15 year old Caucasian female, living in central New Jersey, with history of Lyme Disease for 6 months, history of Obsessive Compulsive Disorder for 9 months, two inpatient psychiatric hospitalizations, follow ups with Lyme Disease specialist and therapist both last seen one week before our evaluation, history of noncompliance with treatment as she completed antibiotic treatment but has been noncompliant with psychotropic medication. Patient was escorted to the Emergency Room by parents due to worsening agitation and assaultiveness towards them for one week. After being diagnosed with Obsessive Compulsive Disorder, her behavior has recurred with symptoms lasting 2 consecutive weeks, then partially resolving for one month. Over the course of one week prior to evaluation, patient became involved in nightly rituals including having her parents do her homework for her, remove her earrings, and brush her teeth. On day of evaluation patient became agitated after her parents refused to do her homework and she made a hole in a wall by kicking it with her foot; parents called police and patient was taken to ER for psychiatric evaluation. Patient was admitted to Child/Adolescent Psychiatry unit. On the unit, she was calm with less anxiety. A family meeting was held after 3 days on the unit and a conclusion was made that she would consult with her specialist and comply with medical treatment first, to then be started on psychiatric treatment. Discussion: Patient's first ELISA test was found to be negative. This test as well as other currently available serological tests can be unreliable, with both false positive and false negative results. Clinicians need to consider clinical factors that would aid in the diagnosis of Lyme disease. These include a history of an erythema migrans rash, and exposure to a Lyme endemic area. Other key parts of the evaluation include CSF studies, structural and functional imaging, as well as tests for cognitive dysfunction including tests of memory, attention, processing speed, and verbal fluency. In addition to clinical factors, neuropsychiatric symptoms such as forms of psychosis, agitation, anxiety and behavioral disturbance could also be a manifestation of the infectious disease caused by the spirochete *Borrelia burgdorferi*. Even before

official diagnosis of Lyme Disease, patients should be educated about neuropsychiatric symptomatology and should be aware of any behavioral changes. It is also very important for the clinician him or herself to always consider Lyme disease as a rule out diagnosis with new onset neuropsychiatric presentations, especially when the patient is exposed to endemic areas.

### NR3-28

#### PERSONALITY DISORDERS IN FEMALE ADOLESCENTS IN A RESIDENTIAL PROGRAM

*Chair: Samuel Neubut M.D.; Author(s): Diana L. Santiago, M.D., John E. Lewis, Ph.D., Mercedes Briones, Psy.D., and Jon A. Shaw, M.D.*

#### SUMMARY:

**INTRODUCTION:** Twenty-five adolescent females in a residential program were assessed for ADHD, personality trait/disorders, and a history of sexual abuse. Personality traits/disorders have been documented as occurring in the adolescent population (Krueger & Carlson, 2001). **HYPOTHESIS:** A history of sexual abuse will be correlated dimensionally with the number of personality trait items on the SCID-II-PQ. **METHODS:** Subjects (mean 15.1 years) were administered the SCID-II-PQ (Crawford et al., 2005), Stop-Signal Task (Aron & Poldrak 2005), and the Trauma Symptom Checklist for Children (Singer et al., 1995). The sexual abuse was confirmed by multiple sources. **RESULTS:** The most common Axis I diagnoses were Mood Disorder NOS (58%), Depressive Disorders (34%), PTSD (12%), Conduct Disorder (88%), and ADHD (100%). Utilizing the Stop-Signal Task, all of the females met the threshold criteria for ADHD. Ninety-two percent of adolescents were found to have a personality disorder; the most common being Antisocial (72%), Borderline (52%), and Passive Aggressive (28%) personality types. **CONCLUSION:** We found that 60% of the adolescent females had a well-documented history of sexual abuse. The history of sexual abuse was significantly related to the number of endorsed personality trait items on the Cluster B modules and on the total SCID-II-PQ score. Of the top ten personality trait items endorsed by the sexually-abused subjects, only two came from the Borderline Personality Disorder module. **DISCUSSION:** The high prevalence of personality traits/disorders found to be co-morbid with ADHD is consistent with previous literature (Burket et al., 2005). The finding that sexual abuse is related to the number of endorsed personality disorder trait items on both Cluster "B" modules and on the total SCID-II-PQ score suggests the value of a dimensional approach to understanding the psychological ramifications of

sexual abuse in our population. **References:** Aron, A. & Poldrak, R. (2005). The cognitive neuroscience of response inhibition: Relevance for genetic research in attention-deficit/hyperactivity disorder. *Biological Psychiatry*, 57, 1285-1292. Burket, R., Sajid, M., Wasiak, M., Myers, W. (2005). Personality comorbidity in adolescent females with ADHD. *Journal of Psychiatric Practice*, 11(2), 131-136. Crawford TN, Cohen P, Johnson JG, Kasen S, First MB, Gordon K, Brook JS. (2005), Self-reported personality disorder in the children in the community sample: convergent and prospective validity in late adolescence and adulthood. *J Pers Disord*. 19(1):30-52. Krueger, R. & Carlson, S. (2001). Personality disorder in children and adolescents. *Current Psychiatry Reports*, 3, 46-51. Singer MI, Anglin TM, Song L, Lunghofer L (1995), Adolescents exposure to violence and associated symptoms of psychological trauma. *Journal of the American Medical Association* 273: 477-482.

### NR3-29

#### IS THERE AN ASSOCIATION BETWEEN COHEN SYNDROME AND ATTENTION DEFICIT HYPERACTIVITY DISORDER?

*Chair: Ayme Frometa M.D.; Author(s): Bharat Nandu, M.D., Mark Diamond MS III, Michelle Thorpe, M.D.*

#### SUMMARY:

Cohen Syndrome is a rare autosomal recessive genetic disorder with variable expression. The most common genetic mutation is located on Chromosome 8, at the 8q22-q23 loci. Disease characteristics include early-onset developmental delays, psychomotor retardation, variable ophthalmic abnormalities, distinctive facial features, and various musculoskeletal abnormalities including joint hypermobility and hypotonia. Patients with Cohen Syndrome are often described as having a cheerful disposition and overly friendly approach. Some maladaptive and autistic-like behaviors may also be noted. No significant psychological co morbidities have been directly linked with Cohen Syndrome at this time; however ADHD might be linked with some of the behavioral abnormalities seen in these children. We present a case of 8 year old Caucasian female who was diagnosed with Cohen syndrome at age 4. She was further diagnosed to have ADHD hyperactive-compulsive type at age 5. Extensive neuropsychiatric evaluation showed delay in visual and motor perceptions, fine motor skills, organizational skills, and adaptive functioning. Substantial delays across a range of cognitive skill areas and moderate delay in nonverbal skills was also demonstrated.

**NR3-30**  
**POST-TRAUMATIC STRESS DISORDER**  
**AMONG HOSPITALIZED CHILDREN**  
**& ADOLESCENTS: PREVALENCE,**  
**CO-MORBIDITIES AND ASSOCIATED**  
**VARIABLES**

*Chair: Pavan Madan M.D.; Author(s): John Goethe, M.D.*

**SUMMARY:**

**Objective:** We set out to determine the prevalence, demographic variables, comorbidity, medications used and health care utilization variables associated with PTSD. **Methods:** All psychiatric inpatients between the ages 4-17, discharged between 1/1/2000 and 9/30/2008 from an urban community hospital were retrospectively identified from the hospital database (n=2751). Patients with a clinical diagnosis of PTSD (n=727) were compared to those without it on demographic, diagnostic and treatment variables using independent t-tests, chi-square analysis and logistic regression. **Results:** PTSD was found to be present in 26.4% (n=727) of patients aged 4-17. It was found to be highly comorbid with M.D.D (31%), Depression NOS (23%), other anxiety disorders (60%), ADHD (22%), ODD (14%) and Bronchial Asthma (18%). The variables that were more likely to be associated with PTSD were ages 4-12 (OR=1.54, p<0.001), female gender (OR=1.67, p<0.001), Hispanic race (OR=1.6, p<0.001), african-american race (OR=1.8, p<0.001), bronchial asthma (OR=1.3, p=0.03), use of antipsychotics (OR=2.5, p<0.001) or mood stabilizers at the time of discharge (OR=1.4, p=0.004), length of hospital stay 14 days or more (OR=1.5, p<0.001) and readmission within 3 months (OR = 2.1, p<0.001). **Conclusion:** PTSD is a highly prevalent condition among child and adolescent inpatients, especially females. It is highly comorbid with depressive disorders, other anxiety disorders, ADHD, ODD and Bronchial Asthma. Subjects with PTSD are hospitalized for a longer duration and readmitted much more frequently. Further studies are warranted among child and adolescent-inpatients to determine the prevalence and associated variables with PTSD.

**NR3-31**  
**CORRELATION BETWEEN SELF-REPORTS**  
**OF CHILD'S DEPRESSION AND PARENT'S**  
**ASSESSMENT OF CHILD'S BEHAVIOR**

*Chair: Kwon Yunyoung M.D.; Author(s): YM Shin, M.D.*

**SUMMARY:**

**Background:** Depression is common not only in adults but in also adolescents and children. Because childhood is a significant period with numerous

developmental tasks to be accomplished, childhood depression has a negative implication on various developmental areas including cognition, emotion, social skill, academic achievement, and ability to cope with stress. Furthermore, early identification and diagnosis of childhood is quite challenging, since the child's depressed mood often accompanies behavioural problem, which is called "masked" depression. The purpose of this study is to determine the correlation between child's depression scale and parent's assessment scale of child's behaviour. **Methods:** Subjects were recruited from the Suwon Project, a cohort comprising a non-random convenience sample of 226, 10-year-old ethnic Koreans in their 4th year of elementary school and their parents. All participants underwent several tests including Children's Depression Inventory(CDI) and Korean version of Child Behavior Check List(K-CBCL). Depression were evaluated using the Children's Depression Inventory(CDI) and Korean version of the Child Behavior Check List(K-CBCL) was used for the assessment of child's behaviour. K-CBCL is divided into social competence and behavior problems, and the former provides total social competence, school, social problems, the latter provides one total behavior problem, two second-order factor scores (internalizing problems and externalizing problems), and eight syndrome scales (aggressive behavior, anxious/depressed, delinquent behavior, attention problems, social problems, thought problems, withdrawn, and somatic complaints). **Results:** 226 children consisting of 166 boys(73.5%) and 60 girls(26.5%) participated in the study. The average Children's Depression Inventory(CDI) of the participants was 14.57(SD=7.54). Two contents of the K-CBCL, total scale of adjustment scale and social withdrawal problem were found to be closely related to the CDI. **Conclusion:** The results suggested that children with behavioral problems may be closely associated with depression, after controlling for covariates, although much still needs to be elucidated. **REFERENCES:** 1) Kim SY, Ha JH, Hwang WS, Yu JH. Association of Psychosocial Factors in Developing Childhood Depression and ADHD in a Community Low Income Family Children. J Kor Acad Child Adolescence Psychiatry 2008;19:76-81 2) Shin YM, Cho H, Lim KY, Cho SM. Predictors of Self-Reported Depression in Korean Children 9 to 12 Years of Age. Yensei Med J 2008;49:37-45

**NR3-32**  
**PSYCHOLOGICAL REACTIONS OF**  
**CHILDREN AND ADOLESCENTS TO THE 2005**  
**EARTHQUAKE IN PAKISTAN: EFFECTS OF**  
**RELOCATION**

*Chair: Nisha Warikoo M.B.B.S Author(s): Wanda Fremont,*

*M.D.; Mobsin Ali, M.D.; Nancy Newman, Busbra Naz, M.D.; Stephen V Faraone, M.D.*

#### SUMMARY:

**OBJECTIVES** This study evaluated the psychological consequences in children and adolescents exposed to the 2005 Pakistan Earthquake. **METHODS** Data was collected within 1 month after earthquake in Pakistan from those children and adolescents exposed to the earthquake using self-reported questionnaire in 3 groups of subjects. Group I comprising of 25 subjects stayed in shelters next to their homes (Khagran), group II with 25 subjects relocated to Muzaffarabad, within the quake zone and group III with 26 subjects, was relocated to a more developed city outside the quake zone in Islamabad. **RESULTS** Significantly greater number of subjects were attending school in group II, compared to I and III. Subjects in Group II had significantly higher mean scores in re-experiencing domain compared to those in Groups I or III. No significant difference emerged in the mean ASD, PTSD and depression scores and percentage of subjects with PTSD in the 3 groups. Depression was significantly correlated with PTSD and trauma. On average, children attending school had lower re-experiencing score than those who did not attend school. For ASD, depression and 3 symptom domains of PTSD, site was not a statistically significant predictor. **CONCLUSION** Children and adolescents who relocated to areas within the quake zone were at higher risk of developing re-experiencing symptoms compared to those who continued to stay near their homes or relocated to more developed areas outside the quake zone. Relocation to areas with better facilities may be an option while planning disaster relief operations. Clinical evaluation and therapeutic intervention should address these reactions and take into account those factors in planning disaster relief operations.

#### NR3-33

### ANOREXIA NERVOSA AND FOLIE A DEUX: A CASE REPORT

*Chair: Raman Baweja M.D.; Author(s): Aggarwal, Richa M.D.; Mahr, Fauzia M.D..*

#### SUMMARY:

**Introduction/case:** Folie à deux is a rare delusional disorder shared by two people with close emotional ties. Anorexia Nervosa is a severe eating disorder characterized by intense fear of gaining weight, a refusal to maintain body weight above 85% of the expected weight for a given age and height, three consecutive missed periods and either refusal to admit the seriousness of the weight loss, undue influence of shape or weight on one's self image, or a disturbed

experience in one's shape or weight (DSM-IV TR). We report the unique case of Anorexia Nervosa with Folie a Deux in which shared delusion was contributing to the psychopathology of Anorexia Nervosa. Here we present a case of 15-year-old girl who was transferred to the child and adolescent psychiatry unit for management of Anorexia Nervosa. She had shared paranoid delusion with her mother against her father. Her mother was primary person with these paranoid delusions and was inducing these delusions in the patient. Her shared delusion indirectly was contributing to her eating problem. Her psychiatric treatment included nutritional rehabilitation, monitoring her eating disorder behaviors, supportive therapy, individual and group therapy, and family therapy. Her delusional beliefs got weakened after separation from mother. **Discussion:** "Anorexia a deux" has been described for familial occurrence of anorexia nervosa in the literature. A clear mechanism for development of Anorexia nervosa in family is unknown. Most acceptable theories are genetic theory in twins and induction theories between family members. The progression of delusional symptoms between the family members is thought to reflect an attempt of a family to maintain cohesiveness in the presence of a perceived hostile environment. **Conclusion:** Clinicians should be aware about complex family dynamics in treating patient with Anorexia nervosa. Proper recognition of a rare disorder like folie a deux can result in successful treatment outcomes by separation of patients, behavioral treatment and psychopharmacological treatment.

#### NR3-34

### PERIOPERATIVE SUPPORTIVE PSYCHOTHERAPY CAN REDUCE POSTOPERATIVE DELIRIUM IN PATIENTS AFTER CARDIAC SURGERY: A RETROSPECTIVE STUDY

*Chair: Jeewon Lee M.D.; Author(s): Jai Sung Noh, M.D., Joon-ho Jung, M.D.*

#### SUMMARY:

**Background:** Postoperative delirium is associated with many important consequences such as higher mortality, increased length of hospital stay, higher hospital costs, and cognitive and functional decline. The risk that delirium will develop is increased in patients who undergo cardiac operations. Several interventions to prevent delirium have been developed and proved effective. Yet there is limited research evidence on effectiveness of psychiatric intervention to prevent delirium. **Objective:** The objective of this study was to determine the efficacy of perioperative supportive psychotherapy on postoperative delirium prevention in patients after elective cardiac surgery. **Methods:**

We conducted a retrospective study of patients who underwent cardiac surgery from July 1st to October 31st, 2011 in Ajou University Hospital, comparing to those who underwent cardiac surgery from July 1st to October 31st, 2010, in Ajou University Hospital. Subjects who had cardiac surgery in 2011 had received perioperative supportive psychotherapy based on a structured protocol and those in 2010 had not. All medical records of the subjects were collected and reviewed. The primary end point was the incidence of postoperative delirium within 7 days after surgery, and secondary end points included amount of antipsychotics used for delirium, number of days antipsychotics were used, and length of intensive care unit stay. Results: The incidence of postoperative delirium was significantly lower in the supportive psychotherapy group than in the control group. The supportive psychotherapy group had smaller amount and shorter length of days of antipsychotics used for the treatment of delirium. Also, the length of intensive care unit stay was shorter in the supportive psychotherapy group than in the control group. Conclusion: In the current era of escalating health care costs and high technology, supportive psychotherapy during perioperative period may be an effective strategy to decrease incidence and attenuate symptoms of postoperative delirium.

**NR3-35**  
**SYMPTOM MAGNIFICATION IN PATIENTS WITH A TRAUMATIC BRAIN INJURY COVERED BY WORKERS' COMPENSATION**

*Chair: Kyoung-Sae Na M.D.; Author(s): Han-Yong Jung, M.D., Ph.D. Soyoung Irene Lee, M.D., Ph.D. Shin-Gyeom Kim, M.D. Hyun Jung Park, M.D. Won Woo Kim, M.D.*

**SUMMARY:**

**Objectives:** Patients with traumatic brain injury (TBI) experience various neuropsychiatric symptoms such as cognitive impairment and depression. A widespread notion exists that patients with TBI show symptom magnification in the context of litigation such as for workers' compensation. However, few studies have examined this notion. We investigated whether patients with TBI and covered by workers' compensation showed more memory deficits and subjective depression compared with patients with TBI but no workers' compensation. **Methods:** Patients with mild to moderate TBI defined by the International Classification of Diseases, tenth revision were recruited from among patients referred for neuropsychological evaluation at the psychiatric department. Patients with comorbid mood disorders and mental retardation were excluded. Memory deficit was measured by the Rey 15-item test, on which lower scores represent more exaggerated

memory deficits. Frequency of malingering behaviors was assessed with a cut-off score of 9 (=8 is regarded as malingering behavior) on the Rey 15-item test. Many investigators have suggested that even patients with severe TBI are able to recall at least nine of the 15 items. Subjective depression was measured by the Beck Depression Inventory (BDI) and represented as T scores based on normative data. Results: In total, 131 patients with TBI with (n = 55) and without (n = 76) workers' compensation were recruited. No differences in age, gender, education, or severity of brain injury were observed between the two groups. Patients with TBI and workers' compensation had significantly lower scores on the Rey 15-item test and higher scores on the BDI compared with those in patients with TBI without workers' compensation. The frequency of malingering behavior was significantly higher in the workers' compensation group than that in the non-workers' compensation group. Scores on the BDI were negatively correlated with the Rey 15-item test only in the workers' compensation group, whereas no correlations were found in the non-workers' compensation group. Neither the Rey 15-item test nor the BDI was significantly different between patients with mild and moderate TBI. Conclusions: Our results suggest that patients with TBI covered by workers' compensation had a tendency to underperform cognitively and exaggerate subjective symptoms. Clinicians should use a thorough assessment to validate symptoms in the population.

**NR3-36**  
**COGNITIVE DETERIORATION AND VOIDING DIFFICULTY IN PATIENT WITH NEUROSYPHILIS: CASE REPORT**

*Chair: Jongha Lee M.D.*

**SUMMARY:**

Syphilis is an infectious disease caused by *Treponema pallidum* and transmitted by sexual activity, and blood transfusion, etc. The rates of syphilis have been increased in the United states, as well as in several European country. Infection of syphilis can be divided three stages according to the duration of being infected and symptoms. Neurosyphilis is one part of the tertiary stage and in this stage, personality change, decline of cognitive function and other psychotic symptoms can appear. It is not easy to differentiate diagnosis of neurosyphilis or other psychotic disease, for example dementia and psychotic depression. If correct diagnosis is delayed, the symptoms of patients will become worsen and permanent disability can be remained. The authors present a case of 59-year-old man with acute cognitive deterioration, which was identified as a manifestation of neurosyphilis after admission to a

psychiatric ward. He was treated with psychotropic medication and penicillin G for neurosyphilis. During admission, psychiatric symptoms were improved, but the other symptoms appeared, voiding difficulty. This case emphasizes differential diagnosis of neurosyphilis which is characterized for cognitive deterioration, personality change, and mood instability and general medical condition accompanied by neurosyphilis. **Keywords:** Neurosyphilis, Cognitive deterioration, Dementia, Voiding difficulty, Personality change

**NR3-37****TELEPSYCHIATRY: AN EMERGING MODALITY IN BEHAVIORAL HEALTH**

*Chair: Asim Rizvi M.D.; Author(s): Yakir K. Vaks, M.D., Sarah Sheikh, M.D.*

**SUMMARY:**

Background: Telepsychiatry has proven to be reliable, effective, and efficient in treating hard to reach patients with mental illness. Previous studies examining the effect of therapeutic alliance, provider satisfaction, and the overall effectiveness of telepsychiatry show a strongly positive result. Improved access to pediatric and geriatric patient populations is one such favorable outcome of using videoconferencing to engage psychiatric patients. Overall, telepsychiatry has had an empowering effect on patients, providers, educational programs, and communities. Although telepsychiatry is not a novel concept (the earliest documentation on the subject is from the University of Nebraska in the 1950s using a two way closed circuit television system) and previous literature reviews on the subject have been published, significant advances in consumer technology in recent years coupled with the reduction of cost of such videoconferencing equipment has the potential to make telepsychiatry even more empowering and accessible. The advent of tablet computers and smartphones with high definition movie capabilities only helps to spawn an era where a larger number of psychiatrists can treat mental health patients in distant areas. **Methods:** A review of the current literature, utilizing the search terms: telepsychiatry, effective treatment modalities, remote assessment, child psychiatry, geriatric psychiatry, community psychiatry, technology in psychiatry. 17 articles were identified, reviewed and the results were synthesized by the study team. **Results:** The most current published literature on the subject of telepsychiatry indicates that the modality is clinically efficacious and an increasingly more efficient tool that can be utilized to great effect by psychiatrists. A 2004 survey of telemedicine programs in which 88 programs responded showed that 49% of such programs were predominantly focused on mental health. In addition to

its increasing prevalence, one randomized investigation of 23 youths evaluated through both telepsychiatry and face-to-face, 96% of the diagnoses and treatment recommendations were comparable across the two modalities, with comparable family satisfaction. **Conclusion:** The most current published literature on the subject of telepsychiatry shows that it is a clinically efficacious and increasingly more efficient tool that can be utilized to great effect by psychiatrists, both in hard to reach populations and in areas with better availability of psychiatric care.

**NR3-38****SHOULD WE ROUTINELY ASK ABOUT PROBLEMATIC COMPUTER AND INTERNET USE AS PART OF THE PSYCHIATRIC HISTORY?**

*Chair: Himanshu Tyagi M.D.; Author(s): Ankush Vidyarthi MRCPsych*

**SUMMARY:**

Internet mediated communications have revolutionised the asynchronous forms of interpersonal communications. Changes in our preferred mode of communications are increasingly being reflected in the various societal systems e.g. education (Mark Prensky 2001), relationships (Tyagi 2008) and governments (Arab Spring 2011). Proposals to include pathological computer use in DSM V indicate that technology related problems are now being acknowledged by the mental health profession. This study was conducted to identify some of the arguments for and against these changes and to establish some patterns or name the categories for the arguments. **Method** Our study investigated attitudes of mental health professionals toward internet, and knowledge and understanding of internet related problems and internet related generational differences along with the specific primary question of the inclusion of the assessment of dysfunctional computer and internet use in psychiatric assessments. Data was collected via a survey amongst mental health professionals in USA, UK and India. Out of 1830 requests made, 379 responses were received (20.71% response rate) and 315 responses qualified for the final data analysis. Quantitative data was analysed by using SPSS software and qualitative thematic analysis was performed for free text answers. 72.7% of respondents were psychiatrists, with 41.6% of the total sample being that of those working as consultants with an average clinical experience of 11 years in psychiatry. **Results** 45.1% (n=142) of respondents were in favour of including the assessment of computer and internet use as a routine question. 21.9% (n=69) were against and 33.0% (n=104) were undecided. A qualitative

analysis of the free text answers for our primary question produced some interesting themes (included in poster). Professional working in children and adolescent services were most aware about the internet related problems. Significant background effects of demographic variables were also apparent: differences by age and clinical status were found. Some culture-specific characteristics of understanding internet related problems could be observed in our study.

### NR3-39

#### THE VIRTUAL OBJECT AND ITS ROLE IN TRAUMATIC ATTACHMENT: A CASE REPORT

*Chair: Kerrigan Sean M.D.; Author(s): William Kates, M.D. and John Reichard, M.D..*

#### SUMMARY:

**Introduction:** In object relations theory, an initial attachment is gradually formed to a “primary love object” who needs to be seen as omnipotent, capable of complete protection, and consistently containing any threat. In such relationships, the separation of a distinct “self object” can be traced and is often dependent on the availability of transitional objects and an anchoring ego ideal. This case report explores how relationships with “virtual” objects (such as characters in television programs or video games) may emerge in response to primary loss or perceived abandonment from a primary love object in early development to fill holes in a fractured ego. **Materials:** The clinical case describes Mr. B, a man who presents to treatment with difficult object relationships and a history of traumatic attachment. His chronic dependence on television and video games to cope with interpersonal stress and distillation of his identity are discussed, as well as how particular virtual relationships have had the potential to help him process prior emotional trauma. **Discussion:** In exploring the treatment of Mr. B and his virtual dependence, it became useful to consider how celebrated features of virtual personalities could illuminate perceived flaws in his arrested sense of self. He was able to describe in detail the benefits of “substituted living” through characters offering possible representations of an ideal self who could survive in a mirrored fantasy realm without the need to seek the approval of a parental figure. By taking the form of several “invincible” characters that have the ability to generate power independently, Mr. B is allowed to experiment with an identity that is otherwise completely unavailable to him, a transition from a self-object that is helpless when abandoned. The properties of Mr. B’s virtual objects within “screens” are also explored as potentially replicating sensory cues of secure attachment, hijacking the senses and skewing threatening objects seen in the real world into something safer for an underdeveloped intrapsychic experience. The theoretical persistence of transitional objects into adult life is also considered relative to Mr. B, particularly in how such virtual objects lie between two elusive real-world objects (the other

and the self), serving to process new learning about his changing environment and the formation of an ego ideal in a way that is grounding and destimulating. **Conclusions:** In exploring the treatment of Mr. B, several insights can be reached into the potential utility of “virtual” objects to repair and course-correct the development of a meaningful self-object in the wake of real world traumatic attachments. Mr. B’s choice of virtual relationships can be seen as a “record” of his instinctual response to repeated failures of a distant parent, and he appears to be drawn to “invincible” and “self-reliant” characters as a means to access an otherwise unavailable ego strength.

### NR3-40

#### PSYCHIATRY ON YOUTUBE: INFORMATION OR MISINFORMATION?

*Chair: Rajnish Mago M.D.; Author(s): Aashna Mago (presenting author), Rabul Gupta, Rajnish Mago*

#### SUMMARY:

Background YouTube is the world’s most popular online video community, allowing billions of people to watch and share originally-created videos. However, its content may be harmful or helpful to patients and families. Methods Searches were conducted on www.YouTube.com using search terms related to psychiatry: “psychiatry,” “antidepressants,” “antidepressant side effects,” “bipolar disorder,” “suicide,” etc. Data was systematically gathered on content themes, number of views, number of “likes/dislikes,” and uploaders. Videos were rated by two independent raters as predominantly negative or positive about psychiatric treatment. Results Videos were predominantly negative for 60% (psychiatry) to 100% (antidepressants) of the top videos. Commonest theme for “psychiatry” was that mental disorders are arbitrary. For “antidepressants,” commonest themes were that antidepressants don’t work and have dangerous side effects. Suicide attempts in the news items was the commonest theme for “suicide.” For “How to commit suicide,” none of the top videos were either helpful or specifically facilitated suicide. Prank videos from juveniles and videos of attempted suicide were had view counts up to 1,138,790. For “suicide,” the National Suicide Prevention Lifeline was “promoted” by YouTube to the top of the list, the only example of helpful promotion in our searches. Videos were infrequently uploaded by psychiatry professionals/ organizations in 0% (antidepressants) to 30% (psychiatry) cases. More frequently they were uploaded by patients, therapists, non-profits, law firms, etc. Credentials of uploaders were indeterminable for 25% to 44% of videos. Of 10 leading organizations, only APA has a “channel” on YouTube, and only 4 videos have been posted by APA over 2 years. Of 10 leading psychiatry departments, only Yale (one video)

and Duke (TV interviews only) have YouTube channels. Most videos (99.3%) were not rated as either “Likes” or “Dislikes” by viewers. “Likes” exceeded “Dislikes” in all cases. Discussion YouTube mainly contains videos likely to negatively affect the views of patients and their families about psychiatric treatment. Ratings by viewers are rare and not a protection against misinformation. Majority of the videos are posted by persons whose identity, qualifications, and motivation are questionable or indeterminate. YouTube should require a statement about the uploader’s qualifications and “promote” videos from reputable sources. Psychiatry organizations and departments are urged to develop channels and post scientifically accurate and balanced videos helpful to mental health professionals, patients, families, and the public.

### NR3-41

#### 32 YEAR OLD IRAQ VETERAN MAN PRESENTING WITH PSYCHOSIS

*Chair: Jamsheed Khan M.D.; Author(s): Amel Bader, M.D.; Moosa Fadhel, MS 3rdYear; Yakir Vaks, M.D.*

#### SUMMARY:

This patient is a 32-year-old single, unemployed, Korean male with a past psychiatric history of schizoaffective disorder for three years. He was brought into the Bergen Regional Medical Centre emergency room where he was assessed and admitted due to worsening psychotic symptoms and violent behavior. In the emergency room, the patient was anxious but cooperative and was not willing to discuss the events that brought him to the ER. He served in active combat in Iraq from 2004–2008. For a few months prior to admission, the patient reported hearing voices calling him derogatory names and he was seen breaking windows by his neighbors. He was brought in by local police because he started acting violently at home. According to his father who accompanied him, he was banging on the walls, destroying furniture and attempted to break a window sill. After unsuccessfully trying to calm him down, his father called the police. The patient reported one previous psychiatric hospitalization in 2009 at the VA hospital in NJ where he was diagnosed with schizoaffective disorder. The patient has a history of aggressive behavior and destruction to property but has no legal charges. The patient reported smoking half a pack of cigarettes per day, no other substance use. The patient denied any recent stressors or history of sexual/physical abuse and there was no family history of psychiatric illness. No medical history was reported. On exam, the patient appeared his stated age and was well nourished, but was unkempt and disheveled. His affect was not congruent with his mood because he

was laughing inappropriately while being questioned. His speech was normal and he displayed goal directed activity. Although his thought association was intact, he displayed minimal insight and poor judgment. His memory was intact. He was anxious but cooperative and reported no auditory or visual hallucinations. He denied suicidal or homicidal ideation at the time of the interview. The patient was not currently taking any medications. After being medically cleared from the ER, he was sent to an acute adult care unit for observation. During this time, he was given Risperidol 1mg orally BID. The patient was also given a nicotine patch 14mg daily. The patient was adherent with his medications and there was no clinical improvement except the psychosis, later Risperdal was discontinued and SSRI was started and patient showed clinically significant improvement on it. Discussion PTSD is a common mental illness diagnosed in war veterans and its prevalence is on the rise. In addition to the constellation of symptoms experienced by PTSD patients, suicide risk is also becoming another major cause of concern in war veterans diagnosed with PTSD. Some patients also present with psychosis as the first presenting symptom and frequently get misdiagnosed and the diagnosis of PTSD is missed and patients are left untreated making them more prone for increasing depression and development of suicidal ideation

### NR3-42

#### EMOTION DYSREGULATION AND TREATMENT RESPONSE IN BINGE EATING DISORDER SUBTYPES

*Chair: Iris Lin M.A.; Author(s): Debra L. Safer M.D.*

#### SUMMARY:

**Background:** According to the dual pathway model described by Stice et al (1999), affect dysregulation, dietary restraint or a combination of the two explain the development of binge eating disorders. This model is supported by a cluster-analysis identifying two subtypes: dietary restraint (DR) and dietary-negative affect (DNA). These subtypes have shown stability over time and across the spectrum of binge eating disorders. The DNA subtype is associated with greater psychiatric comorbidity and is more treatment resistant. **Objectives:** To explore whether 1) affect dysregulation differs between the two subtypes at baseline and 2) a stronger relationship exists between improvement in emotion regulation skills and outcome for the DNA compared to the DR subtype after an affect regulation-focused treatment. **Method:** 101 men and women with DSM-IV Binge Eating Disorder (BED) criteria were randomly assigned to Dialectical Behavior Group Therapy (DBT) adapted for BED (n=50) or to a control

group (n=51). Measures at baseline and post-treatment included the Eating Disorder Examination (EDE) to assess for the frequency of binge eating (defined as binge eating days over the past 28) and the Difficulties in Emotion Regulation Scale (DERS) to measure emotion dysregulation. Independent-sample t-tests analyzed whether baseline DERS scores were significantly higher in the DNA than DR subtype. Correlations were used to examine if significant correlations between decreased emotion dysregulation and decreased binge eating would be present only in the DNA subtype randomized to DBT and not in the DNA subtype randomized to the control group or DR subtypes in either condition. Results: In the cluster analysis, 36 of the 101 subjects (35.6%) were DNA subtypes and 65 (64.4%) were DR subtypes. Of the 36 DNA subtypes, 21 (58.3%) were randomized to DBT and 15 (41.7%) to the supportive group control. Of the 65 pure DR subtypes, 29 (44.6%) were in the DBT and 36 (55.4%) in the control group. Percentages of the DR and DNA subtypes did not significantly differ by treatment condition. Baseline levels of emotional dysregulation were significantly higher in DNA than DR subtypes ( $p < .001$ ). When the subtypes were examined within each treatment condition, a statistically significant correlation between lowered DERS scores and lowered binge eating frequency was only found among the DNA subtypes randomized to DBT-BED ( $r = .642$ ,  $p = .005$ ). Conclusions: To our knowledge, this is the first study with evidence to support the dual-pathway hypothesis that DNA subtypes have significantly more affect dysregulation than the DR subtype. This confirmation is important as affect dysregulation is considered a central triggering mechanism for binge eating. Findings from the current study suggest that different eating disordered populations make therapeutic improvements through specific mechanisms. More targeted affect regulation interventions could increase the treatment response of the DNA subtypes.

**NR3-43**  
**PREVALENCE OF MAIN PSYCHIATRIC DISORDERS IN RELATION TO URBANIZATION IN GYEONGGI PROVINCE BY USING THE K-MINI**

*Chair: Seongjin Cho M.D.; Author(s): Yongchon Park, M.D., Ph.D. Chungyeub Chung, M.D. Hyeonjin Chung, M.D.*

**SUMMARY:**

Objectives Epidemiological studies have supplied growing evidence of an association between the prevalence of psychiatric disorders and the urban/rural division. We investigated the prevalence and risk factors of the main psychiatric disorders in two

areas of Gyeonggi Province of South Korean with different levels of urbanization. Methods A survey was conducted of the adult population (over 40 years of age) in Yangpyeong-gun (lower level of urbanization ; n=639) and Guri-si (higher level of urbanization ; n=335) in Gyeonggi Province. The Korean version of the Mini-International Neuropsychiatric Interview (K-MINI) was used as a structured psychiatric diagnostic interview instrument. Major depressive disorder (M.D.D), suicidality, alcohol dependence, alcohol abuse, generalized anxiety disorder (GAD), somatoform disorder, bipolar disorder, and schizophrenia were selected as the 8 main psychiatric problems. Results The prevalence of the 8 main psychiatric disorders in Guri-si (25.6%) was higher than those of Yangpyeong-gun (15.1%,  $p < 0.05$ ). In particular, the prevalence of M.D.D, suicidality, and GAD, which are thought to be strongly influenced by psychosocial factors, were significantly higher in Guri-si ( $p < 0.05$ ). Conclusion A greater prevalence of almost all major psychiatric disorders is associated with higher levels of urbanization, exceptions being somatoform disorders and bipolar disorder. This urban-rural difference may be related to environmental risk factors.

**NR3-44**  
**VARIATION BY MONTH AND DAY OF THE WEEK IN INTERNET SEARCHES FOR SUICIDE IN THE UNITED STATES**

*Chair: Jacob Taylor M.P.H.; Author(s): Matthew D. Burkey, M.D., M.P.H.*

**SUMMARY:**

Background: Tracking internet search terms related to health is an emerging epidemiologic tool. This technique has already proven helpful in tracking influenza infection patterns and in psychiatry the study of internet search terms has provided evidence in support of the seasonality of depressive symptoms, with stronger effects seen further from the equator. With respect to suicide, early evidence has suggested that the proportion of internet searches which contain the word "suicide" is correlated both temporally and geographically with completed suicide attempts. Studies of completed suicide have consistently showed that rates differ by month and some evidence suggests that there are also significance differences in suicide rates by day of the week. The objective of this study is to investigate whether individuals in the United States are more likely to make searches related to suicide on particular days of the week and in particular months of the year. Methods: Day-by-day and month-by-month records of the relative frequency of Internet searches that contain the word "suicide" in the United States from January 1,

2004 through September 30, 2011 were extracted using Google Insights for Search, a publicly available database of Internet search terms. Analysis of variance methods were used to compare mean relative frequencies of searches that contain the word “suicide” across months of the year and day of the week. Results: Both month of the year and day of the week are independently associated with relative frequency of searches that contain the word “suicide.” These results were highly statistically significant ( $p < 0.01$ ) in both cases. Searches for “suicide” follow a clear seasonal trend, with peaks in October-November and March-April with relatively fewer searches during the summer months. In terms of days of the week, searches for “suicide” are 1.05 times more common on Sundays compared with other days ( $p < 10^{-4}$ ). The least common day for searching “suicide” was Friday ( $p < 0.01$ ). Conclusions: This study shows that there are statistically significant temporal trends in Internet searches using the word “suicide” in the United States. The peak in “suicide” searches in March-April corresponds to the months with the highest suicide rates in the United States as suggested by large scale epidemiologic studies (March - May). The peak in October-November corresponds to a smaller peak in suicide rates that has been noted in these large studies. The small but highly statistically significant peak in searches for “suicide” on Sunday does not correspond with a large study that suggests that more people commit suicide on Wednesday than any other day in the United States. However, research from Japan suggests that more suicides occur on Monday than any other day. More research is needed to delineate the complex relationship between internet search activity and suicidal acts.

**NR3-45**  
**UNDERSTANDING RISK FOR SUICIDE ATTEMPTS: A LATENT CLASS ANALYSIS OF MULTIPLE RISK FACTORS IN A NATIONALLY REPRESENTATIVE SAMPLE OF U.S. ADULTS**

*Chair: Daniel Rasic B.S.; Author(s): James Bolton, M.D., Robert Pietrzak Ph.D., Norbert Schmitz Ph.D., Jitender Sareen, M.D.*

**SUMMARY**

Multiple risk factors contribute to suicide attempts and suicide. Recent U.S. data suggests that individuals who complete suicide can be classified into patterns of risk factors. We sought out to understand the patterns of risk factors among people who survived a suicide attempt in a nationally representative sample of U.S. adults. The purpose of the study was to classify individuals who attempted suicide into classes of risk factors and to compare these classes to identify similarities and

differences with existing data of classes of risk factors for people who died by suicide. Data were drawn from Wave 2 of the National Epidemiologic Survey of Alcohol and Related Conditions (N=34,653; Response Rate 70.2%) and a latent class analysis was conducted on all individuals with a history of a suicide attempt. Included risk factors included a history of major depression, mania or hypomania, an anxiety disorder and cluster B personality disorders; alcohol and drug use disorders; financial, legal, interpersonal stressors; history of sexual abuse; and physical disabilities. Early analysis suggests that five classes of risk factors best characterized suicide attempters. One class was characterized by moderate probability of depression and high probability of disability. A second class was characterized by high probability of all mental disorders. A third class had low probability of mental disorders but high likelihood of alcohol and drug use disorders. A fourth class was characterized by high probability of affective and cluster B disorders but low levels of disability. A final class had a low probability of all studied risk factors. A history of sexual abuse had a moderate to high prevalence in all classes except one. Further analyses will be conducted to determine the sociodemographic correlates and help-seeking across latent classes. These data will provide detailed information regarding the patterns of risk factors of suicide attempters that could be used to help guide preventative strategies.

**NR3-46**  
**UNDERGRADUATE MEDICAL STUDENTS' ATTITUDE TOWARDS PSYCHIATRY: A COMPARATIVE STUDY FROM INDIA AND JAPAN**

*Chair: Jatinder Chawla M.D.; Author(s): Takahira Kato, Yatan Pal Singh Balhara, Tateno Masaru, Rajesh Sagar, Geetanjali Chugh*

**SUMMARY:**

Background: The knowledge of attitude and awareness of undergraduate medical students towards psychiatry, mental health and psychiatric disorders is of utmost importance as they are going to be involved in care of these patients either directly or indirectly during the later years of their careers. Aims: Understanding and comparing attitudes and beliefs of medical students from India and Japan towards psychiatric illness and psychiatry. Study design: Cross sectional assessment. Methods: Consented third year medical students at the two study sites (India and Japan) were given semi-structured questionnaire to evaluate the attitudes and beliefs of undergraduate students towards psychiatric disorders. It had questions pertaining to five domains viz., emotion experienced if faced with

psychiatric patients, etiology of psychiatric disorders, help seeking for psychiatric disorders, treatment of psychiatric disorders, and psychiatry as a future career choice. Results: 79 Indian students and 77 Japanese students participated in the study. 45.6% from India and 26% from Japan ( $p < .05$ ) reported they could not describe their emotion if faced with psychiatric patients. Role of excessive emotions ( $p < .05$ ) and loneliness ( $p < .05$ ) in causation of psychiatric disorders was reported by significantly more Japanese medical students. Whereas, Indian students were more likely ( $p < .05$ ) to find evil spirits as a causative factor for psychiatric illness. Most medical students (> 90%) from both study sites favored psychiatrists for treatment of psychiatric illness. 92.4 % Indian v/s 80.5% Japanese ( $p < .05$ ) reported that psychiatric disorders are treatable. 50.6% Indian students favored use of electroconvulsive therapy, while 51.9% Japanese students were not sure of their view on the issue. 54.4% Indian students did not favor psychiatry as a future career option, while 41.6% Japanese students either refused psychiatry as a career choice or reported uncertainty on this issue. Conclusion: In spite of limited generalizability, the findings of the current study do suggest that existing model of medical education is not effective in bringing about the change in knowledge and attitude of the students towards psychiatric illness during the first half of the medical training.

### NR3-47

#### THE EFFECTIVENESS OF MODERN TREATMENT MODALITIES ON REDUCING RECIDIVISM IN SEXUAL OFFENDERS: A SYSTEMATIC REVIEW AND META-ANALYSIS

*Chair: Monica Chawla M.D.; Author(s): Jodi Bond, M.D., Carmen Fulton, M.D., M.P.H., Seth Himelhoch, M.D., M.P.H.*

#### SUMMARY:

Context: Sexual offense crimes are an increasingly focused upon topic in American news and politics. Little is known about effects of any form of treatment on sexual offenders. Objective: The examiners wished to determine whether any form of treatment for sexual offenders impacted rates of repeated sexual offense in people with history of sexual offense charges. Interventions examined included various forms of therapy, including CBT, multisystemic therapy, and group therapy. Data Sources: Searches of the Cochrane database, PubMed, and PsychInfo were performed for studies published through September 2010 to identify studies regarding sex crimes. Study Selection: Studies included were randomized control trials of sex offenders exposed to some form of treatment in an attempt to prevent reoffense. These studies were required to

follow subjects for at least 18 months and examined males and females ages 12-65. Two independent raters examined studies meeting criteria to ensure that the inclusion criteria were met. A total of three studies were found to meet eligibility criteria. Data Extraction: Random-effects meta-analysis was performed with between-study heterogeneity assessed using the Q statistic. Results: Rates of sexual reoffense in 935 adults randomized to receive treatments showed no significant difference in rates of reoffense. Meta-analysis of these studies shows that overall there is no statistically significant improvement in rates of reoffense compared to offenders who did not receive a variety of treatment modalities (RR 0.96 (CI 0.90-1.02)). Rates of reoffense in 48 adolescents who received treatment versus usual community services showed significant decrease in rates of reoffense in the therapy group suggesting treatment interventions in this population may be more effective than in adult offenders. Each study included showed high risk of bias through Cochrane risk of bias assessments and heterogeneity was calculated  $I^2 = 82.8\%$ . Conclusions: The study results show thus far there are no therapeutic interventions found to be helpful in decreasing rates of sexual reoffense among sex offenders. However, more research is needed, particularly in the juvenile population since research seems promising that this population may show significant improvements in rates of reoffense.

### NR3-48

#### RESTORING GUN RIGHTS: WHAT IS THE ROLE OF THE PSYCHIATRIST?

*Chair: George Annas M.D.*

#### SUMMARY:

Under United States federal law those “adjudicated as mental defectives or incompetents or those committed to any mental institution” are ineligible to possess, receive, ship, or transport firearms or ammunition (1968). In addition to the federal law, 34 states and the District of Columbia provide additional statutes in regard to restrictions for those who are mentally ill, as of 2010. Some jurisdictions are beginning to offer a process by which a person may obtain a relief of disability and be eligible, once more, to purchase a firearm. This leads to the challenge of how one determines if such a person should regain this right. As psychiatrists, we would all prefer our patients remain unarmed and it would be unethical to actually recommend a patient buy a firearm. However, the second amendment is important to a great deal of our patients and the desire to regain these rights should not be dismissed. In this poster, I will introduce the topic of performing a risk assessment for the restoration of gun rights. I will also discuss the

challenges involved as well as what research still needs to be done in order to move towards a standardization of these assessments. References: Federal Gun Control Act, 18 USC § 922 (1968) Harlow M, Davidson C, Haun J, Wernsing S. Restriction Laws for the Mentally Ill. Poster Presentation for the American Association of Psychiatry and the Law, meeting, presented October 22, 2010.

### NR3-49

#### TESTING A DIATHESIS-STRESS MODEL: POTENTIAL GENETIC RISK FACTORS FOR DEVELOPMENT OF DISTRESS IN CONTEXT OF CANCER DIAGNOSIS AND TRANSPLANT

*Chair: Magdalena Romanowicz M.D.; Author(s): S. Ehlers, D. Walker, P. Decker, J. Rundell, G. Shinozaki, M. Litzow, W. Hogan, D. Mrazek, J. Black*

#### SUMMARY:

Purpose: Brain-derived neurotrophic factor (BDNF) is a nerve growth factor that has antidepressant-like effects in animals and may be implicated in the etiology of mood-related phenotypes, specifically in the context of stressful life events. We hypothesized that this single-nucleotide polymorphism will predict the development of psychological distress among patients diagnosed with acute leukemia and preparing for HSCT (Hematopoietic Stem Cell Transplant). We also explored the relationship of other genetic factors to psychological distress including 5HTTLPR and STin2, FKBP5 and the CRHR1 TAT haplotype. Experimental Design: In a retrospective cohort design, 107 adult acute leukemia survivors preparing for HSCT at a major medical center completed a pre-HSCT psychological assessment and volunteered to donate blood to the HSCT Cell and Serum Research Repository for future research studies. Results: There was evidence of a potential association between BDNF (Val66Met) and psychological distress. More specifically, rs6265, was related to both personal mental health history ( $p=0.09$ ,  $0.06$  adjusted) and diagnosis of depression/adjustment disorder at time of pre-transplant evaluation ( $p=0.11$ ,  $0.09$  adjusted). Other genetic factors were unrelated to distress. Conclusion: The BDNF Val66Met polymorphism may contribute to development of depressive symptomatology in patients undergoing stressful life events, such as diagnosis of acute leukemia and preparation for HSCT. The SNPs in BDNF might be applicable in identifying patients at risk for developing psychological distress and depression in the context of coping with stressful medical conditions. Polymorphism in other genes (FKBP5, CRHR1, and 5HTT) did not show any significant relationships. Replication studies are needed with larger samples of people undergoing similar significant life stressors.

### NR3-50

#### ASSOCIATION OF SEROTONIN TRANSPORTER LINKED POLYMORPHIC REGION (5-HTTLPR) AND ESCITALOPRAM ANTIDEPRESSANT TREATMENT RESPONSE IN KOREAN PATIENTS WITH M.D.D

*Chair: Eunsoo Won M.D.*

#### SUMMARY:

Background : Conflicting results exist on whether or not polymorphisms in the serotonin transporter gene promoter region (5-HTTLPR) influence antidepressant response to selective serotonin reuptake inhibitors (SSRIs). Various studies have shown that short(s) / long(l) polymorphisms of the 5-HTTLPR might predict treatment outcomes to selective serotonin reuptake inhibitors (SSRIs), however ethnic variation as well as choice of drug and length of assessment may influence genetic effects on antidepressant response. The purpose of this study was to evaluate the association between 5-HTTLPR and clinical response to escitalopram treatment in Korean subjects with major depressive disorder (M.D.D). Methods : One hundred and fifteen Korean patients diagnosed with major depressive disorder were evaluated during 8 weeks of escitalopram treatment at a dose of 5-40mg/day. Patients were genotyped for short(s)/long(l) polymorphisms in the 5-HTT promoter region (5-HTTLPR) using polymerase chain reaction (PCR). Clinical symptoms were evaluated by the 21-item Hamilton Depression Rating (HAM.D.-21) scale during the 8 weeks of treatment. Results : Treatment response to escitalopram at 8 weeks was moderated by 5-HTTLPR, with better response rates for s-allele carriers than l-allele homozygotes. The proportion of s allele carriers in responders was higher than that in non-responders at 8 weeks (96.6% vs. 85.7%) of treatment (odd ratio = 6.24,  $P=0.026$ ). However, the frequencies of genotypes in remitters and non-remitters were comparable ( $P>0.05$ ). The percentile decline of HAM.D.-21 in patients possessing the s allele ( $59.86 \pm 3.23\%$ ) was larger than that in l allele homozygotes at 8 weeks of escitalopram treatment ( $43.13 \pm 11.49\%$ ,  $P=0.029$ ). Conclusions : Our data showed a relationship between SSRI response and polymorphisms in the serotonin transporter gene promoter region, which suggests 5-HTTLPR genotype may act as a marker that predicts long-term response to escitalopram treatment in patients with M.D.D.

### NR3-51

#### WITHDRAWN

### NR3-52

**RELATIONSHIP BETWEEN WORKING/  
VOLUNTEER STATUS AND SUCCESSFUL  
AGING IN THE SUCCESSFUL AGING  
EVALUATION (SAGE) STUDY**

*Chair: Steve Koh M.D.; Author(s): Colin Depp, Ph.D., and Dilip Jeste, M.D.*

**SUMMARY:**

Large-scale studies of community-dwelling older adults examining bio-psycho-social aspects of successful aging have been rare. It has been reported that self-report of aging successfully may not be directly related to degree of disease and disability. Few studies have focused on the importance of engagement in productive activities, such as through working and volunteering, on self-perceptions of successful aging and on other indicators of mental health. Nevertheless, it has been suggested that changes in employment such as through mandatory retirement can contribute to increased symptoms of depression and overall poor health outcome in older adults. Those who maintain active employment and/or voluntary work may have improved life satisfaction and perception of being successfully aged regardless of their degree of physical illness, disability or cognitive decline. We used data from the Successful AGing Evaluation (SAGE) study, a structured multi-cohort longitudinal design to study successful aging in 1,300 randomly-selected community-based men and women in San Diego County, over the age of 50, with an over-sampling of people in the 80s and 90s. Participants in the SAGE study were assessed along various dimensions of physical, cognitive, emotional, and psychosocial functioning and participants were randomly selected community dwelling to be representative of the San Diego population. Participants completed a 25-minute telephone interview was followed by a comprehensive survey. We compared indicators of successful aging across working or volunteering status, physical functioning (i.e. IADL or SF-36), cognitive functioning (ie. TICS), and depression (PHQ-9). Results indicated that individual's working or volunteering status was not related to independent living status. Full-time employment status was significantly related to perception of active engagement with life and sense of mastery or growth. Fully employed individuals had higher cognitive ability (TICS total score), lower rates of depression (PHQ9 score) and better score on SF36 physical composite scale. Being employed part-time, however, did not show significant relationship with PHQ9 score. Interestingly, volunteering did not have any significant associations with any of the measures studied. These results may indicate that not all forms of productive activity engagement produce the same effects on indicators of successful aging.

**NR3-53**

**HALLUCINATIONS IN OLDER ADULTS WITH  
SCHIZOPHRENIA ON 4.5 YEAR FOLLOW-UP**

*Chair: Audra Yadack M.D.; Author(s): Biswarup Ghosh, M.D., Ifeanyi Izediuno, M.D., Carl I. Cohen, M.D.*

**SUMMARY:**

**OBJECTIVES:** There are little data available on the prevalence, course, associated factors, and impact of hallucinations in later life. This longitudinal study of older persons with schizophrenia explores: (1) the changes in the prevalence of hallucinations over time; (2) clinical and social variables at baseline that predict hallucinations on follow-up; (3) the effect of baseline hallucinations on various clinical and social outcomes; (4) variables associated with changes in hallucination status. **METHODS:** The study consisted of 254 persons with schizophrenia spectrum disorders aged 55 and over living in NYC who developed the disorder prior to age 45. Data on 103 patients followed for a mean of 52 months are presented. Mean age was 61 years, 55% were male, and 55% were white. Hallucinations consisted self-reported auditory, visual, or olfactory symptoms. **RESULTS:** There was no significant difference between the means of the PANSS hallucination scale at Time 1 (T1;  $2.0 \pm 1.6$ ) and Time 2 (T2;  $1.8 \pm 1.5$ ). and 33% and 26% of subjects had hallucinations at T1 and T2, respectively. None of these differences were significant. Notably, only 16% had hallucinations at both T1 and T2, 57% never had hallucinations, 10% developed hallucinations, and 17% no longer had hallucinations. Although several T1 variables predicted presence of T2 hallucinations, in logistic regression only the presence of hallucinations (OR=5.8) and lower Community Integration Scale (OR=.60) scores at T1 remained significant predictors. The presence of hallucinations at T1 did not significantly correlate with any clinical variables at T2. Change from hallucinations at T1 to no hallucinations at T2 was associated with having higher Community Integration Scale scores and more confidantes at T1. **CONCLUSIONS:** Although point-prevalence of hallucinations is fairly low (less than one-third) there were fluctuations in symptoms so that 43% had hallucinations during the study period. There were few long-term predictors of hallucinations, although persons who had better community integration—a measure of independent living, life quality, and social engagement—had better outcomes. The findings suggest that hallucinations do not remain stable in later life, and commonly may disappear or re-emerge. Identifying age appropriate strategies for enhancing community integration may help maintain and increase the likelihood symptom remission.

## NR3-54

**QUALITY OF LIFE IN OLDER ADULTS WITH SCHIZOPHRENIA: A LONGITUDINAL POPULATION BASED STUDY**

*Chair: Elena Garcia-Aracena M.D.; Author(s): Carolina Jimenez, M.D., Helen Ryu, M.D., Carl I. Cohen, M.D.*

**SUMMARY:**

**Objectives:** In the past, researches made about quality of life (QOL) among older adults with schizophrenia have been mostly cross - sectional studies. There have been only a few longitudinal studies that have examined younger populations. In 2025 the number of older adults with schizophrenia is expected to double, so it will become very important to understand all the factors that are associated with improved QOL in this population. This study examines fluctuations, predictors, and impact of QOL, in a 4-year follow-up study of older adults with schizophrenia. **Methods:** The study consisted of 252 persons with schizophrenia spectrum disorder, aged 55 and older, living in NYC, who developed the disorder prior to the age of 45. Data on 98 follow-up interviews are presented with a mean follow-up of 51 months (range 12 to 95 months). We used an adaptation of Lehman's QOL model that consists of four variables sets (demographic, objective, clinical, and subjective) comprising 10 independent variables. The dependent variable was the Quality of Life Index (QLI). The sample was also divided into high and low QOL based on mean general population scores for the QLI. **Results:** In linear regression analysis, the following baseline variables were found to be significant predictors of the QLI at follow-up: higher QLI ( $\beta=.45$ ), fewer depressive symptoms ( $\beta=-.22$ ), and fewer mental health services ( $\beta=-.17$ ). On follow-up, there was a non-significant decrease in the percentage of subjects with high QLI (46 % baseline; 44 % follow up); 31 % had high QLI at both assessments, 41 % had low QLI at both assessments, 13 % went from low QLI to high, and 15 % went from high QLI to low. Partial correlations controlling for gender, age and baseline values of the outcomes variables indicated that baseline QLI predicts fewer positive symptoms ( $r=-.30$ ) and fewer depressive symptoms ( $r=-.25$ ) at follow up. **Conclusion:** The longitudinal data indicate that cross-sectional findings regarding QOL have probably been over-estimations, and that only about one-third of older adults maintain a high QOL and slightly more than one-fourth fluctuate between high and low QOL. Moreover, the data indicate that improving QOL can diminish subsequent positive symptoms and depression, although the latter also affects subsequent QOL. It is not clear if mental health services have any benefit on QOL. The clinical and public policy

implications of these findings will be discussed

## NR3-55

**GENDER DIFFERENCES IN THE IMPACT OF OPTIMISM ON SUCCESSFUL AGING AND MENTAL HEALTH**

*Chair: Ipsit Vahia M.D.; Author(s): Colin Depp Ph.D., Matthew Allison M.D., J. Kellogg Parsons M.D., Dilip V Jeste, M.D.*

**SUMMARY:**

**Introduction:** Optimism has been associated with benefits to physical and emotional health, as well as successful aging. However, it remains unclear whether there exist gender-associated differences in the impact of optimism on indicators of successful aging and mental health in older adults. In order to assess this, we compared correlates of optimism in a sample of community-dwelling older men and women in San Diego. **Methods:** We recruited male participants from the San Diego site of the Selenium and Vitamin E Cancer Prevention Trial (SELECT) and female participants from the San Diego site of the Women's Health Initiative (WHI) study. All participants were mailed a self-report successful aging questionnaire which included standardized validated measures of successful aging associated domains including cognition, depression, physical and emotional function and positive psychological traits. Optimism was measured using the Lifetime Orientation Test – a 6 item questionnaire scored from 5 (least) to 30 (most optimistic). **Results:** On average the sample of men (N= 621) was younger (mean age = 65.6 years) than the women (N=1979) (mean age = 72.9 years). The groups rated themselves similarly in terms of self rated successful aging (7.96 in men compared to 8.04 in women). Scores on the optimism scale were also comparable (23.5 in men vs. 24.3 in women). Among both, higher optimism was most strongly correlated ( $R > 0.4$ ,  $p < 0.001$  for all comparisons) with greater personal mastery, higher self-efficacy, lower perceived stress and higher resilience. However, the correlation with chronological age was significant among women, but not men. **Conclusions:** There may be gender-related differences in the correlates of successful-aging related variables and optimism. Overall, optimism is associated with greater resilience, lower perceived stress and greater perceived control over one's function (personal mastery and self-efficacy)

## NR3-56

**SERVICE USE AND BARRIERS TO MENTAL HEALTH CARE IN MAJOR DEPRESSION AND COMORBID SUBSTANCE USE DISORDERS**

*Chair: Lian Yu Chen M.D.; Author(s): Rosa M. Crum, M.D., M.H.S., Silvia Martins, M.D., Ramin Mojtabai, M.D., Ph.D., M.P.H.*

#### SUMMARY:

**Objective:** Mental disorders in community and clinical settings are often comorbid with substance disorders. Yet, relatively little is known about the implications of this comorbidity for service use patterns and barriers to care. This study examines the service utilization patterns and perceived barriers to care among participants with major depressive episodes (M.D.E) with and without comorbid substance disorders in a large and representative community sample. **Methods:** We analyzed data from 187,864 adults aged 18 and above drawn from the National Survey on Drug Use and Health 2005-2009. We investigated differences in socio-demographic profiles, mental health service use patterns, and perceived reasons for not seeking mental health care among four groups of individuals: participants with past-year M.D.E only (N=11,192), past-year M.D.E with alcohol abuse/dependence (M.D.E+ALC, N=2,640), past-year M.D.E with illicit drug abuse/dependence (M.D.E+DRUG, N=998), and past-year M.D.E with alcohol and/or illicit drug abuse/dependence (M.D.E+ALC/DRUG, N=4699). Basic contingency analyses were followed by weighted bivariate and multivariate logistic regression analyses. **Results:** Compared to participants with M.D.E only, preliminary results showed that those with comorbid disorders were younger, more likely to be male and uninsured. Participants with M.D.E+DRUG showed significantly higher odds of inpatient care, outpatient care, medication treatment, and daycare program; while M.D.E only and M.D.E+ALC showed no significant differences with regard to these treatment modalities. However, participants with comorbid disorders were more likely than those with M.D.E only to report an unmet need for mental health care (M.D.E+ALC, aOR=1.51[1.28-1.78] and M.D.E+DRUG, aOR=2.39 [1.89-3.04]). Participants with comorbid disorders were more likely than those with M.D.E only to report fear of stigmatization, confidentiality concerns and transportation difficulty as barriers to mental health care seeking. Moreover, participants with M.D.E+ALC were more likely to endorse a pessimistic view on mental health treatments. **Conclusion:** Participants with comorbid substance disorders have a distinct pattern of service utilization and perceived for mental health care and experience a different set of barriers to mental health treatment seeking. The findings can contribute to planning of services and public health campaigns aimed at improving access to mental health services for this large group of individuals with mental health condition in community settings.

#### NR3-57

### PREVALENCE OF MEDICAL ILLNESSES IN PATIENTS WITH PSYCHOTIC DISORDERS: A RETROSPECTIVE CHART REVIEW STUDY

*Chair: Amy Shah M.D.; Author(s): Jessica Lammers, M.D., John Vraciu, M.D., John Wirick, M.D., Henry Nasrallah, M.D.*

#### SUMMARY:

Many studies have shown that patients with psychiatric disorders such as psychosis often suffer from one or more medical illnesses. There is a large body of literature about the presentation of obesity, diabetes, hyperlipidemia, and hypertension, referred to as the metabolic syndrome, which can be caused or exacerbated by some antipsychotic medications. In addition, medications chosen by primary care physicians to combat medical disorders in patients suffering from psychosis may occasionally worsen psychiatric symptoms. Therefore, good clinical care of patients suffering from psychotic and coexisting medical illnesses requires a background as a physician and as a psychiatrist. This chart review project will be conducted to assess the prevalence and type of serious medical problems in patients who are treated by senior psychiatric residents for a psychotic disorder in the setting of a teaching mental health outpatient facility, which is part of a UC Health system. **Methods:** Randomly selected medical records of up to 100 patients with psychotic disorders will be selected from the workload of each of several outpatient psychiatrists at a community mental health agency. The research psychiatrist(s) will screen each patient's chart for the following data: current age, age at diagnosis, weight and height, BMI currently and at first diagnosis, current AIMS score, involvement of a primary care physician, most recent lab data including TSH, renal, liver, lipid panels, most recent blood pressure, current living situation, current diagnoses, medications trials, and current medication regimen, as well as evaluation of when any medical problems started. **Procedures and data analysis:** At the completion of the data collection, the information will be analyzed using standard statistical software to assess for trends which demonstrate 1) the prevalence of serious medical problems in psychiatric patients with psychosis and 2) establish the importance and necessity of medical training, skills, and knowledge in the practice of psychiatric care.

#### NR3-58

### AN OVERVIEW OF SPECIALIZED FOLLOW UP OF CHILDREN WITH CONCURRENT AXIS I AND AXIS III DIAGNOSES

*Chair: Cristian Penciu M.D.; Author(s): Bharat Nandu, M.D., Rumana Rabmani, MS IV, Brittney Schumann, MS III, Anita Sinha, MS III, Syed Hussaini, M.D., Gary Rosenberg, M.D.*

#### SUMMARY:

Background: The U.S. residency training is steadily adopting system based learning through combining psychiatry residency programs within different specialties. As of December 2011, FREIDA Online database contains 11 combined internal medicine/psychiatry programs, 10 combined pediatrics/psychiatry/child and adolescent psychiatry programs and 7 family medicine/psychiatry programs. Pediatric emergency room (ER) visits due to psychiatric reason account for a significant number of ER visits. Objective: To analyze the coexistence of medical and psychiatric diagnosis within pediatric population referred to emergency room due to psychiatric conditions. Methods: We conducted a retrospective study in which we collected information about ER visits of the pediatric population over the past 1 year. We collected information about their referral sources, axis I diagnosis spectrum, axis III diagnosis, and their discharge disposition. Results: Our population consists of 323 pediatric ER visits because of psychiatric reasons. In our sample, 77(22%) were referred by a medical health professional, 56 (17%) were following up with a child psychiatrist, 125 (39%) carried an Axis III diagnosis. Their discharge dispositions were as follows: 224 (69%) were discharged with advice to follow-up with a psychiatrist, 46 (14%) were discharged to their families without further follow-up recommendation, 26 (8%) to other mental health professional/organization other than psychiatrist and 2 (1%) were discharged with plan to follow up with their medical doctor. Conclusion: Within our sample, a significant number of patients were found to have a medical diagnosis concurrent with a psychiatric diagnosis. More than half were recommended to follow up with a psychiatrist. This would suggest the need for supplemental combined specialties. None of our patients were followed by a combined specialty physician.

#### NR3-59

#### EFFECTIVE TREATMENT OF TRICHOTILLOMANIA WITH ARIPIPRAZOLE, AS AN ADJUNCT, IN A PATIENT WITH MAJOR DEPRESSIVE DISORDER: A CASE REPORT

*Chair: Yakir Vaks M.D.; Author(s): Sarah Sheikh, M.D., Amando Garza MSIII; Aditya Alawat MSIII; Arpi Koltougian MSIII.*

#### SUMMARY:

Background: TTM is a variant of the Obsessive Compulsive Disorder spectrum, and its symptoms have similarity shown to be influenced not only by serotonin but also by dopamine levels in different areas of the brain. Recent studies have also supported this theory by successfully treating patients with SSRI resistant TTM using pharmacological agents that block or decrease levels of dopamine. Aripiprazole, like most atypical anti-psychotics, acts on both the dopamine D2 and serotonin 5-HT1A receptors. It also manifests antagonistic effects at 5-HT2A receptors and postsynaptic D2 receptors. Several case studies have suggested that Aripiprazole may be a promising treatment for TTM. Other atypical anti-psychotic agents including Risperidone, Olanzapine and Quetiapine have also shown significant positive statistical outcomes in patients with SSRI-resistant TTM. Patients who completed at least 1 week of the atypical anti-psychotic Olanzapine during a flexible dose study were evaluated for hair pulling. The majority of patients showed a significant decrease in symptoms with a mean reduction of 66% from baseline using the MGHHPs. Methods: A patient was followed over the years in an outpatient clinic in a community psychiatric hospital in New Jersey. The study collected data by medical chart review. No contact with the patient was required, however, patient was given treatment on an outpatient basis. Data collected included dates the medication was prescribed with regular follow-up, medications prescribed for treatment on outpatient basis, DSM-IV diagnosis established from the initial visit to the current visits. Current literature was explored, a review of more than 10 articles was done and synthesized to be included in the study. Results: Several case studies have suggested that Aripiprazole may be a promising treatment for TTM. In a flexible dose study using Aripiprazole as a treatment modality on 12 subjects with TTM, the majority of subjects had greater than 50% reduction in hair pulling symptoms as per The Massachusetts General Hospital Hair Pulling Scale (MGHHPs). In our case report the patient had a significant improvement of hair pulling symptoms as well. Conclusion: Despite following the current evidence based treatment guidelines, many patients have poor response. According to the literature reviewed, as evidenced by several individual cases where patients have been successfully treated with different anti-psychotics, dopamine may have a much larger role in TTM symptoms than previously thought. Augmentation of an SSRI with aripiprazole can be an effective strategy for patients with TTM. Considering that aripiprazole is one of the atypical anti-psychotics with a better side effect profile in this class of medications, it should be viewed as an ideal candidate for further research in the treatment

of SSRI resistant TTM.

### NR3-60

#### A CASE OF KLEPTOMANIA TREATED WITH NALTREXONE AS AN ADJUNT TO FLUOXETINE

*Chair: Adrezza Ferrer M.D.; Author(s): Bharat Nandu, M.D., Daniela Kloos MS III*

##### SUMMARY:

Kleptomania is one of the least understood and studied psychiatric disorders and many times it is hidden by the coexistence of other psychiatric disorder including other impulse disorders. Many conflicting ideas are being presented about the etiology of this disorder. Some blame neurotransmitter imbalances and some categorize this illness as a symptom rather than a disorder. The reality is that patients suffering from this disorder also are experiencing constant emotional, financial and legal problems. Experience of guilt and shame consequent to kleptomaniac act, consequences of being caught or arrested and continuously violating the law are the outcomes of this psychopathology. The possibility of successful treatment by various psychotropic medications remained the long term area of concern. The aim of this case report is to discuss the unique case of kleptomania with uncontrollable stealing urges in a female patient who responded to nalrexone as an adjunct to fluoxetine and her urge related symptoms remain under controlled.

### NR3-61

#### COMPARING VIDEO GAME PLAY IN IMPULSE CONTROL DISORDER AND CONTROL CHILDREN

*Chair: Cristian Penciu M.D.; Author(s): Bharat Nandu, M.D., Syed Hussaini, M.D.*

##### SUMMARY:

**Background:** Children with Impulse control disorder tend to have difficulty sustaining tasks and play. There has been speculation that this tendency also applies to video game play, with Impulse control disorder children playing for shorter durations than children without Impulse control disorder. Limited research has been conducted in correlating video game use with Impulse control disorder, with one study concluding that there was no difference in video game use. **Objective:** This study compares video game playing time, in terms of hours per week and hours per session, between Impulse control disorder and control children. **Methods:** A randomized sample of 59 children aged 7-18 years presenting in an acute psychiatric setting

were administered a 21-item questionnaire to assess the different types of video games that they play, as well as the amount of time spent playing them. From the sample of 59 children, data was not included for a patient if the diagnosis, hours played per week, or hours played per session were not known. This divided our groups into 18 children with Impulse control disorder and 37 control children without Impulse control disorder. **Results:** The 18 children with Impulse control disorder averaged 13.9 hours of video game play time per week and 2.8 hours per session while the 37 children without ADHD averaged 12.8 hours per week and 2.5 hours per session. There was no significant difference in either of these groups at 95% and 90% confidence intervals. **Conclusion:** There is no significant difference in the video game usage of children with or without Impulse control disorder. Children with Impulse control disorder do not play for shorter durations than children without ADHD.

### NR3-62

#### ACNE EXCORIEE: A REVIEW

*Chair: Jillian Wong B.A.; Author(s): John Y. M. Koo, M.D.*

##### SUMMARY:

**Background:** Acne excoriée is a psychodermatological condition that refers to the behavior of picking or scratching at acne or skin with minor epidermal abnormalities. Though the patient has a skin condition, there is a primary psychiatric disturbance that focuses on acne. Patients with acne excoriée can have a variety of underlying psychopathology, but depression and anxiety appear to be the two most common underlying psychiatric conditions. Many patients also report compulsion for picking at the skin associated with poor self-image. We performed a literature review to illustrate the clinical presentation, work up, and treatment for acne excoriée. **Methods:** We conducted a search of Pubmed's Medline database of articles. Articles in English containing the words "acne excoriee" were reviewed. We examined reference lists to identify any missing articles, and 22 articles were included in the review. **Results:** **Clinical Presentation:** A patient with acne excoriée most commonly presents as a young Caucasian female with excoriated acne and scars. Patients tend to excoriate regions that are easily accessible. The patient with acne excoriée can have a distribution of lesions resembling the shape of butterfly wings on the back, referred to as the "butterfly sign." In the butterfly sign, there is sparing of the upper, lateral sides of the back bilaterally. **Work-up:** The approach for work up includes taking a thorough history, conducting a detailed physical examination, and assessing the patient for an underlying psychiatric disorder that may

be related to the condition. In particular, evaluating the patient for the exact nature of the underlying psychopathology such as depression, anxiety, and OCD is key. Treatment: For a patient with depression as the underlying cause, an antidepressant with psychotherapy can be provided. A patient with anxiety as the underlying source can use an anti-anxiolytic medication combined with psychotherapy. Patients with obsessive thoughts and compulsive urges can be given anti-OCD medication such as paroxetine and fluoxetine along with behavioral therapy to reduce the obsessions and compulsions. For mixed depression-OCD patients, SSRIs are the preferred choice of therapy. Pharmacologic therapy alone may not be effective if the patient is not motivated to control the compulsive urges; establishing therapeutic rapport is key. Conclusion: Working closely with the patient to serve his or her specific needs and establishing a solid therapeutic alliance can significantly improve outcomes.

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### **NR3-63 ASSOCIATION OF ATTACHMENT STYLE TO MEASURES OF IMPULSIVITY IN PSYCHIATRIC INPATIENTS**

*Chair: Melanie Kopp M.D.; Author(s): Azra Qizilbash, Thabell Tanis, Reetuparna Bhattacharjee, Dilini Herath, Irina Kopeykina, Igor Galynker, M.D., Ph.D., Lisa J. Cohen, Ph.D.*

#### **SUMMARY:**

**Objective:** Impulsivity and attachment styles have both been found to be associated with treatment outcome. There is little data, however, which evaluates the relationship between impulsivity and attachment styles. The current study aims to explore the relationship between three measures of impulsivity and four attachment styles. **Methods:** Impulsivity and attachment were assessed among 40 psychiatric inpatients (age 18-65) in treatment at urban medical center. Impulsivity was measured by the Barratt Impulsivity Scale (BIS-11), a 34 item self report questionnaire that assesses six components of impulsivity: attentional, motor, self-control, cognitive complexity, perseverance and cognitive instability impulsivity. Impulsivity was also measured by two neurocognitive tasks: the Balloon Analogue Risk Task (BART) a computerized behavioral task of risk taking propensity, and the Computerized Mirror-Tracing Task (MTPT-C) a non-verbal visuospatial test of distress tolerance. Attachment was measured with Relationship Style Questionnaire (RSQ), a 30-item self report measure with evaluates secure, fearful, preoccupied and dismissing attachment styles. **Results:** Correlations were computed between measures of attachment style (RSQ) and impulsivity (BIS-11,

BART, MTPT-C) for our sample of 40 psychiatric inpatients. Of these correlations we found that secure attachment was significantly negatively correlated with the attentional impulsivity and self-control problems on the BIS, but was not correlated with the neurocognitive measures of distress tolerance (MTPT-C) and risk taking propensity (BART). Preoccupied attachment was positively correlated with self-control problems, marginally correlated with attentional impulsivity and positively, though marginally, correlated with risk taking propensity. Dismissing attachment did not correlate with any impulsivity measures, while fearful attachment correlated marginally and positively with self-control problems. **Conclusions:** Attachment style may be related to impulsivity in psychiatric inpatients. As attachment styles and impulsivity have been found to be associated with treatment outcome, these findings warrant a greater consideration of both attachment styles and impulse control in the treatment of major psychiatric disorders. **References:** Bankston S, Carroll D, Cron S, Granmayeh L, Marcus M, Moeller F, Liehr, P: Substance abuser impulsivity decreases with a nine-month stay in a therapeutic community. *Am J Drug Alcohol Abuse* 2009; 35: 417-420. Joyce AS, Ogrodniczuk JS, Piper WE, Sheptycki AR: Interpersonal predictors of outcome following short-term group therapy for complicated grief: A replication. *Clin Psychol Psychot* 2010; 17: 122-135.

### **NR3-64 INTEGRATION OF MENTAL HEALTH AND PRIMARY CARE IN SCREENING AND TREATMENT OF POSTTRAUMATIC STRESS DISORDER IN THE VA CLINICAL SETTING**

*Chair: Elliot Lee M.D.; Author(s): Rachel Molander, M.D. Rachael Pluim-Bergmann Eileen Ahearn, M.D., Ph.D. Dean Krabn, M.D., MS*

#### **SUMMARY:**

In an effort to create seamless, population-based, veteran-focused care, the Veterans Administration has integrated mental health care into the primary care setting. The integrated model depends on PTSD screening for all primary care patients, followed by further evaluation by primary care physicians for positive screens. In this model, psychiatrists are embedded in primary care and serve as consultants to primary care physicians. Subsequent mental health care delivery can occur in the primary care setting for uncomplicated cases or may subsequently occur in specialty mental health clinics. The integrated care approach has been studied in the treatment of depressed primary care patients, but less is known about the successful level of referral and engagement of this



approach for Posttraumatic Stress Disorder (PTSD). In this study, we describe the care management of veterans who screened positive for PTSD in various VA primary care clinics. During the 1 year period of September 2009-2010, 804 veterans in primary care screened positive for PTSD using the 4 question PC-PTSD screen. One hundred and ten of the veteran were already enrolled patients in the mental health clinic. Sixty eight percent of the remaining 694 veterans had an integrated care evaluation by mental health staff in the primary care setting and 32% were diagnosed with PTSD. The use of telemental health allowed veterans at both rural and urban clinics to receive integrated care evaluation with equal likelihood in either setting. We analyzed the OIF/OEF veteran population separately to better understand the referral process for our newest veterans. Of the 305 OEF/OIF veterans who screened positive, 71.8% had an integrated care assessment and 67% of these veterans were subsequently referred to the mental health clinic. Ninety eight percent of veterans had documented assessment of a positive screen, with documented follow up from primary clinic or integrated care regarding treatment of their mental health symptoms. This high rate of follow up of mental health symptoms is indicative of the success of screening and the integrated care approach in the primary care setting for OEF/OIF veterans with PTSD symptoms.

**NR3-65**  
**DEPRESSION IN SARCOIDOSIS PATIENTS OF A TERTIARY CARE GENERAL HOSPITAL IN SOUTH INDIA**

*Chair: Arjun Lakshmana Balaji M.B.B.S Author(s): Abhishek Hulegar Ashok Ravindra Mehta M.D. FCCP Naveen C Kumar M.D.*

**SUMMARY:**

**Introduction:** Sarcoidosis is chronic multisystem granulomatous disorder of unknown etiology commonly affecting the respiratory system. Western literature describes varying rates (18-60% prevalence) of depression in patients with sarcoidosis. Direct neurological effect of sarcoidosis on central nervous system, chronicity of the disease, prolonged therapy is some of the factors hypothesized to be involved in the evolution of depression. This issue remains unexplored in developing countries like ours. Here we are reporting prevalence of depression in a cross-sectional sample of patients with sarcoidosis. **Methods:** Sample included 148 consecutive patients with a biopsy proven diagnosis of sarcoidosis, who visited department of pulmonology of Fortis Hospital, a private tertiary care general hospital, Bangalore, India, between September 2009 and October 2011. Hamilton depression rating scale

(HDRS) was administered to all patients. Patients with a score 7 or more were considered to be 'cases' of depression. **Results:** There were 63 (42.6%) males and 85 (57.4%) females in our study. Mean age was 48.14 years (SD= 12.6). Mean duration of symptoms was found to be 3.3 months (SD= 2.1). Prevalence of depression was found to be 25.7 % (Mild=23%, Moderate=2.7%). Mean HDRS score was 10.5 amounting to 25.7% depression. **Conclusion:** Prevalence of depression in patients with sarcoidosis appears to be higher than that of the general population. To our knowledge this is the first study in India to report prevalence of depression in sarcoidosis patients. Though, there are limitations (not a random sample, no structured interview was used to diagnose depression, not a prospective study, no comparative sample from the general population/patients with other medical disorders), this study brings to notice an important clinical issue consultation liaison psychiatry. Further prospective studies are urgently needed to study depression in sarcoidosis.

**NR3-66**  
**TRUE INTEGRATED CARE: THE ROLE OF COMBINED TRAINING IN FAMILY MEDICINE-PSYCHIATRY AND INTERNAL MEDICINE-PSYCHIATRY IN THE ERA OF INTEGRATION**

*Chair: Monika Jindal M.D.; Author(s): Erik Vanderlip, M.D.; Alison Lynch, M.D.*

**SUMMARY:**

The new APA President has boldly labeled the decade of 2010 to 2020 the era of collaboration between physical health/primary care and mental health. As more patients are enrolled in expanding coverage programs, it has become increasingly clear that psychiatrists will be working with primary care clinicians to expand their reach and effectiveness for the benefit of the population. The current fragmented system does not effectively take care of the whole patient. Persons suffering from chronic and severely disabling mental illness frequently have poor preventive health care. Moreover, many medical illnesses co-occur frequently with psychiatric disorders. For the last three decades, combined post-graduate training programs in internal medicine-psychiatry and family medicine-psychiatry have been created to address these issues and bridge the gap between mental health care and primary care. Combined graduates are experts in integrating medicine and psychiatry, and offer new models for psychiatric practice in integrated care settings. This includes pioneering psychiatrists' functionality in a) the patient centered medical home, b) collaborative care, c) accountable care organizations. It also includes training tailored to "borderland"

settings, such as pain centers, comprehensive heart centers, HIV clinics, substance abuse centers, sleep centers, and medicine-psychiatry units. In the evolving era of integrated care, the demand for this skill set and expertise is ever-increasing. However, competition for spaces in programs fluctuates dramatically and numerous programs have closed or are in the process of closing. A moratorium on the creation of new combined programs by the American Board of Psychiatry and Neurology has contributed to the uncertain future of combined training. This poster will feature a brief overview of the history of combined training programs in internal medicine-psychiatry and family medicine-psychiatry, evaluate the benefits of combined training on individual patient levels and larger system levels of care, and critically appraise the role of combined training within the context of greater mental health and primary care integration.

**NR3-67**  
**AN EXPERIMENT IN INTEGRATED CARE**  
**EDUCATION**

*Chair: Sosunmolu Shoyinka M.D.; Author(s): Rubin Moore M.D.*

**SUMMARY:**

With the current critical shortage of mental health care professionals (1)Integrated Care is poised to become a key model of mental health care delivery in the United States. There is evidence that up to 70% of mental health care is delivered in primary care settings while no show rates for specialty mental health care are high. Integrating Behavioral Health into Primary Care offers expanded access, reduced stigma and population-based psychiatric care. While the concept of Integrated care is rapidly gaining grounds in the mental health services arena, less attention is being paid to training the next generation of psychiatrists in delivering care within this model. The University of Missouri Community Psychiatry program offers a newly developed elective for senior residents in Integrated Care. This elective was developed specifically to expose residents in their 4th year to clinical experiences in delivering psychiatric care in an Integrated system. The Family Health Center in Columbia, Mo is a Federally Qualified Health Center that has recently partnered with the Burrell Behavioral Health system, a private, not for profit organization that provides a wide range of mental health services for individuals and families, under the auspices of a Missouri State grant, to develop integrated services. FHC serves 3 counties in Missouri, with a potential population of over 50,000 individuals. This population has a high prevalence of mental health needs, yet it's psychiatric services are limited to one psychiatrist half a day per

week, a mental health nurse, and a counselor. Beginning in July 2011, in partnership with the university of Missouri dept. of psychiatry, a yearlong half-day per week elective rotation was developed that enables a 4th year psychiatry resident to collaborate with Behavioral Health Consultants (master's level SW)to provide real-time consults to primary Care providers and thus both increase access as well as decreasing wait times to see the psychiatrist and APRN. The residents have access to attending supervision at all times but are encouraged be flexible and use their initiative ins solving problems, using an outpatient consultation - liaison model. The elective also offers valuable experience in treating co-occurring disorders. Initial feedback has been strongly positive both from the clinic staff and the trainee.

**NR3-68**  
**EXAMINING QUALITY OF LIFE IN A SAMPLE**  
**OF NARCOLEPTIC PATIENTS**

*Chair: Harnek Kablon, M.D.; Author(s): Meagan L. Dwyer, Ph.D., Suzanne Stevens, M.D., Shumaila Younas, M.D., Barry Liskow, M.D.*

**SUMMARY:**

Background: Narcolepsy is a sleep disorder characterized by excessive daytime sleepiness, cataplexy, sleep paralysis and hypnagogic hallucinations. Disturbed sleep at night, depression and anxiety has also been implicated in Narcolepsy. Narcolepsy impacts quality of life. The aim of the current study is to determine the impact of daytime sleepiness, disturbed nighttime sleep, cataplexy, and depression and anxiety symptoms on mental and physical aspects of narcoleptic patients' quality of life. Methods: Study sample consisted of 27 subjects who are treated in the sleep medicine clinic at the University of Kansas Medical Center. All subjects met the diagnostic criteria for narcolepsy, based on ICSD-R classification. Subjects filled out the questionnaire packet consisting of: Beck Depression Inventory-II (BDI-II), Beck Anxiety Inventory (BAI), Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), SF-36 for depression, anxiety, day time sleepiness, disturbed sleep at night and mental & physical health quality of life respectively. SPSS version 20 was used for all statistical calculations. Results: Participants endorsed an average Global PSQI score of 11.12 (SD = 4.61), a mean ESS score of 16.70 (SD = 5.66), average BDI- II score of 17.78 (SD = 12.42), and an average BAI score of 17.11 (SD = 12.10). 30% reported experiencing cataplexy. Linear regression was used to examine the impact of key variables on patients' mental and physical quality of life using SF-36 scores. The first model showed that ESS, PSQI, BAI, and BDI-II scores, along with the

patients' experience of cataplexy, significantly impacted their overall mental health quality of life (MQOL) ( $F = 7.23, p > .001$ ). However, only the BDI-II score was shown to be a unique significant predictor. This model accounted for 56.5% of the variance in MQOL. The second model showed that the same variables were significantly impacting patients overall physical health quality of life (PQOL) ( $F = 6.59, p > .001$ ). The second model accounted for 53.8% of variance in PQOL. In this model, only the PSQI global score was a unique significant predictor. Conclusion: In the current sample of Narcoleptic patients, many reported significant symptoms of anxiety and depression which appear to be common in this clinical population. We found that ESS, PSQI, BAI, BDI-II, and experience of cataplexy accounted for over 50% of the variance in both mental and physical QOL scores. However, only BDI-II was a unique significant predictor of MQOL, and only PSQI was a unique significant predictor of PQOL. The current study is somewhat limited, notably by the small sample size. The current findings imply that along with the typical sleep disturbances associated with Narcolepsy, depression and anxiety symptoms also play key roles in patients' QOL. Clinically this may suggest that providers assess for and treat these potentially comorbid conditions to improve patient QOL.

**NR3-69**  
**COMPARISON OF CLINICIAN RATED MHCT(HONOS-PBR)SCORES IN CLUSTER WITH STANDARD:IMPLICATIONS FOR A NEW FINANCING MENTAL HEALTH MODEL IN ENGLAND**

*Chair: Pratima Singh M.D.*

**SUMMARY:**

**Objective:** To examine to what extent the 'must score' items match to the MHCT gold standard when allocating patients to one of the 21 mental health payment by results care clusters. **Method:** This audit was undertaken as a part of a primary cluster validation exercise for the payment by results (PbR) implementation in a London mental health trust. The sample ( $n=2782$ ) consisted of all the MHCT clustering assessments done for working age adult and older adult patients allocated to a PbR cluster in the secondary care mental health trust in a 3 month period (Nov 2010-Jan 2011). The percentage of MHCT scores compatible with the range of acceptable 'must score' for the cluster was calculated for each cluster. For each of the 3 superclass- Non-psychotic, psychotic and organic there are cluster determining HONOS questions that must be scored within a range for a cluster membership. These are denoted by red 'must score' items in the

MHCT booklet which is the clinical gold standard to determine the correct cluster based on scores. The MHCT assessments were examined to see how closely they matched these definitions. The point of clustering for each assessment was then examined in turn to find out at which point was there most agreement between the clinical allocation and the MHCT. Results: This audit showed a wide variation (2-72%) in the clinician allocated score for a cluster compared to the required 'must score items for the cluster in the MHCT booklet. Agreement was better in clusters which have clear diagnostic coherence For Eg. Organic clusters 18-21 (91%), Cluster 15- Severe psychotic depression (78%) and in those clusters which have a wider range of acceptable 'Must score' HONOS scale. Eg Cluster 10- First episode psychosis (73%), Cluster 14- Psychotic crisis (85%) and Cluster 17- Difficult to engage (75%). The agreement between clinician and MHCT was best at the 'Significant change in need' and 'Discharge' points of clustering and lowest at new referral. Conclusion: The reasons behind variation in allocation of scores are multiple. It can be argued that the cross check for clustering accuracy by comparing clinician allocated score with the gold standard MHCT is a crude method as it does not take into account the full clinical complexity of a case. This way of checking for accuracy probably also applies only at the first assessment rather than at other points in the care pathway. After treatment has started a clinical change in the patients presentation (improvement, no change or decline) will make the scores fall out of those defined for the cluster. While the commissioners will seek assurance that clinician allocate patients to a PbR cluster accurately and while a national algorithm to guide cluster allocation is being built, more study is needed to explore reasons behind the variation and to tailor training targeting these issues to overcome some clinical biases.

**NR3-70**  
**PSYCHOTROPIC MEDICATION COST AWARENESS: A COMPARISON SURVEY EVALUATING KNOWLEDGE AND ATTITUDES OF RESIDENT AND ATTENDING PRIMARY CARE PROVIDERS**

*Chair: Satinder Mahal D.O.; Author(s): Aweekshit Tripathi M.D.*

**SUMMARY:**

**Background:** The treatment of patients with psychotropic medications is expensive. In 2009, there were 380 million total retail prescriptions for psychotropic medications with a net dollar cost over \$22 billion (Greenblatt et al 2011). Many physicians are unaware of medication costs as demonstrated

by previous studies (Wilbur 2008, Singh et al 2010). Expensive medications are prescribed despite the availability of cheaper medications with equal efficacy and availability (Lee 2004). These staggering costs present a financial burden to patients. Many of these studies have focused on general practitioners and fewer studies have evaluated psychotropic medications specifically. Here we will present data comparing the pharmacoeconomic knowledge, and attitudes of those practitioners who often prescribe psychotropic medications (primary care and psychiatry). Methods: Participants were recruited from a psychiatric and family medicine residency program and involved both attending and resident physicians. Data was collected during CME events. A questionnaire was designed addressing physician attitudes about decisional factors related to prescribing decisions (i.e. cost, tolerability, efficacy, availability and compliance). In addition, participants were asked to correctly price a month's supply of 25 most commonly prescribed psychotropic medications (Grohol 2010) at common starting doses. The opinions about previous academic training in pharmacoeconomics was also explored. Results: Preliminary data on a limited number of questionnaires (n=10 for each group) demonstrates total correct responses for the primary care group (mean= 16.4%) and for psychiatric physicians (mean = 20.4%). Both groups had similar attitudes with 80% of primary care and 70% of psychiatrists citing cost as an important factor. In addition, nearly 85% of total responders indicated that they felt their previous academic training did not adequately prepare them for cost conscious prescribing. Further data analysis is necessary to verify and expand upon these results. Conclusions: While most physicians rated cost as an important decisional factor, a majority were unable to identify the correct pricing of several commonly prescribed psychotropic medications. Furthermore, an overwhelming majority expressed a lack of education about pharmacoeconomics. This has profound implications for patient care. At the time of the conference, more data analysis, limitations, improvements, and directions for future research will be discussed.

**NR3-71  
DISRUPTED RESTING-STATE FUNCTIONAL CONNECTIVITY OF THE HIPPOCAMPUS IN MEDICATION-NAÏVE PATIENTS WITH MAJOR DEPRESSIVE DISORDER**

*Chair: Xiaobua Cao Ph.D.; Author(s): Zhifen Liu, Cheng Xu, Jianying Li, Qiang Gao, Ning Sun, Yong Xu, Yan Ren, Chunxia Yang, Kerang Zhang*

**SUMMARY:**

**Objective:** The hippocampus has been reported to exhibit structural and functional alterations in patients with major depressive disorder (M.D.D). But the functional relationships between this area and other regions are seldom investigated. The present study was to explore the functional connectivity patterns of the hippocampus in patients with M.D.D. **Methods:** Seed-based correlation analyses were performed in the resting-state functional magnetic resonance imaging data to examine differences in functional connectivity of the hippocampus between medication-naïve patients with M.D.D and healthy adults. Correlation analyses were done between clinical variables and the strength of functional connectivity in regions showing group differences. **Results:** Positive functional connectivity with the hippocampal-ROIs was seen mainly in bilateral limbic system, subcortical areas, temporal lobe, medial and inferior prefrontal cortex while negative functional connectivity was observed in bilateral prefrontal cortex, parietal and occipital cortex and the cerebellum. Group comparison showed decreased functional connections with the hippocampus in M.D.D, with decreased positive functional connectivity with the right hippocampal-ROI in the limbic regions and the cingulate gyrus, and decreased negative functional connectivity with the left hippocampal-ROI in bilateral prefrontal and parietal cortex. Negative correlations were seen between illness duration and the strength of functional connectivity in the prefrontal and parietal cortex. **Conclusion:** The above results suggest that abnormal functional relationships between the hippocampus and areas in the cortical-limbic mood regulation circuit may underlie the pathophysiology of M.D.D.

NR3-72

**LURASIDONE MONOTHERAPY FOR THE TREATMENT OF BIPOLAR I DEPRESSION: RESULTS OF A 6-WEEK, DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY**

*Chair: Presenters: Antony Loebel, M.D.*

*Authors: Josephine Cucchiaro, Ph.D., Robert Silva, Ph.D., Kaushik Sarma, M.D. Ph.D., Hans Kroger, MS, .; Joseph R. Calabrese, M.D. , Gary Sachs, M.D.*

**Summary:**

**Objective:** To evaluate the efficacy and safety of lurasidone, flexibly dosed at 20-60 mg/day or 80-120 mg/day, in the treatment of major depressive episodes in patients with bipolar I disorder without psychotic features.

**Methods:** Subjects meeting DSM-IV-TR criteria for bipolar I depression, with or without rapid cycling, with a Montgomery Asberg Depression Rating Scale (MADRS) score  $\geq 20$  and a Young Mania Rating Scale score  $\leq 12$ , were randomized to 6 weeks of once-daily, double-blind treatment with either lurasidone 20-60 mg (LUR20-60), lurasidone 80-120 mg

(LUR80-120) or placebo (PBO). Primary and key secondary endpoints were change from baseline to week 6 endpoint in MADRS and CGI-bipolar severity (CGI-BP-S) scores, respectively, analyzed using mixed model repeated measures (MMRM). Additional secondary outcome measures were analyzed using ANCOVA.

Results: Study completion rates were 74.1% in the LUR20-60 group (N=166; mean modal dose, 34.9 mg), 73.4% in the LUR80-120 group (N=169; mean modal dose, 92.3 mg) and 74.7% in the PBO group (N=170). Lurasidone treatment resulted in significantly greater MADRS score reduction at Week 6 endpoint for both the LUR20-60 group (-15.4;  $p < 0.001$ ; effect size=0.45 [based on ANCOVA-LOCF]) and the LUR-80-120 group (-15.4;  $p < 0.001$ , effect size=0.45) vs. PBO (-10.7). Both LUR groups separated significantly from PBO from week 2 onward. Lurasidone treatment resulted in significantly greater endpoint reduction in CGI-BP-S scores for both the LUR20-60 group (-1.8;  $p < 0.001$ ) and the LUR80-120 group (-1.7;  $p < 0.001$ ) compared with PBO (-1.1). Responder rates (reduction in MADRS  $\geq 50\%$ ) were significantly higher for LUR20-60 (53%) and LUR80-120 (51%) compared with PBO (30%;  $p < 0.001$  for both comparisons). Both LUR20-60 and LUR 80-120 groups also showed significant improvement vs. PBO ( $p < 0.01$ ) on the Hamilton Anxiety Rating scale, the Sheehan Disability Scale, the self-rated Quick Inventory of Depressive Symptomatology, and the Quality of Life, Enjoyment and Satisfaction Questionnaire. Discontinuation rates due to adverse events for LUR20-60 (7%) and LUR-80-120 (6%) were similar to PBO (6%). For LUR20-60, LUR80-120, and PBO, respectively, the most frequently reported adverse events were nausea (10.4%, 17.4%, 7.7%), headache (14.0%, 9.0%, 11.9%), and akathisia (7.9%, 10.8%, 2.4%). Minimal changes in weight, lipids and measures of glycemic control were observed.

Conclusion: Monotherapy with lurasidone, flexibly dosed at 20-60 mg/day or 80-120 mg/day, significantly reduced depressive symptoms in patients with bipolar I depression. Lurasidone treatment also significantly improved anxiety, self-rated quality of life and ability to function. Tolerability and safety of lurasidone was consistent with results of previous studies in schizophrenia. Sponsored by Sunovion Pharmaceuticals Inc., Marlborough, MA, and Fort Lee, NJ.

**SUNDAY MAY 06, 2012**

**New Research Poster Session 4**

## **MOOD DISORDERS**

### **NR4-01**

#### **THE TEMPERAMENT AND CHARACTER OF KOREAN SOLDIERS WITH MILITARY MALADJUSTMENT: A PRELIMINARY STUDY**

*Chair: Kyoungbo Han M.D.; Author(s): Sungbu Lee, M.D.*

#### **SUMMARY:**

Objective: Recently, there have been more increasingly discharged soldiers for military inadequacy with maladjustment after enlistment although the

qualification of medical and psychological screening tests on conscription in the Republic of Korea Army. Because these soldiers adversely affect the morale of the military force and efficacy, it's imperative to assess the characteristics of them. We supposed they have common personality problem. This study investigated the temperament and character of soldiers with military maladjustment based on Cloninger's psychological model. Methods: Maladjustment was defined as the soldier who was hospitalized at the medical unit to evaluate military discharge for maladjustment. Control that was defined as the soldier on active service at the medical unit participated in this study. Forty eight maladjustment soldiers and forty controls were enrolled from June to Nov. 2011. The Temperament and Character Inventory(TCI) measured the personality of participants. Chi square test, Fisher's exact test, Mann-Whitney test, multivariate analysis of covariance, logistic regression were performed to analyze the data. This study protocol was approved by the IRB of the Armed Forces Medical Command. Results: Maladjustment group showed significantly lower rank and shorter duration of service than control. The harm avoidance(HA) scores were significantly high in maladjustment group while reward dependence(RD), persistence(P), self-directedness(SD) and cooperativeness(C) scores low after controlling for rank and duration of service. Both groups had no significant difference in novelty seeking(NS) scores. The low C scores had significant effects on the military maladjustment. Conclusion: These results suggest that low level of C predict the military inadequacy Soldiers with maladjustment seem to have different personality characteristics from normal. They may have vulnerable personality not to adapt to military organization and experience premature military failure. Therefore, early detection of the soldiers with personality flaw by the assessment of personality may be important. Further researches with a large sample are necessary to confirm these results. Key Words: Military Maladjustment, Temperament, Character

### **NR4-02**

#### **EPIDEMIOLOGY OF ANXIETY DISORDER AMONGST HIGH SCHOOL STUDENTS (GRADE 5 TO 10) OF AN URBAN-METRO COMMUNITY IN MUMBAI**

*Chair: Amresh Shrivastava M.D.; Author(s): Anjali Karira, M.D., Nilesh Shab. M.D.,DPM,DNB, Amresh Shrivastava, M.D., DPM,MRCPsych, Anjali karira, Nilesh Shab, Amresh Shrivastava*

#### **SUMMARY:**

Introduction: Anxiety disorders constitute the most

common disorders of childhood and adolescence, which has marked effect on a child's development. Several studies show its prevalence ranging from 20-to-25% in general population and a lifetime estimate of approximately 15%. Several Psychosocial and environmental factors are associated with pattern and prevalence of anxiety disorder. It has impact on school performance and productivity and complex. Not much research has been done to explore prevalence and pattern of anxiety disorder in school going adolescents in urban population. We examined high school students in a population study for anxiety disorders. Methods: The study was conducted in the catchment area of the general teaching hospital in Mumbai. Study design was cross-sectional, population-based survey along with a clinical assessment done by trained mental health clinicians. Data was recorded in a structured interview format and analyzed using SPSS. Results: We conducted a survey of 450 students and conducted clinical evaluation of 111 students. Results showed that 36.7% students had DSM-IV anxiety disorder. Parents and students were successfully able to report anxiety as confirmed by clinical diagnosis; these students were young (mean age 11.2 years), with significant female predominance (female, 64.7% and male, 35.3%, ratio 1.8:1). Presence of anxiety was not associated with family type; language spoken or level of education in the parents. Interestingly more than 50% had no siblings. Commonest diagnosis was generalized anxiety disorder (17.8%) followed by social anxiety (15.8%), panic disorder (13.3%), and separation anxiety (5.6%). Discussion: Our findings suggest higher rate of anxiety disorder. It is likely that urban economic, and social factors are contributing to the psychopathology. We could not study the impact of anxiety disorder on performance and personality development, which could have given more clear idea of nature of intervention required. Conclusion: More than one third high school students in urban metro population of Mumbai suffer from a clinical and DSM diagnosis of anxiety disorder which was successfully identified by parents.

**NR4-03**  
**INTERNET SCREENING FOR ANXIETY DISORDERS: EFFECTS ON TREATMENT-SEEKING IN A THREE-MONTH FOLLOW-UP STUDY**

*Chair: Michael Van Ameringen M.D.; Author(s): William Simpson, BS Beth Patterson, BScN, Bed*

**SUMMARY:**

Objectives: The internet is an extensive resource for health information, which has assisted curious individuals to research their medical symptoms. This

may be especially common for sensitive, stigma-prone mental health issues. Numerous barriers prevent people from seeking proper mental health treatment, however little is known about the relationship between internet self-diagnosis and treatment seeking behaviour. Methods: A link to the MACSCREEN (a validated, self report screening tool for anxiety and depression) was posted on our research centre homepage as a free anxiety screening test. Three months after completing the MACSCREEN and a variety of symptom severity scales, respondents were emailed a follow up questionnaire asking about their treatment seeking behaviour. Results: Of the 494 participants who completed the MACSCREEN, 48 also completed the follow up questionnaire. The majority were highly educated, married (54.2%) women (83.3%) with a mean age of 33.5 ( $\pm$  11.4). Prior to completing the survey, 89.6% had planned to use the information in the MACSCREEN to seek further assessment. At 3 month follow up 62% reported seeking treatment from a health professional, and 58.3% reported searching the internet for further anxiety information. For those who did not seek treatment, the most common barriers were fear/lack of desire to take medication (50%), cost of therapy (27.8%) and symptoms not sufficiently severe (27.8%). In order to seek treatment, 50% reported that treatments would have to be more affordable and 39% said the severity of their anxiety would have to increase. When compared to those who did not complete the follow-up questionnaire, follow-up participants had higher rates of college education ( $p < 0.05$ ), and were more likely to have received previous treatment ( $p < .01$ ). All follow-up participants were assessed as having clinically significant diagnoses ( $p < .001$ ). Higher scores were found on the Sheehan Disability Scale ( $p < .01$ ), suggesting greater functional impairment as well as higher rates of Obsessive Compulsive Disorder ( $p < .001$ ), Generalized Anxiety Disorder ( $p < .05$ ) and Major Depressive Disorder ( $p < .001$ ) in the follow-up participants compared with those who did not complete the follow-up questionnaire. Conclusions: Individuals with significant mental health issues are using the internet to self diagnose. Two-thirds of respondents reported seeking treatment following the MACSCREEN, while 1/3 did not. Medication and cost of therapy were the largest factors preventing individuals from seeking help. While rates of specific disorders were higher in the follow-up group, there were no differences in severity measures, suggesting that perceived impairment is a stronger predictor of treatment seeking rather than overall disorder severity. Limitations include a potential selection bias, given the increased functional impairment and rates of prior treatment found in the sample who completed the follow-up questionnaire.

## NR4-04

**PHARMACOTHERAPY OF PANIC DISORDER: TAPERING OUT CLONAZEPAM AND PAROXETINE AFTER THREE YEARS OF TREATMENT**

*Chair: Antonio Nardi M.D.; Author(s): Marina D Mochcovitch, M.D.; Roman Amrein, M.D.; Rafael C Freire, M.D.; Alexandre M Valença, M.D.; Flavia Paes, MSc; Sergio Machado, MSc; Adriana C da Silva, Ph.D.; M Versiani, M.D.*

**SUMMARY:**

Efficacy and safety during treatment and drug discontinuation in panic disorder (PD) are mainly established in short- and intermediate term studies. We describe the successful tapering out of PD patients treated for 3 years with clonazepam or paroxetine or their combination. We selected 94 patients being asymptomatic from their PD for at least one-year after three years of drug treatment and wishful to leave the medication participated in this trial. The protocol envisaged a dose discontinuation phase protracted over 8 weeks and 12 months of follow-up. Patients were seen biweekly during the first 2 months and monthly afterwards. The dose of clonazepam was decreased in 2-week intervals by decrements of 0.5mg clonazepam until reaching 1 mg/day followed by weekly dose reduction of 0.25 mg; or 10 mg paroxetine until reaching 20mg/day followed by weekly dose reduction of 5mg. We used scales for anxiety, withdrawal symptoms and checked for recurrence of panic attacks. The mean dose at starting the tapering out was  $1.9 \pm 0.3$  mg/day of clonazepam and  $38.8 \pm 3.9$  mg/day of paroxetine. 57.8% of clonazepam and 18.2% of paroxetine patients were free of the medication after the 2 months of tapering as the protocol. 19 (26.0%) needed another 3 months to leave the medication. 9 (12.3%) of this last group used also mirtazapine as adjunct therapy during this period. 3 (4.1%) patients gave up the tapering due to return of anxiety symptoms. The withdrawal symptoms were mild and observed in 55 (75.3%) patients. No serious adverse events were observed. Insomnia, tremor, nausea, sweating, headache, and subjective anxiety were the main complains. Patients of the clonazepam group had during the withdrawal period fewer side effects/withdrawal symptoms than those of the paroxetine or combination group and significantly more patients of the clonazepam group were drug free, asymptomatic and without AE at the end of the first follow up year. It is possible to take the clonazepam and paroxetine slowly out even after a long treatment without any major withdrawal symptom. The dose should be tapered slowly and some adjunct drug may be useful for some cases.

## NR4-05

**LU AA21004 IN THE PREVENTION OF RELAPSE IN ADULT PATIENTS WITH GENERALISED ANXIETY DISORDER**

*Chair: David Baldwin M.B.B.S Author(s): Henrik Loft MSc, Ioana Florea M.D..*

**SUMMARY:**

**Purpose:** This study investigated the long-term maintenance of efficacy of Lu AA21004 at 5 or 10mg/day in the prevention of relapse in patients with generalised anxiety disorder (GAD) who had responded to acute treatment with Lu AA21004. This multimodal psychotropic agent is thought to work through a combination of two pharmacological modes of action: reuptake inhibition and receptor activity. In vitro studies indicate that Lu AA21004 is a 5-HT<sub>3</sub> and 5-HT<sub>7</sub> receptor antagonist, 5-HT<sub>1B</sub> receptor partial agonist, 5-HT<sub>1A</sub> receptor agonist and inhibitor of the 5-HT transporter [1]. In vivo nonclinical studies have demonstrated that Lu AA21004 enhances levels of the neurotransmitters serotonin, noradrenaline, dopamine, acetylcholine and histamine in specific areas of the brain [2]. **Methods:** 687 adult patients with a primary diagnosis of GAD (DSM-IV criteria) and a baseline Hamilton Anxiety (HAM-A) total score =20 received 20-week, open-label, flexibly dosed Lu AA21004 5 or 10mg/day treatment. From Week 8 onwards the dose remained fixed. 459 patients responded to treatment (HAM-A total score =10 at both week 16 and 20) and were randomised to 24-56 weeks of double-blind treatment with Lu AA21004 (n=229) or placebo (n=230). The pre-defined primary efficacy endpoint was the time to relapse in the double-blind period using a Cox model and the key secondary efficacy endpoint, under multiplicity control, was the time to relapse for patients responding to treatment for at least 12 weeks prior to randomisation. Relapse was defined as a HAM-A total score =15, or an insufficient therapeutic response, according to the investigator's clinical judgement. **Results:** The mean HAM-A total score was 28.4 at baseline and had decreased to 4.4 for patients randomised. The primary analysis showed a statistically significant effect of Lu AA21004 relative to placebo on the time to relapse of GAD, with a hazard ratio of 2.71 (Cox model,  $p < 0.0001$ ). Fewer Lu AA21004-treated patients relapsed (15%) compared with placebo (34%). The key secondary analysis also showed a statistically significant effect of Lu AA21004 relative to placebo in the 82% of patients who were stable responders with a hazard ratio of 3.06 (Cox model,  $p < 0.0001$ ). Lu AA21004 was well tolerated, with withdrawal rates due to adverse events (AEs) of 9% in the open-label period, and of 4% and 3% for Lu AA21004 and placebo, respectively, in the

double-blind period. In the open-label period, 76.9% patients reported an AE. In the double-blind period, the incidence of AEs was 53.9% (placebo) and 55.5% (Lu AA21004). The type and incidence of AEs reported after abrupt discontinuation of treatment suggest that Lu AA21004 did not cause discontinuation symptoms. No clinically relevant changes over time were seen in clinical laboratory tests, vital signs, weight, or ECG parameters. Conclusion: Lu AA21004 was efficacious in preventing relapse and was well tolerated in the maintenance treatment of GAD in this study.

#### NR4-06

### PSYCHOSIS IN SOCIAL ANXIETY PATIENTS: FRONTIERS OF PSYCHOPATHOLOGY

*Chair: Andre Veras M.D.; Author(s): Jeffrey P. Kahn, M.D. Antonio E. Nardi, Ph.D.*

#### SUMMARY:

Notably, patients with severe Social Anxiety Disorder (SAD) can experience self-referential psychotic perceptions. Four explanations seem possible for these psychotic manifestations in SAD: (1) preoccupation with any perception of criticism; (2) SAD is caused by a primary thought abnormality, leading to intense concern about the opinions of others; (3) heightened SAD and associated physiological stress contribute to yet more pronounced mental disorders such as delusional disorder; (4) SAD can evolve into a hypomanic state, often with psychotic symptoms. Case series: SAD patients who later developed psychotic symptoms. 1. Male. After a few weeks of abstinence from crack cocaine, he became unusually concerned about neighbors' opinions. He believed that local youths, with whom he had previously been involved in physical fights, mocked and teased him. 2. Male. He developed concerns about travelling alone on the street, which gradually intensified to the point where he had the strong impression that neighbors and passers-by laughed when he passed by, and made comments that indirectly questioned his sexual orientation. 3. Female. She had the impression that people avoided her when she walked on the street. She then began to worry that she had an offensive smell. During a family meeting, someone referred to her as "stinking." From then on, she was convinced she had a foul odor. 4. Female. After initial psychological stabilization, she developed an episode that included psychotic symptoms that her colleagues deliberately excluded her, that her parents had caused her marital separation, and that her psychiatrist was able to read her mind and feelings. 5. Male. He initially presented with SAD, responding well to SSRI and psychotherapy. About ten years later, long off medication, he returned to treatment. In addition

to recurrent SAD, he also had thoughts that people could read his mind, and that customers and colleagues viewed him negatively and dismissively. 6. Male. With a pronounced history of shyness and SAD since childhood, a young man later developed the conviction that people can read his mind, and that they could send him special messages. The distinction between anxious concern and delusion may be imprecise, and may fluctuate throughout the disorder's evolution. New diagnostic subcategories or the enlargement of the social anxiety diagnostic spectrum may better reflect this clinical phenomenology. There appears to be a symptomatic spectrum that ranges from shyness to SAD to psychotic features and on to delusional disorder.

#### NR4-07

### PREVALENCE OF SMOKING IN MODERATE TO SEVERE OCD

*Chair: Himanshu Tyagi M.D.; Author(s): Lynne M Drummond MRCP MRCPsych*

#### SUMMARY:

Background The prevalence of smoking is significantly higher in people with existing mental illness than those without mental health problems. Various reports from western countries indicate that 40-60% of all cigarettes smoked by general population are smoked by people with mental health problems. Data from the Adult Psychiatric Morbidity Survey 2007 in general population in England indicates that 32% of people with a common mental disorder smoke regularly as compared with 20% of people without a mental illness and 57% of people who had attempted suicide in the past year were smokers. Smoking rates vary with type of mental illness with the highest incidence in psychotic illness, followed by affective disorders. However the data for smoking in OCD appears to suggest huge variations, with some studies estimating the rates of smoking in OCD as lesser than that of the general population and others more in line with other anxiety disorders and depression. In light of this relative lack of conclusive research evidence, we decided to conduct this study. Method We investigated the prevalence of smoking in people who obtained outpatient treatment for OCD from a specialised service in south-west London over the period of one year between April 2009 and April 2010. We then compared the smoking rates in this sample with another large sample consisting of people receiving outpatient treatment for serious mental illness (psychosis or treatment refractory depression) from a community mental health team based in the same geographical area. Smoking data for every patient in our sample was collected and revised throughout the year as part of a quality improvement target for the local healthcare

commissioning body. OCD was diagnosed via diagnostic clinical interview in the specialised service. Standardised measures were used to capture information about the severity and nature of OCD symptoms. A factor analysis was performed to correlate prevalence of smoking with the severity of OCD. As a secondary aim, smoking rates in people receiving inpatient treatment for OCD were also calculated by using a sample from the National OCD treatment service based in south west London. Results Preliminary results indicate that the rates of smoking in OCD are significantly lower than that of general population and those treated for serious mental illness. This difference becomes even more significant with more severe OCD patients requiring inpatient treatment. Data for smoking in psychiatric inpatients without OCD is still being analysed.

**NR4-08**  
**PREVALENCE AND RELATED VARIABLES**  
**TO RISK OF ANXIETY DISORDERS IN**  
**COLOMBIAN MEDICAL STUDENTS**

*Chair: Adalberto Campo-Arias M.D.; Author(s): Heidi C. Oviedo, M.D. Edwin Herazo, M.D., MSc*

**SUMMARY:**

Background: Anxiety disorders are more frequent mental disorders in Colombian general population. Although, little information is available about the prevalence and related variables to risk of anxiety disorders in Colombian medical students. Objective: To know the prevalence and some related variables to risk of anxiety disorders in students from two medical schools in Colombia. Method: A cross-sectional study was designed. Medical students over 18 years old filled out a five-item version of the Zung's Rating Anxiety Scale (ZRAS); students with scores higher than ten were considered as at risk of anxiety disorders. A model of logistic regression was done to adjust related variables. Results: A sample of 667 medical students accepted to participate in the research. The mean of age was 20.9 years old (SD=2.7), 54.1% between 18 and 20 years; and 60.6% were females. The short version of ZRAS showed high reliability (Cronbach alpha 0.789 and McDonald omega 0.790). A total of 227 students (41.5%) were at risk of anxiety disorders. Female gender (OR=3.0; 95%CI 2.4-4.2), and younger age (between 18 and 20 years) (OR=1.4; 95%CI 1.0-1.9) were related to risk of anxiety disorders. Conclusions: A high percentage of Colombian medical students is at risk of anxiety disorders. Female and younger students present high risk. It is necessary to screen anxiety disorders among medical students.

**NR4-09**  
**INTERPERSONAL PSYCHOTHERAPY (IPT)**  
**FOR POSTTRAUMATIC STRESS DISORDER**

*Chair: John Markowitz M.D.*

**SUMMARY:**

Most empirically-based psychotherapies for posttraumatic stress disorder (PTSD) are based on exposing patients to reminders of trauma. Consensus and organizational (American Psychiatric Association, Institute of Medicine) guidelines endorse this approach. Exposure-based treatment works, yet not all patients tolerate this sometimes-grueling treatment. Moreover, individuals with high levels of dissociation may fare poorly in exposure-based treatments. We have developed interpersonal psychotherapy (IPT), a time-limited treatment with demonstrated efficacy in treating mood disorders and bulimia, as a non-exposure-based alternative to treating PTSD. IPT focuses 1) on affective attunement, which emotionally detached patients need; 2) on rebuilding social skills and interpersonal trust, which PTSD damages; and 3) on mobilizing social supports, whose lack predisposes to PTSD and whose provision aids recovery. This paper will present encouraging pilot data supporting IPT as a treatment for PTSD and describe an ongoing, NIMH-funded randomized clinical trial comparing 14 weeks of treatment with Prolonged Exposure, Relaxation, and IPT. This study assesses Reflective Function (emotional/interpersonal understanding) as a potential mediator and moderator of treatment outcome. The author will also present a social support theory of PTSD. IPT potentially offers an affect- and attachment-focused alternative to exposure-based treatments for PTSD.

**NR4-10**  
**COULD REM SLEEP BE A BIOLOGICAL**  
**BIOMARKER FOR ANXIETY DISORDERS?**

*Chair: Abid Malik M.D.*

**SUMMARY:**

Although interest in finding biological biomarkers for psychiatric illnesses has been longstanding, efforts to find biological biomarkers have not been very successful. It has been known for quite some time that most antidepressants suppress REM (rapid eye movement) sleep in depressed patients, normal controls and laboratory animals 1. Thus it is postulated that increased REM density could be a possible biological biomarker for depression 2. Several anti-depressant medications are FDA approved for anxiety disorders as well, such as Generalized Anxiety Disorder, Obsessive Compulsive Disorder and Panic Disorder, implying there may some commonality in the pathophysiology of depressive and anxiety disorders. There is a relative paucity of articles looking at electroencephalographic sleep

patterns in anxiety disorders. This review is an effort to summarize the REM sleep abnormalities in Generalized Anxiety Disorder, Obsessive compulsive disorder and panic disorder. Further research is needed to clarify the relationship of REM sleep in anxiety disorders. Reference: 1. Steiger A, Kimura M: Wake and sleep EEG provide biomarkers in depression : J Psychiatr Res. 2010 Mar;44(4):242-52. 2. Pillai V, Kalmbach DA, Ciesla JA: A meta-analysis of electroencephalographic sleep in depression: evidence for genetic biomarkers. : Biol Psychiatry. 2011 Nov 15; 70(10):912-9.

#### NR4-11

### **METHYLPHENIDATE TRANSDERMAL SYSTEM IN TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY DISORDER: ANALYSIS OF RESPONSES IN YOUNGER VS. OLDER ADOLESCENTS**

*Chair: Raun Melmed M.D.; Author(s): Robert L. Findling, M.D.*

#### SUMMARY:

Background: Attention Deficit Hyperactivity Disorder (ADHD) is a neurobiological disorder that may begin in childhood and often persists into adolescence. Treatment considerations in adolescents include a perceived need for symptom control, and desire for flexibility regarding treatment options. Efficacy and safety of the methylphenidate transdermal system (MTS) was reported in a Phase IIIb study of adolescents (162 males and 55 females). Efficacy and tolerability of MTS as a function of younger vs. older subjects from that study has not been previously reported. Methods: A randomized, double-blind, parallel-group, placebo-controlled, naturalistic study with dose optimization was conducted in subjects ages 13 to 17 years old diagnosed with ADHD by DSM-IV TR® criteria. A 5-week dose optimization period for both placebo transdermal system (PTS) and MTS (10 mg, 15 mg, 20 mg or 30mg M.P.H.) with 9-hr patch wear time was followed by 2 weeks of dose maintenance for both groups. Efficacy evaluations were post hoc analyses of the original study primary endpoint [mean change from baseline at study endpoint in ADHD-Rating Scale (RS)-IV total scores]. Results: Baseline mean (standard error, SE) ADHD-RS-IV total scores were 37.6 (0.81; MTS/n=76) and 38.3 (1.23; PTS/n=38) for 13-14 year-olds (Y), and 35.0 (0.87; MTS/n=67) and 34.7 (1.29; PTS/n=34) for 15-17Y. At study endpoint (last observation carried forward), the mean changes from baseline scores were: -18.6 (1.38; MTS) and -8.3 (2.02; PTS) for 13-14Y (P<0.001), and -18.9 (1.79; MTS) and -9.5 (1.89; PTS) for 15-17Y (P=0.001). This represents an approximate two-fold reduction in total

score for the MTS group, regardless of age group. Common treatment-emergent adverse events reported by =5% in the 76 MTS-treated 13-14Y were decreased appetite (n=21; 27.6%), irritability (n=11; 14.5%), headache (n=9; 11.8%), upper respiratory infection (URI; n=8; 10.5%), abdominal pain upper, nausea, anorexia, insomnia or dizziness (n=6; 7.9% each), weight decreased (n=5; 6.6%), and fatigue or nasopharyngitis (n=4; 5.3% each). In the 69 MTS-treated 15-17Y these events were decreased appetite (n=16; 23.2%), headache (n=9; 13%), nausea (n=8; 11.6%), URI (n=7; 10.1%), or irritability (n=5; 7.2%). Conclusions: Efficacy and tolerability of MTS is comparable in 13 to 14 and 15 to 17 year-old adolescents. MTS is an effective and tolerable long-acting treatment for ADHD, particularly in adolescents who may prefer the flexibility of the patch wear time.

#### NR4-12

### **A COMPARISON OF RATES AND REASONS FOR URGENT CARE UTILIZATION AMONG CHILDREN WITH ADHD TREATED WITH ATYPICAL ANTIPSYCHOTICS VS. NON-ANTIPSYCHOTICS**

*Chair: Keith Betts Ph.D.; Author(s): Steven R. Pliszka M.D. Vanja Sikirica, Phar M.D., M.P.H. Ryan Dammerman, M.D., Ph.D. Paul Hodgkins, Ph.D., MSc Tom Samuelson, B.A. Jipan Xie, Ph.D., M.D. Brigitte Robertson, M.D. Eric Q. Wu, Ph.D. M. Haim Erder, Ph.D.*

#### SUMMARY:

Objective: Atypical antipsychotics (AAPs) are sometimes prescribed for children with attention deficit/hyperactivity disorder (ADHD). This study compares the real-world rates and reasons for urgent care utilization between stimulant-treated ADHD children (6 to 12 years old) who switched to or augmented stimulants with AAPs vs. non-antipsychotic (NAP) medications (stimulants, guanfacine, atomoxetine, and clonidine). Methods: Patients aged 6-12 with an ADHD diagnosis (ICD-9 CM: 314.0x) and at least one stimulant fill between 01/2005 and 12/2009 were identified from a large U.S. commercial medical/pharmacy claims database. Patients were classified into two treatment groups based on whether they had a subsequent claim for an AAP or NAP medication, respectively. Patients with a psychiatric diagnosis for which AAPs are indicated were excluded. Patients in the AAP group were matched 1:1 to those in the NAP group using propensity score matching requiring an exact match on whether the AAP or NAP being a switched-to vs. augmenting drug. Propensity scores were generated from a logistic regression including demographics, treatments, resource utilization, costs and comorbidities during the 6 months

prior to treatment initiation. Reasons for urgent care utilization were analyzed using the ICD-9 CM code for the primary diagnosis. Mental health diagnoses were further categorized based on the DSM-IV. The percentage of patients with  $\geq 1$  hospitalization and  $\geq 1$  emergency room (ER) visit as well as the top reasons for urgent care utilization and ADHD-related utilization during the 12 months post treatment initiation were compared using McNemar's tests. Results: A total of 1,857 patients (358 switchers, and 1499 augmenters) were included in each of the matched cohorts. The baseline characteristics were well-balanced between the two cohorts. A significantly greater proportion of patients in the AAP group experienced hospitalization (84 [4.5%] vs. 34 [1.8%];  $P < 0.001$ ) and had  $\geq 1$  ER visit than in the NAP group (441 [23.8%] vs. 344 [18.5%];  $P < 0.001$ ) during the 12 months after AAP or NAP treatment initiation. Mood disorders were the most common reason for hospitalization among AAP patients and occurred significantly more frequently than in NAP patients (34 [1.8%] vs. 4 [0.2%];  $P < 0.001$ ). The leading cause of ER visits was accidents/injuries with a significantly higher rate in AAP patients (224 [12.1%] vs. 179 [9.6%];  $P=0.017$ ). The rates of ADHD-related hospitalization and ER visits were also numerically higher in the AAP group (14 [0.8%] vs. 7 [0.4%];  $P=0.127$  and 9 [0.5%] vs. 3 [0.2%];  $P=0.083$ , respectively). Conclusions: Stimulant-treated ADHD children who switched to or augmented with AAPs had significantly higher rates of urgent care utilization than NAP patients. Accidents/injuries and mood disorders were the primary reasons for ER visits and hospitalizations, respectively, and were less common in the NAP group. Supported by Shire Development Inc.

**NR4-13**  
**METHYLPHENIDATE TRANSDERMAL**  
**SYSTEM FOR TREATMENT OF ATTENTION**  
**DEFICIT HYPERACTIVITY DISORDER**  
**(ADHD) IN ADOLESCENTS: GENDER**  
**SUBGROUP ANALYSES**

*Chair: Robert Findling M.D.*

**SUMMARY:**

Background: Efficacy and safety of the once-daily methylphenidate transdermal patch (MTS) in teenagers was first reported in a Phase IIIb study of adolescents with 162 males and 55 females (ITT population). There is a greater prevalence of (ADHD) in males, and effects of MTS were not previously reported in adolescents by gender. Methods: A randomized, double-blind, parallel-group, placebo-controlled, naturalistic study with dose optimization was conducted in subjects ages 13 to 17 years old diagnosed with ADHD by

DSM-IV TR® criteria. A 5-week dose optimization period for both placebo transdermal system (PTS) and MTS (10mg, 15mg, 20mg or 30mg M.P.H.) with 9-hr patch wear time was followed by 2 weeks of dose maintenance for both groups. Efficacy evaluations were post hoc analyses of the original study primary endpoint [mean change from baseline at study endpoint in ADHD-Rating Scale (RS)-IV total scores]. Results: Mean (standard error, SE) baseline ADHD-RS-IV total scores were 36.9 (0.69; MTS/n=107) and 36.5 (1.00; PTS/ n=53) for males, and 35.1 (1.2; MTS/n=36) and 36.9 (2.08; PTS/n=19) for females. At study endpoint (last observation carried forward), the mean changes from baseline scores were: -19.0 (1.29; MTS) and -7.1 (1.47; PTS) for males ( $P < 0.001$ ), and -17.9 (2.22; MTS) and -13.8 (3.03; PTS) for females ( $P=0.290$ ). Among males, MTS therapy resulted in a reduction from baseline that was 2.6 times greater than observed for placebo. The corresponding reduction for females on MTS was 29% greater than placebo. Females on placebo exhibited a greater reduction than males treated with placebo, an observation that may have contributed to the lack of significance for that group, since the mean reduction for MTS among males and females was comparable. Common treatment-emergent adverse events reported by  $\approx 5\%$  in the 109 MTS-treated males were decreased appetite (n=25; 22.9%), nausea, headache, or upper respiratory tract infection (n=12; 11% each), irritability (n=11; 10%), and weight decrease, anorexia, dizziness, or insomnia (n=6; 5.5% each). In 36 MTS-treated females, common events were decreased appetite (n=12; 33.3%), headache (n=6; 16.7%), irritability (n=5; 13.9%), abdominal pain upper, influenza, nasopharyngitis, upper respiratory tract infection, or insomnia (n=3; 8.3% each), or weight decrease, nausea, dizziness, vomiting or viral infection (n=2; 5.6% each). Conclusions: In both males and females, MTS was associated with greater improvement from baseline compared to placebo. Failure to reach statistical significance among females may have been a function of the somewhat higher placebo response in that subgroup. MTS may be an effective and tolerable treatment option for either male or female adolescents with ADHD.

**NR4-14**  
**METHYLPHENIDATE TRANSDERMAL**  
**SYSTEM FOR TREATMENT OF ATTENTION**  
**DEFICIT HYPERACTIVITY DISORDER**  
**IN ADOLESCENTS: IMPACT OF PRIOR**  
**STIMULANT USE**

*Chair: Robert Findling M.D.*

**SUMMARY:**

**Background:** Efficacy and safety of the once-daily methylphenidate transdermal system (MTS) in teenagers was first reported in a Phase IIIb study of 217 adolescents ages 13 to 17 years. In that study, 56% of subjects were stimulant treatment-naïve (Naïve), and 44% had prior exposure to stimulant medication (STIM). Differences in MTS effects in these subjects have not previously been reported. **Methods:** A randomized, double-blind, parallel-group, placebo-controlled, naturalistic study with dose optimization was conducted in subjects ages 13 to 17 years diagnosed with Attention Deficit Hyperactivity Disorder (ADHD) by DSM-IV TR® criteria. STIM underwent 14-30 days washout of medication before the study. A 5-week dose optimization period for both placebo transdermal system (PTS) and MTS (10mg, 15mg, 20mg or 30mg M.P.H.) with 9-hr patch wear time was followed by 2 weeks of dose maintenance for both groups. Efficacy evaluations were post hoc analyses of the original study primary endpoint [mean change from baseline at study endpoint in ADHD-Rating Scale (RS)-IV total scores]. **Results:** Baseline mean (standard error) ADHD-RS-IV total scores were 36.0 (0.78; MTS/n=85) and 35.2 (1.22; PTS/n=36) for Naïve, and 37.0 (0.93; MTS/n=58) and 38.0 (1.32; PTS/n=36) for STIM. At study endpoint (last observation carried forward), mean changes from baseline scores were: -17.5 (1.44; MTS) and -10.8 (1.99; PTS) for Naïve (P=0.010), and -20.5 (1.72; MTS) and -6.9 (1.89; PTS) for STIM (P<0.001). Among the Naïve group, this represented a 62% greater reduction from baseline among adolescents receiving MTS compared to placebo; among STIM adolescents receiving MTS, the reduction was almost three-fold greater compared to placebo. Common treatment-emergent adverse events reported by =5% in the 86 MTS-treated Naïve subjects were decreased appetite (deAPP; n=25; 29.1%), irritability (n=15; 17.4%), headache (HA; n=14; 16.3%), upper respiratory tract infection (URI; n=10; 11.6%), nausea (NA; n=8; 9.3%), weight decreased or insomnia (n=7; 8.1% each), abdominal pain upper, anorexia or dizziness (n=6; 7% each), or fatigue (n=5; 5.8%). In the 59 MTS-treated STIM subjects, these events were deAPP (n=12; 20.3%), NA (n=6; 10.2%), URI (n=5; 8.5%), HA, nasopharyngitis or pharyngitis streptococcal (n=4; 6.8% each), application site pruritus, influenza, pharyngolaryngeal pain, epistaxis, or pyrexia (n=3; 5.1% each). **Conclusions:** MTS is associated with salutary effects in adolescents who were stimulant treatment-naïve or those with a history of stimulant treatment. MTS represents an option for patients with ADHD, who may benefit by switching to a flexible duration, long-acting stimulant medication, regardless of prior stimulant treatment.

**NR4-15****EFFICACY OF GUANFACINE EXTENDED RELEASE ADMINISTERED IN THE MORNING OR EVENING AS ASSESSED BY THE CONNERS' PARENT RATING SCALE-REVISED: SHORT FORM**

*Chair: Thomas Rugino M.D.; Author(s): Margaret D. Weiss, M.D., Carla White, BSc, CStat, Jonathan Rubin, M.D., MBA. Ryan Dammerman, M.D., Ph.D.*

**SUMMARY:**

**Objective:** To examine the efficacy, as assessed by Conners' Parent Rating Scale-Revised: Short Form (CPRS-R:S) total and subscale scores, of guanfacine extended release (GXR), administered either in the morning or evening, in children with attention-deficit/hyperactivity disorder (ADHD). **Methods:** Children (N=340 enrolled; 6-12 years) with ADHD were enrolled in this 8-week, double-blind, double-dummy, randomized, placebo-controlled, multicenter, dose-optimization study. GXR (1-4 mg/d) was administered once daily, either in the morning (GXR AM) or evening (GXR PM). The CPRS-R:S is a parent/guardian-completed assessment that consists of 27 questions grouped into 4 subscales: oppositional, cognitive problems/inattention, hyperactivity, and ADHD Index. Safety assessments included treatment-emergent adverse events (TEAEs). **Results:** Subjects in the GXR groups had significantly greater improvement from baseline to endpoint in overall CPRS-R:S total scores compared with placebo. At endpoint, placebo-adjusted least squares (LS) mean (95% CI) changes from baseline in the all-active, GXR AM, and GXR PM groups were: -11.6 (-16.2, -7.1), -12.5 (-17.8, -7.3), and -10.8 (-16.0, -5.6), respectively (P<0.001 for all). The GXR groups also had significantly greater improvements at endpoint compared with placebo in all CPRS-R:S subscales. At endpoint, placebo-adjusted LS mean (95% CI) changes from baseline for each subscale were: -2.0 (-2.9, -1.0), -2.2 (-3.3, -1.1), -1.8 (-2.9, -0.6) for oppositional; -2.7 (-3.9, -1.4), -2.7 (-4.2, -1.2), -2.7 (-4.1, -1.2) for cognitive problems/inattention; -3.1 (-4.2, -2.1), -3.5 (-4.7, -2.3), -2.8 (-4.0, -1.6) for hyperactivity; and -5.3 (-7.5, -3.1), -5.6 (-8.1, -3.1), and -5.0 (-7.5, -2.5) for ADHD index, respectively (P<0.003 for all). Effect sizes in the all-active, GXR AM, and GXR PM groups at endpoint for each subscale were: 0.664, 0.714, and 0.616 for CPRS-R:S total; 0.523, 0.579, and 0.469 for oppositional; 0.547, 0.551, and 0.542 for the cognitive problems/inattention; 0.761, 0.852, and 0.676 for hyperactivity; and 0.625, 0.660, and 0.590 for ADHD index, respectively. The most common TEAE in each group was somnolence (44.3%, 46.7%, 42.1%, and

12.5% for all-active, GXR AM, GXR PM, and placebo, respectively). Mean (SD) optimal doses were 2.9 (0.95), 2.9 (0.92), and 3.0 (0.98) mg in the all-active, GXR AM, GXR PM, and placebo groups, respectively. TEAEs of somnolence, sedation, or hypersomnia were reported by 55.7%, 57.0%, 54.4%, and 15.2% in the all-active, GXR AM, GXR PM, and placebo groups, respectively. Conclusion: Morning or evening administration of dose-optimized GXR was effective and generally well-tolerated in treating ADHD-related symptoms, as assessed by CPRS-R:S total scores. Additionally, in both dosing regimens GXR was similarly efficacious across all symptom domains: oppositional, cognitive problems/inattention, hyperactivity, and ADHD index.

**NR4-16**  
**EFFECT OF LISDEXAMFETAMINE DIMESYLATE ON SYMPTOMS OF HYPERACTIVITY/IMPULSIVITY AND INATTENTION IN CHILDREN AND ADOLESCENTS WITH ADHD**

*Chair: David Cogbill M.D.; Author(s): Richard Civil, M.D.; Andrew Lyne, MSc; Liza A Squires, M.D.*

**SUMMARY:**

**Objective:** To evaluate the effect of lisdexamfetamine dimesylate (LDX), the first long-acting, prodrug stimulant therapy for attention-deficit/hyperactivity disorder (ADHD), on symptoms of hyperactivity/impulsivity and inattention in children and adolescents with the disorder. **Methods:** This randomized, double-blind, placebo-controlled trial of an optimized dose of LDX (30mg, 50mg or 70mg) was conducted in children and adolescents (6–17 years of age) with ADHD at 48 sites in the European Union. The trial consisted of a 4-week dose-optimization period followed by a 3-week dose-maintenance period. Symptoms of hyperactivity/impulsivity and inattention were assessed using relevant subscales of the ADHD-rating scale (ADHD-RS). Osmotic release oral system methylphenidate (OROS-M.P.H.) was included in the study as a reference arm. **Results:** Of 336 randomized patients, 317 were included in the full analysis set (LDX, n=104; placebo, n=106; OROS-M.P.H., n=107) and 196 patients completed the study. At baseline, mean (SD) ADHD-RS hyperactivity/impulsivity subscale scores were similar across the treatment groups (LDX, 18.3 [6.27], placebo, 19.2 [5.10], OROS-M.P.H., 18.7 [5.48]), as were inattention subscale scores (LDX, 22.4 [3.41]; placebo, 21.8 [3.72]; OROS-M.P.H., 21.8 [3.50]). The difference between LDX and placebo in least-squares (LS) mean change from baseline (95% confidence interval [CI]) in hyperactivity/impulsivity subscale scores was statistically significant at study

endpoint (–8.7 [–10.3, –7.2],  $p < 0.001$ ), and at every on-treatment visit (weeks 1–7). For hyperactivity/impulsivity subscale outcomes at endpoint, the effect size (the difference in LS mean change between active drug and placebo divided by the root mean square error) for LDX was 1.603. Similarly, the difference between LDX and placebo in LS mean change from baseline in inattention subscale scores was statistically significant at endpoint (–3.8 [–5.3, –2.3],  $p < 0.001$ ). For inattention subscale outcomes at endpoint, the effect size for LDX was 1.715. At endpoint, there were also statistically significant differences in LS mean change from baseline between the reference OROS-M.P.H. and placebo for the hyperactivity/impulsivity subscale (–6.0 [–7.5, –4.5],  $p < 0.001$ ; effect size 1.107) and inattention subscale (–2.0 [–3.4, –0.5],  $p = 0.008$ ; effect size 1.218). Conclusion: At endpoint, symptoms of hyperactivity/impulsivity and inattention were reduced in children and adolescents with ADHD receiving LDX compared with placebo. Clinical research was funded by Shire Development Inc.

**NR4-17**  
**LISDEXAMFETAMINE DIMESYLATE IMPACT ON 2 SUBJECTIVE QUALITY OF LIFE SCALES IN ADULT ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND EXECUTIVE DYSFUNCTION**

*Chair: Lenard Adler M.D.; Author(s): Bryan Dirks, M.D.; Patrick Deas, BS; Aparna Raychaudhuri, Ph.D.; Ben Adeyi, MS; Keith Saylor, Ph.D.; Richard Weisler, M.D.*

**SUMMARY:**

**Objectives:** To examine lisdexamfetamine dimesylate (LDX) efficacy vs. placebo on 2 self-reported quality of life (QOL) measures in adults with attention-deficit/hyperactivity disorder (ADHD) and clinically significant executive dysfunction (EFD). **Methods:** In a randomized, double-blind, 10-week study of LDX vs. placebo of 161 adults (18–55 years) with ADHD and EFD (Behavior Rating Inventory of Executive Function-Adult Global Executive Composite baseline T-score  $\geq 65$ ), 154 participants completed the Adult ADHD Impact Module (AIM-A; key secondary); 54 participants completed both the AIM-A and the Adult ADHD Quality of Life (AAQoL) scales. This post hoc analysis compares results from the 54 participants who completed both self-reported QOL measures. The AIM-A multi-item scores were transformed to a 0 to 100 scale; higher scores indicating a better QOL. Safety assessments included treatment-emergent adverse events (TEAEs) and vital signs. **Results:** All AIM-A multi-item scales were numerically improved with LDX vs. placebo at week 10/endpoint/early termination (ET). Mean (SD) changes from baseline for LDX and

placebo, respectively, were 14.4 (9.59) and 6.3 (11.11) on Living With ADHD, 17.5 (14.75) and 7.9 (13.35) on General Well-Being; 38.9 (30.82) and 16.1 (20.39) on Performance and Daily Functioning; 32.1 (24.51) and 19.8 (25.67) on Impact of Symptoms: Daily Interference; 34.1 (23.14) and 18.4 (25.20) on Impact of Symptoms: Bother/concern; and 25.0 (18.46) and 11.3 (20.67) on Relationships/Communication. Numerical improvement with LDX vs. placebo, respectively, was seen also on the AAQoL. Mean (SD) changes from baseline were 38.6 (24.53) and 16.3 (21.57) for Life Productivity; 19.8 (22.07) and 6.7 (21.57) for Psychological Health; 19.2 (18.29) and 5.2 (12.76) for Life Outlook; 16.4 (19.85) and 10.6 (22.42) for Relationships; and 26.3 (16.19) and 10.7 (16.69) for Total Score. AIM-A multi-item subscales, Question 1: "How much would you rate the overall QOL right now?" and Question 4: "Over the past few weeks, I've had more good days than bad days," were numerically improved with LDX vs. placebo. Detailed safety results were reported elsewhere. The proportion of participants reporting any TEAE ( $\geq 5\%$  in either group) was 78.5% for the LDX group and 58.8% for placebo. Most participants reported TEAEs of mild or moderate severity, and there were no deaths or serious AEs. At week 10/endpoint/ET, small mean increases in vital signs were observed. Conclusions: With LDX, adults with ADHD/EFD showed numerical improvement on key AIM-A and AAQoL self-reported QOL domains. These findings were supported by post hoc analysis of changes for the same subgroup of participants on the AIM-A and AAQoL scales. The post hoc numerical trend toward a positive finding with LDX vs. placebo is promising and bears further study. The safety profile of LDX was consistent with that seen with other long-acting stimulants. Clinical research was funded by the sponsor, Shire Development Inc.

#### NR4-18

### URGENT CARE UTILIZATION FOR ADOLESCENTS TREATED WITH ATYPICAL ANTIPSYCHOTICS OR NON-ANTIPSYCHOTICS: A COMPARISON OF RATES AND REASONS

*Chair: Steven Pliszka M.D.; Author(s): Vanja Sikirica, Phar M.D., M.P.H., Keith A. Betts, Ph.D., Paul Hodgkins, Ph.D., MSc, Tom Samuelson, B.A., Jipian Xie, Ph.D., M.D., Ryan Dammerman, M.D., Ph.D., Brigitte Robertson, M.D., Eric Q. Wu, Ph.D., M. Haim Erder, Ph.D.*

#### SUMMARY:

Objective: Atypical antipsychotics (AAPs) are sometimes prescribed to adolescents for the treatment of attention deficit/hyperactivity disorder (ADHD). This study compares the real-world rates and reasons for urgent

care utilization between stimulant-treated ADHD adolescents who switched to or augmented stimulants with AAPs vs. those who switched to or augmented with non-antipsychotic (NAP) medications (stimulants, guanfacine, atomoxetine, and clonidine). Methods: Patients aged 13-17 with an ADHD diagnosis (ICD-9 CM: 314.0x) and at least one stimulant fill between 01/2005 and 12/2009 were identified from a large U.S. commercial medical/pharmacy claims database. Patients were classified into the AAP or NAP treatment group based on whether they had a subsequent claim for an AAP or NAP medication, respectively. The date of the subsequent claim is the index date. Patients with a psychiatric diagnosis for which AAPs are indicated were excluded. Patients in the AAP and NAP groups were matched 1:1 using a propensity score match requiring an exact match for mode of initiation (switching vs. augmenting). Propensity scores were generated from a logistic regression including demographics, treatments, resource utilization, costs and comorbidities during the 6 months prior to the index date. Reasons for urgent care utilization were analyzed using the primary diagnosis ICD-9 CM code. Mental health diagnoses were further categorized based on the DSM-IV. Rates of all-cause, top-cause, and ADHD-related hospitalization and emergency room (ER) visits were compared using McNemar's tests. Results: A total of 849 patients (187 switchers and 662 augmenters) were included in each matched cohort. The baseline characteristics were well-balanced between the two cohorts. A significantly greater proportion of patients in the AAP group experienced all-cause hospitalization (73 [8.6%] vs. 28 [3.3%];  $P < 0.001$ ) and ER visit (239 [28.2%] vs. 169 [19.9%];  $P < 0.001$ ) during the 12 months post index date. Mood disorders were the most common reason for hospitalization among AAP patients and occurred significantly more frequently than in NAP patients (42 [4.9%] vs. 7 [0.8%];  $P < 0.001$ ). The leading cause of ER visits among both cohorts was accidents and injuries with AAP patients having significantly higher rates (125 [14.7%] vs. 94 [11.1%];  $P = 0.026$ ). Rates of ADHD-related hospitalization were significantly higher (16 [1.9%] vs. 2 [0.2%];  $P=0.001$ ) in the AAP group, while rates of ADHD-related ER visits were numerically higher (3 [0.4%] vs. 2 [0.2%];  $P=0.655$ ). Conclusions: Stimulant-treated adolescents with ADHD who switched to or augmented with AAPs had significantly higher rates of all-cause and ADHD-related hospitalizations and all-cause ER visits than NAP patients. Mood disorders and accidents/injuries were the primary reasons for hospitalization and ER visits, respectively, and were more common in the AAP group vs. NAP cohort. Supported by Shire Development, Inc.

#### NR4-19

**THE HIDDEN COSTS OF ATTENTION DEFICIT/HYPERACTIVITY DISORDER (ADHD): A FOCUS ON SCHOOL AND WORK IN THE UNITED STATES**

*Chair: Doshi Jalpa Ph.D.; Author(s): Paul Hodgkins Ph.D. MSc, Jennifer Kable Ph.D., Vanja Sikirica Ph.D. M.D. M.P.H., Michael Cangelosi M.P.H. MA, Julian Setyawan MS Ph.D., Haim Erder Ph.D., Peter Neumann ScD*

**SUMMARY:**

Background The economic impact of ADHD extends to a variety of sectors besides health care. This review focuses on ADHD costs related to education among children and adolescents with ADHD, and income and productivity losses among adults with ADHD in the US. Methods A systematic review of MEDLINE, PsycINFO, EMBASE, and ERIC identified primary studies published between 1/1/1990 and 6/30/2011 reporting education- or productivity-related costs of ADHD. Only US-based studies in which mean annual incremental costs per ADHD individuals (compared with non-ADHD controls) were reported or could be derived were included. Eleven studies met the inclusion criteria. Data extracted included estimates of incremental costs of ADHD, cost components measured, year of cost data, and age range of the sample. Per person incremental costs were adjusted to 2010 dollars and converted to annual national excess costs of ADHD based on 2010 US census population estimates, ADHD prevalence rates, and employment rates by age group. Results Three studies reported ADHD-related education costs for special education, grade retention, and/or disciplinary incidents. The annual incremental cost of education for 3-4 year olds was reported to be \$12,447 per student whereas that for 5-18 year olds ranged from \$2,222 to \$4,690 per student. These estimates translate into national excess costs ranging from approximately \$15 to \$25 billion among 3-18 year olds in 2010. Two studies examined costs to individuals with ADHD due to lost income (i.e. unemployment or lower wages). One study found that young adults (19-25 years) with a history of ADHD had a significantly higher mean annual salary (\$3,744) than non-ADHD controls, largely because a significantly lower proportion was enrolled in college and thus more likely employed. The second study reported that annual household income was lower by \$10,532 to \$12,189 per ADHD adult when examined across the entire typical working age range of 18-64 years. Employer productivity losses due to employee absenteeism, presenteeism (i.e. poor performance while at work), disability payments, and/or workers' compensation ranged from \$209 to \$6,699 per 18-64 year old employee per year across six studies. These estimates translate into national excess costs

related to income and productivity losses ranging from approximately \$86 to \$138 billion dollars among 18-64 year olds in 2010. Conclusions While there is a wide range in the magnitude of the cost estimates derived from the reviewed studies, this analysis indicates that ADHD is associated with a substantial individual and societal impact in terms of income and productivity losses and education costs in the US. Through improved disease management and adherence to ADHD maintenance treatment(s), the educational and productivity burden of ADHD may be reduced, potentially producing savings for those institutions investing in their students' and employees' mental health.

**NR4-20**

**ADHD SYMPTOMS DURING MORNING, AFTERNOON, AND EVENING WITH GUANFACINE EXTENDED RELEASE TREATMENT ADMINISTERED IN THE AM OR PM**

*Chair: Joel Young M.D.; Author(s): Mark Stein, Ph.D., Carla White, BSc, CStat, Jonathan Rubin, M.D., MBA, Ryan Dammerman, M.D., Ph.D.*

**SUMMARY:**

Objective: To examine the efficacy, as assessed by the Conners' Parent Rating Scale-Revised: Short Form (CPRS-R:S), of guanfacine extended release (GXR), administered either in the morning or evening, in children with attention-deficit/hyperactivity disorder (ADHD). Methods: This 8-week, double-blind, double-dummy, randomized, placebo-controlled, multicenter, dose-optimization study enrolled children (N=340 enrolled; aged 6 to 12 years) with a diagnosis of ADHD. GXR (1-4 mg/d) was administered once daily, either in the morning (GXR AM) or evening (GXR PM). The CPRS-R:S was administered to parents/legally authorized representatives to assess the efficacy of GXR upon awakening (6:00 AM), at midday (2:00 PM), and in the evening (8:00 PM). Safety assessments included treatment-emergent adverse events (TEAEs). The previously-reported primary analysis revealed that GXR monotherapy (all active, AM, or PM administration) resulted in significant reductions in ADHD symptoms compared with placebo as measured by the ADHD Rating Scale IV (P<0.001 for all). Results: At endpoint, placebo-adjusted least squares mean (95% confidence interval) changes from baseline in the GXR all active, GXR AM, and GXR PM groups were: -11.9 (-16.9, -6.9), -13.4 (-19.1, -7.7), and -10.3 (-16.1, -4.6) at the morning assessment; -11.8 (-16.6, -6.9), -12.5 (-18.2, -6.8), and -11.0 (-16.6, -5.4) at the midday assessment; and -12.6 (-17.6, -7.5),

-13.2 (-19.0, -7.3) and -12.0 (-17.8, -6.2) at the evening assessment, respectively, ( $P < 0.001$  for all). Effect sizes in the GXR all-active, GXR AM, and GXR PM groups at endpoint were 0.638, 0.721, and 0.555 at the morning assessment; 0.633, 0.672, and 0.593 at the midday assessment; and 0.664, 0.693, and 0.633 at the evening assessment, respectively. The most common TEAE in each group was somnolence (44.3%, 46.7%, 42.1%, and 12.5% for all active, GXR AM, GXR PM, and placebo groups, respectively). Conclusion: Morning or evening administration of dose-optimized GXR was effective in reducing ADHD symptoms, as measured by the parent-reported CPRS instrument. Further, effect sizes were similar across each of the 3 circadian intervals assessed for the all-active group, as well as the GXR AM and GXR PM groups. These data support the hypothesis that GXR has a positive effect on ADHD symptom reduction throughout the day, regardless of time of administration. Additional studies, such as laboratory classroom studies are needed to further elucidate pharmacodynamic effects. The safety profile of GXR in this study was consistent with its known safety profile and appeared similar for morning or evening administration regimens.

**NR4-21**  
**EFFICACY OF LISDEXAMFETAMINE DIMESYLATE ON SELF- AND INFORMANT-REPORTED EXECUTIVE DYSFUNCTION IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER**

*Chair: Richard Weisler M.D.; Author(s): Lawrence Ginsberg, M.D.; Bryan Dirks, M.D.; Patrick Deas, BS; Ben Adeyi, MS; Lenard A. Adler, M.D.*

**SUMMARY:**

**Objective:** To examine lisdexamfetamine dimesylate (LDX) effects on self- and informant-reported executive function deficits (EFD) using the Behavior Rating Inventory of EF-Adult Version (BRIEF-A) in adults with attention-deficit/hyperactivity disorder (ADHD) and clinically significant EFD. **Methods:** A randomized, double-blind, parallel-group, 10-week study assessed LDX (30-70 mg/d) efficacy and safety vs. placebo in adults (18-55 years) with ADHD/EFD (in a domicile relationship with an informant for  $\geq 6$  months). **Efficacy measures included:** self-reported BRIEF-A Global Executive Composite (GEC) T-score (primary); informant-reported BRIEF-A indexes and subscales (secondary); Pearson correlation analyses of BRIEF-A indexes (post hoc). **Safety measures included** adverse events and vital signs. **Results:** Of 161 randomized, 154 (LDX, 79; placebo, 75) were included in the analysis.

Overall mean percent adherence was 97% for LDX and 99% for placebo at week 10/ early termination (ET). At week 10/ET for LDX and placebo, respectively, mean BRIEF-A GEC T-score change from baseline was -22.3 and -11.1 for self-reported, and -9.8 and -5.7 for informant-reported; LS mean difference (LDX-placebo) was -11.2,  $P < .0001$ , effect size [ES]= 0.74 for self-reported, and -4.9,  $P = .0016$ , ES=0.41 for informant-reported. Mean Behavioral Regulation Index (BRI) T-scores, for LDX and placebo, respectively, were -17.3 and -9.5 for self-reported and -8.3 and -5.9 for informant-reported; LS mean difference was -8.4,  $P = .0002$ , ES=0.55 for self-reported and -3.1,  $P = .0355$ , ES=0.25 for informant-reported. Mean Metacognition Index (MI) T-scores, for LDX and placebo, respectively, were -23.1 and -10.9 for self-reported, and -9.8 and -5.0 for informant-reported; LS mean difference was -11.6,  $P < .0001$ , ES=0.83 for self-reported, and -5.7,  $P = .0003$ , ES=0.49 for informant-reported. With LDX, self-reported subscale scores were lower ( $P \leq .0056$ ); informant-reported subscale scores were generally numerically improved. Pearson correlations of self- and informant-reported BRIEF-A indexes were generally greater at week 10/ET vs. baseline and were moderate. No new or unique safety finding with LDX were observed. Conclusion: LDX improved self- and informant-reported BRIEF-A indexes vs. placebo with medium to larger ES. Overall, ES was numerically greater for self- vs. informant-reported scales similar to other studies assessing self- vs. other ratings. Greater correlations at endpoint between self- and informant-reported BRIEF-A indexes may be related to improved observation over time by informants of impairment/improvement. Improvement may be secondary to greater self- and informant understanding of the nature and effect of core ADHD symptoms. If correct, clinicians who incorporate measurement-based care into traditional clinical care may facilitate awareness of improvement in disease impact and positively affect treatment adherence and outcomes. Clinical research was funded by the sponsor, Shire Development Inc.

**NR4-23**  
**COMPLETED SUICIDES IN THE UNITED STATES BETWEEN 1979 AND 2007: RELATIONSHIP TO AGE, SEX AND ANTIDEPRESSANT PRESCRIPTION PATTERNS**

*Chair: Arif Khan M.D.; Author(s): James Faucett, M.S., Roja Garimella, Maria A. Oquendo, M.D., Richard Weisler, M.D., Ashwin A. Patkar, M.D.*

**SUMMARY:**

Although the Center for Disease Control (CDC)

has been collecting detailed data on suicides and psychotropic use for over thirty years, it is unclear if these data can be used to evaluate suicide patterns associated with age and sex of the decedent. Furthermore, previous attempts to evaluate the relationship between epidemiological factors such as antidepressant use and suicide rates have proven difficult. We evaluated suicide risk for the years 1979 to 2007 using all available data from the Wide-ranging Online Data for Epidemiologic Research database from the CDC website. We based queries of suicide rates/100,000/year on gender and the three age group delineations identified by the Food and Drug Administration as potential markers for "suicidality"; 15-24, 25-64 and 65+. We also conducted a descriptive analysis of antidepressant prescription patterns from 1988 to 2008 with data reported by the National Center for Health Statistics to evaluate any relationship these patterns may have with completed suicides in the U.S. Our analysis addressed the variance of the male to female suicide ratio across age groups as well as the presumption of increased suicide risk in relation to aging for both genders. Suicide rates decreased most markedly (nearly 40%) among those 65 years and overs during the 29 year period. Suicide rates remained stable for adult males throughout the time period, and have increased 25% since 2000 for adult females after a decrease of 34% in that age group from 1979-1999. Male to female suicide ratio was significantly related to age group ( $p < 0.001$ ) with highest risk for males in those 65+ (6.8:1), followed by 15-24 (5.0:1). Male to female suicide risk ratio for adults 25-64 was 3.5:1. Suicide risk was linearly associated with age among men. However, this pattern was not seen among women, with the highest frequency of suicide among those aged 25-64. Although antidepressant prescriptions increased for women and men among all of the age groups in the US in the past three decades, the only reduction in suicide rates was among the older population. These data raise the possibility that there may be a differential response to antidepressant use on suicide rates based on the age of the decedents. This finding is in part supported by previous clinical trial data. In conclusion, the results of our study suggest that the suicide risk has decreased among the older age group in the US in past three decades. Overall, suicide risk is significantly associated with the age and sex of decedents.

**NR4-24**  
**EARLY DETECTION AND TREATMENT OF**  
**MENTAL ILLNESS WITHIN THE WORKPLACE**

*Chair: Helle Sorensen B.S.N.; Author(s): Povl Munk-Jørgensen, Professor, dr.med. Malene Krogsgaard Bording, MScS, Ph.D. student*

**SUMMARY:**

Introduction; Depression and anxiety are the most prevalent mental illnesses among employees leading to an increased number of sick days, decreased social and professional function, job satisfaction and quality of life. Around 25% of the working population is affected by psychiatric symptoms in a way that is painful to the individual, but not of such severity that it qualifies as a genuine disease. Untreated and not early identified these cases could lead to actual mental illness. Moreover, less than half of those currently suffering from depression are provided with the correct diagnosis in general practice, and less than half, diagnosed correctly, receive the proper medical treatment. Objectives; To identify, treat and thereby interrupt pre-existing cases of mental illness in the workplace. To prevent worsening of minor cases of psychiatric illness and symptomatic cases not considered a genuine disease. Aims; To develop models for early tracing and treatment of mental illness in the workplace with consequent improved health status and quality of life for the individual and improved economy for the workplace and the society. Methods; This study includes larger companies with more than 100 employees in the Region of North Denmark. The design is an intervention study using self-reporting questionnaires as a basis for identification of cases of mental illness and follow-up. The questionnaires use already tested instruments, e.g. SCL-90R, CAGE and Effort-Reward Imbalance scale (ERI). For determining the need for treatment, diagnostic clinical interview and examination are used. Results: Over a period of 3 years, 3 companies participated in the study. In general, the prevalence of symptoms decreased in the period. This applies to both the treated cases and the company in general. Within all the participants (N=369) there was a decrease in GSI (Global Severity Index) on 30,8%. For the treated cases (N=35) there was a decrease in GSI on 40,8% during the 12 month period from intervention start to last assessment. Looking solely at the depression subscale the decrease are respectively 32,3% and 56,8% - within the anxiety subscale 50,7% and 44,5%. Conclusion: The prevalence of symptoms decreases not only in the treated cases, but also generally in the company as a whole during the study period. The treatment effect on the treated cases seems to be persistent.

**NR4-25**  
**FACTORS PREDICTING PREMATURE**  
**DROPOUT OF TREATMENT AMONGST**  
**FEMALE SUBSTANCE ABUSERS**

*Chair: Aparna Iyer M.D.; Author(s): Victoria Balkoski, M.D.; Amanda J. Clemence, Ph.D.; Mark Lukowitsky, Ph.D..*

**SUMMARY:**

It is estimated that 21.8 million Americans are current substance users. (1) Substance addiction is a concerning public health issue, and even with treatment relapse rates can be as high as 40-87%. (2) Additionally, quality of life amongst substance users is consistently lower than that of a non-substance abusing individual, and an estimated cost to society of drug use, both in resource allocation and loss in productivity, exceeded \$510.8 billion in 1999 (2,4). In addition to the medical and psychiatric sequelae of addiction, it is especially problematic in women due to teratogenicity from illicit substances, as well as impaired parenting and impaired formation of healthy attachments with infants.(3) Although evidence exists on the effects of substance abuse on the general population as a whole, women with co-occurring substance abuse and mental health diagnoses are a relatively understudied population. Some studies suggest a link between premature dropout from substance treatment and certain variables including type of drug used, age, ethnicity, and gender (5,6,9). Review of the literature suggests an association between stress and prior failed treatments with relapse into substance use (7,8). One study suggests that a history of trauma is predictive of a higher likelihood for relapse amongst women, but not amongst men.(7) Studies indicate that insomnia is also linked to a higher relapse rate for substances. (10,11,12,13) One study reveals that those who are recently sober from alcohol endure some of the greatest sleep disturbances due to sleep-disordered breathing and periodic leg movements during sleep. (14) This study aims to elucidate the characteristics of early dropout and relapse within an already-vulnerable population of female substance users who are treated through a residential chemical dependency program. We conducted a chart review of 71 female patients who were not actively using substances but often continued to report heightened stress and sleep disturbances. These patients received psychiatric treatment through our clinic while concurrently receiving substance abuse treatment from a residential chemical dependency program. We predicted that insomnia, history of trauma, stress and failed prior treatments would be associated with a higher rate of premature dropout from psychiatric and substance treatments. Analyses of variance and chi square statistics were used to examine each variable's unique relationship with relapse, and regression statistics were used to determine which independent variables best predicted relapse when examined together. Results are discussed in reference to the benefit of detecting these characteristics during the admission process and for identifying them as an important part of successful treatment. Additionally, implications for future research are explored including how treatment can be adapted for

these groups of patients by addressing these issues with the goal of improving treatment completion.

**NR4-26****IMPACT OF THE MULTIMODAL ANTIDEPRESSANT LU AA21004 ON SEROTONIN TRANSMISSION IN THE RAT HIPPOCAMPUS**

*Chair: Maurice Lecours B.S.C.; Author(s): Mostafa El Mansari, Ph.D., Pierre Blier, M.D., Ph.D.*

**SUMMARY:**

**Background:** Currently, the majority of depressed patients do not achieve full remission after first-line treatment. Newer classes of antidepressants with more than one mode of action have the potential to increase remission rates and to minimize side effects. Lu AA21004 is a novel multimodal antidepressant that is a 5-HT<sub>3</sub> and 5-HT<sub>7</sub> receptor antagonist, a 5-HT<sub>1B</sub> receptor partial agonist, a 5-HT<sub>1A</sub> receptor agonist, and an inhibitor of the 5-HT transporter in vitro. **Methods:** In vivo electrophysiological recordings and stimulations of the ascending 5-HT bundle originating from the dorsal and median raphe nuclei were used to determine the effects of Lu AA21004 on CA3 hippocampal pyramidal neurons in male Sprague-Dawley rats anesthetized with chloral hydrate. Lu AA21004 was injected intravenously (2-6 mg/kg) in acute experiments or administered subcutaneously for 14 days, at a dose of 5 mg/kg/day via an osmotic minipump. **Results:** The recovery time from complete inhibition of pyramidal neurons after micro-iontophoretically applied serotonin (5-HT), an index of 5-HT transporter activity, was increased after 14-day administration of Lu AA21004. In contrast, the inhibition of CA3 pyramidal neurons after micro-iontophoretically applied 5-HT was unchanged. Injection of the 5-HT<sub>1A</sub> receptor antagonist WAY100635 increased CA3 pyramidal neuron firing, indicating an enhanced tonic activation of post-synaptic 5-HT<sub>1A</sub> receptors. Stimulation of the 5-HT bundle produced a decreased inhibition of the firing of CA3 pyramidal neurons at 5 Hz compared to 1 Hz. **Conclusion:** This study demonstrates that Lu AA21004 blocks 5-HT transporters, but does not dampen the sensitivity of postsynaptic 5-HT<sub>1A</sub> receptors. In addition, Lu AA21004 decreased the function of the terminal 5-HT<sub>1B</sub> autoreceptor, thus showing that its partial agonism led to increased 5-HT release. Long-term Lu AA21004 administration increased the tonic activation of the postsynaptic 5-HT<sub>1A</sub> receptor in the hippocampus, an effect common to all antidepressants. Further experiments are aimed at assessing the role of other 5-HT receptors for which Lu AA21004 possesses high affinity. This study was

sponsored by H. Lundbeck A/S as part of a joint clinical development program with the Takeda Pharmaceutical Company.

**NR4-27****FOUR HYGIENIC-DIETARY RECOMMENDATIONS AS ADD-ON TREATMENT IN DEPRESSION**

*Chair: Mauro Garcia-Toro M.D.; Author(s): Olga Ibarra M.D.; Margalida Gili Ph.D.; M<sup>a</sup> Jesús Serrano MA; Miquel Roca Ph.D., M.D..*

**SUMMARY:**

Individually modifying diet, exercise, sunlight exposure or sleep patterns may be useful in the treatment of Depression. However, these four hygienic-dietary recommendations have so far not been proven to be effective when prescribed together. Eighty depressive outpatients receiving anti-depressant treatment were randomly assigned either to a hygienic-dietary intervention or control group. Outcome measures were blind assessed both before and after the six month intervention period. The primary variable of efficacy of the study was the score of Hamilton Depression 17-item scale (HAM-D). Final Ham-D was 10.7 +/- 7.1 vs. 16.5 +/- 5.8; p:0.00. BDI and GCI also indicated a better evolution of depressive symptoms in the active treatment group. A higher responder and remitters rates and lower psychopharmacological prescription were observed in the hygienic-dietary group. This study suggests that hygienic-dietary recommendations can be an effective antidepressant complementary strategy when applied in daily practice.

**NR4-28****THE IMPACT OF COMORBID ANXIETY DISORDERS IN SUBSYNDROMALLY DEPRESSED PARTICIPANTS PRESENTING FOR A DEPRESSION PREVENTION RESEARCH INTERVENTION**

*Chair: John Kasckow M.D.; Author(s): J Karp M.D., E Whyte M.D., C Brown Ph.D., A Begley MS, S Bensasi BA, CF Reynolds M.D..*

**SUMMARY:**

Background: Subsyndromal depressive disorders in late-life are: 1) common in primary care; 2) associated with functional impairments (Lyness et al. Am J Geriatr Psychiatry, 15:214, 2007); and 3) frequently comorbid with anxiety disorders. Comorbid anxiety may worsen the "high stress" state and exacerbate the negative effect on functioning and health related quality of life. We examined psychiatric comorbidity in

subsyndromally depressed older individuals referred for an indicated depression prevention project that utilized Problem Solving Therapy adapted for primary care. We hypothesized that functioning would be better in those with subthreshold depression alone vs. those with subthreshold depression + comorbid anxiety. Methods: This NIMH-sponsored intervention included 237 participants, age 50 and older with CES-D scores > 10. We determined rates of psychiatric comorbidities among the participants using DSM-IV criteria. Results: Participants had 1 or more of 38 different DSM-IV diagnoses: 21.1% had no DSM-IV diagnosis; 37.1% had 1; 29.6% had 2, 7.6% had 3; 3.8% had 4; and 0.8% had 5 psychiatric diagnoses. The prevalence of these conditions will be presented. We compared levels of health related quality of life and psychosocial functioning in 3 groups of participants: 1) those with subthreshold depression only (n = 126), 2) those with subthreshold depression + a current DSM IV anxiety disorder (n = 58) and 3) those with subthreshold depression + a current comorbid anxiety disorder + a past history of an anxiety disorder (n = 33). Between the 3 groups, there were no differences in RAND12 physical or mental functioning composite scores. However, using the Late Life Function and Disability Instrument, we observed differences in Social Role Domain scores (F(2,173)=3.63, p=0.029). Post hoc testing showed that the 'subthreshold depression only' group had higher Social Role Domain scores than the 'subthreshold depression + current anxiety disorder' group [28.7 (5.5) vs. 21.1 (6.0) respectively]. Conclusions: In this sample of individuals with subsyndromal depression, many were diagnosed with a comorbid psychiatric condition. Many individuals exhibited current or past history of anxiety disorders in addition to having a subthreshold depressive disorder. Those having only subthreshold depression exhibited higher social functioning compared to those with subthreshold depression + a current anxiety disorder. Our findings suggest that it is important to consider screening subsyndromally depressed individuals for current anxiety disorders. Supported by P30 MH090333 and P60 M.D.000207 (CFR). The contents do not represent the views of the Department of Veterans Affairs of the US government.

**NR4-30****LU AA21004, A MULTIMODAL ANTIDEPRESSANT, IS ACTIVE IN A FLUOXETINE-INSENSITIVE RAT MODEL OF DEPRESSION AND ENHANCES COGNITIVE FUNCTION IN RATS**

*Chair: Connie Sanchez Ph.D.; Author(s): Alan Pehrson Ph.D., Thomas Cremers Ph.D., Liliana Pereira Montezinho Ph.D., Crista Trippodi Murphy1 MSc, Yan Li Ph.D., Maria*

*Gulinello Ph.D., Arne Mørk Ph.D.*

**SUMMARY:**

Purpose: Lu AA21004 is an investigational multimodal antidepressant that functions as a 5-HT<sub>3</sub> and 5-HT<sub>7</sub> receptor antagonist, 5-HT<sub>1B</sub> receptor partial agonist, 5-HT<sub>1A</sub> receptor agonist and inhibitor of the 5-HT transporter in vitro [1]. Here we investigate the nonclinical effects of Lu AA21004 on target occupancies, neurotransmitter levels in the brain, and responses in behavioral models of relevance for antidepressant activity and cognitive processing in rats. Methods: Occupancies of Lu AA21004 at the 5-HT<sub>3</sub> and 5-HT<sub>1B</sub> receptor and the 5-HT transporter were measured by ex vivo radioligand binding methods in rat brain slices, and 5-HT<sub>1A</sub> receptor occupancy was measured by in vivo cold competition, binding using liquid chromatography with tandem mass spectrometry detection. Effects on extracellular neurotransmitter levels of 5-HT, NE, DA, ACh and HA were measured in the prefrontal cortex by microdialysis in freely moving rats. The antidepressant potential, measured as performance in the forced swim test, was assessed after repeated dosing of Lu AA21004 (10 mg/kg/day po for 16 days) and compared to fluoxetine (16 mg/kg, po for 16 days) in female rats subjected to multiple progesterone withdrawals [3 rounds of 5-days on and 2-days off progesterone (6 mg ip)]. Finally, effects of Lu AA21004 on acquisition, consolidation and recall of contextual memory in rats were studied in the fear conditioning paradigm, and episodic memory was evaluated in the novel object recognition test. Results: Administration of Lu AA21004 (0.1-10 mg/kg, sc) demonstrated that the compound dose-dependently occupied the studied targets and that the in vivo potency ranking is in agreement with the in vitro potencies measured for the involved targets in the rat. Lu AA21004 (2.5-10 mg/kg, s.c.) dose-dependently increased extracellular levels of 5-HT, NE, DA, ACh and HA in the prefrontal cortex. In the progesterone withdrawal model, Lu AA21004 produced an antidepressant-like response in the forced swim test whereas fluoxetine was inactive. Finally, Lu AA21004 enhanced memory of the rats in the cognition models (5-10 mg/kg, s.c.). Conclusion: In agreement with its in vitro profile, Lu AA21004 engaged several targets at pharmacologically active doses in vivo. The net result of this multimodal mechanism of action was increased activity of several neurotransmitter systems, antidepressant-like effect in a disease relevant model that is insensitive to fluoxetine, and enhanced effects in nonclinical models of cognitive function. The multimodal activity profile of Lu AA21004 may translate into a unique therapeutic profile. 1. Bang-Andersen B, Ruhland T, Jorgensen M, et al (2011). Discovery of 1-[2-(2,4 -Dimethylphenylsulfanyl)phenyl]piperazine

(Lu AA21004): A Novel Multimodal Compound for the Treatment of Major Depressive Disorder. *J Med Chem* 54:3206-21.

**NR4-31**

**LU AA21004 EFFECTS ON ATTENTION AND VIGILANCE MEASURED AS EEG ACTIVITY IN THE RAT**

*Chair: Steven Leiser Ph.D.; Author(s): Paul J. Robichaud, MS Alan Pebrson, PH.D. Connie Sanchez, PH.D.*

**SUMMARY:**

Purpose: Sleep disturbances and electroencephalographic (EEG) measures of sleep are important predictors of depression. Depressed patients generally display disinhibition of REM (rapid eye movement) sleep resulting in shorter latency to the first REM period, longer time spent in REM, and increased REM intensity. Antidepressants, with few exceptions, suppress REM sleep. Serotonin (5-HT) is involved in regulation of sleep and waking functions such as cognition and mood; e.g., 5-HT<sub>1A/B</sub>, 5-HT<sub>2A/C</sub> and 5-HT<sub>3</sub> receptor antagonists promote REM sleep, prolong the duration of slow wave sleep (SWS), and enhance low-frequency (<7Hz) activity in the sleep EEG, a widely accepted marker of sleep intensity. 5-HT<sub>7</sub> receptor antagonists and 5-HT transporter (SERT) inhibitors promote wakefulness. Here we study the effects of the novel antidepressant Lu AA21004 on sleep EEG in rats. In vitro, Lu AA21004 is a 5-HT<sub>3</sub> and 5-HT<sub>7</sub> receptor antagonist, 5-HT<sub>1B</sub> receptor partial agonist, 5-HT<sub>1A</sub> receptor agonist and SERT inhibitor. As the affinity at the rat 5-HT<sub>1A</sub> receptor is lower than at the human receptor (K<sub>i</sub> 230 vs. 15 nM), a combination of Lu AA21004 and flesinoxan is included. Methods: EEGs were recorded from frontal and parietal cortices via a telemetric system (Data Sciences Int.) concurrent with locomotor and neck muscle (EMG) activity. These were manually scored as: SWS, paradoxical (REM) sleep, quiet wake (QW), or active wake (AW). A multi-day, 8-armed, Latin square, cross-over design (n=9) was used. Vehicle, flesinoxan (2.5), Lu AA21004 (5 & 10), alone or with flesinoxan, duloxetine (10), and escitalopram (2) mg/kg, s.c. were dosed between 9-10am (lights on at 6am) and analyzed 90-min pre-and 4-h post-dose. Results: The post-dose time to SWS was not significantly different for vehicle, escitalopram or Lu AA21004 (30, 40 & 65 min). Duloxetine, Lu AA21004 (5 or 10) plus flesinoxan, and flesinoxan alone significantly increased SWS latency (83, 133, 142 & 169 min). All treatments suppressed the total amount of REM. The total amount of SWS was suppressed by duloxetine, Lu AA21004 (5 or 10) with flesinoxan, and flesinoxan alone. QW was moderately higher with all treatments. AW was

increased 2.5-3 fold in all groups, except escitalopram. Quantitative EEG analysis showed that Theta, Alpha, Beta, and Gamma power were significantly increased during AW by Lu AA21004 (5 or 10) plus flesinoxan, and flesinoxan alone. The changes in EEG power were greater in the frontal cortex, a brain region that is central to high-level cognitive functions. Conclusions: Lu AA21004 may be uniquely primed for enhancing vigilance states through 5-HT<sub>1A</sub> receptor agonism, 5-HT<sub>7</sub> receptor antagonism and SERT inhibition, potentially without disrupting sleep quality due to its 5-HT<sub>3</sub> receptor antagonism. The elevated Alpha and Gamma power following Lu AA21004 in combination with flesinoxan suggests a strong role for the compound in modulating the cortical networks recruited during cognitive behaviors.

#### NR4-32

### EARLY IMPROVEMENT AS A PREDICTOR OF LATER TREATMENT RESPONSE IN ACUTE MANIC OR MIXED EPISODES USING CGI ASSESSMENTS: A POOLED, POST-HOC ANALYSIS

*Chair: Armin Szegedi M.D.; Author(s): Jun Zhao, Ph.D.*

#### SUMMARY:

**Objective:** To determine whether early improvement assessed using the Clinical Global Impression scale [CGI-BP mania or CGI- BP overall illness) can be used to predict treatment outcome in manic or mixed episodes in bipolar disorder. **Methods:** Pooled data from two 3-week randomized, double-blind trials were analyzed post hoc based on CGI-BP mania or CGI-BP overall illness scores. **Treatment groups:** flexible-dose asenapine (ASE; 5/10mg twice daily; n=372), olanzapine (OLA; 5–20mg once daily; n=391), or placebo (PBO; n=197). **Early improvement:** reduction from baseline CGI (baseline =4) by at least 1 point at days 2, 4 and 7; **Treatment response:** a score of “minimally ill” or “not at all ill” at Week 3; **Remission:** defined as “not at all ill”. **Odds ratios (OR)** measured the associations between early CGI-BP severity scores and later treatment outcome. **Sensitivity (SN), specificity (SP), and positive (PPV) and negative (NPV) predictive values** were also calculated. **Missing treatment outcomes for individual patients** were treated as treatment failures. **Results:** Early improvement was positively associated with treatment outcome. For CGI-BP severity of mania, associations were observed with ASE at day 2 for both mania response (P<0.03) and remission (P<0.01), OLA at day 4 for response (P<0.02) and remission (P<0.01), and PBO on day 7 for response (P<0.001) and remission (P<0.02). For CGI-BP overall illness, positive associations were observed with ASE at day 4

for both response (P<0.0001) and remission (P<0.0001), with OLA at day 4 for response (P<0.02) and remission (P<0.04), and PBO on day 7 for response (P<0.001) and remission (P<0.01). The OR [95%CI] for early improvement at day 2, 4 and 7 leading to later mania response were: 2.0[1.1-3.6], 5.1[3.0-8.7], 7.2[3.5-15.0] for ASE; 1.4[0.4-3.9], 1.8[1.1-2.9], 3.8[2.0-7.4] for OLA; and 1.2[0.4-3.9], 1.2[0.5-2.9], 5.8[2.2-15.8] for PBO. Respective mania response for SN, SP, PPV, and NPV at day 4 were: 71%, 68%, 42%, and 88% for ASE; 58%, 56%, 35%, and 77% for OLA; and 29%, 75%, 20%, and 83% for PBO. Odds ratios [95% CI] for early improvement at day 2, 4, and 7 leading to later mania remission were: 3.0[1.4-6.4], 11.8[4.0-34.4], infinite) for ASE; 1.8[0.8-4.0], 2.9[1.3-6.5], 4.5[1.3-15.4] for OLA; and 0.9[0.1-7.0], 1.3[0.3-5.1], 6.0[1.2-29.7]) for PBO. Respective remission for SN, SP, PPV, and NPV at day 4 were 88%, 63%, 19%, and 98% for ASE; 71%, 54%, 13%, and 95% for OLA; and 30%, 75%, 7%, and 95% for PBO. Overall illness yielded comparable OR data to mania. **Conclusion:** Early improvement with ASE, OLA, and PBO was associated with week 3 CGI-BP response and remission. A simple CGI assessment can be used by clinicians to tailor individual treatment within the first week of treatment. **Educational Objective:** Participant should be able to understand the clinical utility of CGI assessment in predicting later treatment outcomes in bipolar disorder. **Supported by Merck, Whitehouse Station, NJ.**

#### NR4-33

### MAINTENANCE TREATMENT WITH RISPERIDONE LONG-ACTING INJECTION VS PLACEBO IN SUBJECTS RECENTLY DIAGNOSED WITH BIPOLAR DISORDER: A SUBGROUP ANALYSIS

*Chair: Larry Alphs M.D.; Author(s): Dong-Jing Fu, M.D., Ph.D., Jennifer Kern Sliwa, Phar M.D., BCPP, Yi-Wen Ma, Ph.D., Cynthia A. Bossie, Ph.D.*

#### SUMMARY:

**Introduction:** Bipolar disorder is frequently associated with denial, poor insight, and poor adherence to medication. Recent evidence suggests that both pharmacotherapy and psychotherapy are more effective if instituted early in the course of treatment. Long-acting injectable therapies may be a valuable option because of knowledge of adherence and the wider window for follow-up dosing. This analysis evaluated the role of risperidone long-acting injection (RLAI) as maintenance treatment in subjects recently diagnosed with bipolar I disorder. **Methods:** A post hoc subgroup analysis of a randomized, double-blind study of RLAI monotherapy vs. placebo in the maintenance treatment

of bipolar I disorder (NCT 00132678) assessed subjects recently diagnosed ( $\leq 5$  years since diagnosis) or chronically ill ( $> 5$  years). Subjects who maintained response to RLAI for at least 26 weeks in an open-label stabilization phase were randomized 1:1 to placebo injections or RLAI (at open-label response dose) for up to 24 months. Recurrence was defined as (1) meeting DSM-IV-TR criteria for any bipolar mood episode; (2) intervention with a mood stabilizer, antipsychotic, benzodiazepine (beyond dosage allowed), or antidepressant; (3) hospitalization for any bipolar mood episode; (4) YMRS  $> 12$ , MADRS  $> 12$ , or CGI-S  $> 4$ ; or (5) increase in RLAI (or placebo) or supplementation with another antipsychotic or mood stabilizer.

Kaplan-Meier estimates of time to recurrent event were calculated, and log-rank tests compared groups. Results: 140/275 (50.9%) subjects were recently diagnosed and entered the double-blind maintenance phase ( $n=70$  RLAI,  $n=70$  placebo); 135/275 (49.1%) subjects were chronically ill ( $n=70$  RLAI,  $n=65$  placebo). For recently diagnosed subjects, time to recurrence of a mood episode was significantly longer with RLAI than placebo ( $P<0.001$ ). Median time to recurrence was not reached for RLAI and was 195 days for placebo. Recurrence rates were 31.4% and 60.0%, respectively ( $P<0.001$ ). Time to study discontinuation for any reason (including relapse) was significantly longer with RLAI than placebo ( $P<0.001$ ). Discontinuation rates were 48.6% and 82.9%, respectively ( $P<0.001$ ). For chronically ill subjects, time to recurrence of a mood episode was significantly longer with RLAI than placebo ( $P=0.002$ ). Median time to recurrence was not reached for RLAI and was 265 days for placebo. Recurrence rates were 28.6% and 52.3%, respectively ( $P=0.02$ ). Time to study discontinuation for any reason (including relapse) was significantly longer with RLAI than placebo ( $P=0.006$ ). Discontinuation rates were 50.0% and 70.8%, respectively ( $P=0.01$ ). Conclusions: RLAI significantly delayed the time to recurrence of a mood episode compared with placebo in both recently diagnosed and chronically ill subjects with bipolar I disorder. Placebo data suggest recently diagnosed subjects may perform worse during treatment withdrawal than chronically ill subjects. Funding, Janssen Scientific Affairs, LLC

#### NR4-34

### THE MULTIMODAL ANTIDEPRESSANT LU AA21004 BUT NOT ESCITALOPRAM REVERSES COGNITIVE DYSFUNCTION PRODUCED BY SEROTONIN DEPLETION IN RATS

*Chair: Alan Pebrson D.Phil.; Author(s): Kristian Gaarn du Jardin Nielsen BS, Jesper Borno Jensen BS, Connie Sanchez, DSc*

#### SUMMARY:

**Background:** Major depression is frequently associated with impaired cognitive function, including memory deficits, and the degree of the cognitive dysfunction is inversely related to response to antidepressants [1]. Acutely lowering central serotonin (5-HT) using tryptophan depletion causes dysfunction in mood and memory performance [2]. Here we describe cognitive deficits caused by 5-HT depletion in rats and evaluate the ability of escitalopram or the multimodal antidepressant Lu AA21004 to reverse these deficits. Lu AA21004 is a multimodal antidepressant that functions as a 5-HT<sub>3</sub> and 5-HT<sub>7</sub> receptor antagonist, 5-HT<sub>1B</sub> receptor partial agonist, 5-HT<sub>1A</sub> receptor agonist and inhibitor of the 5-HT transporter (SERT) in vitro. **Methods:** General design: 5-HT was depleted in female rats by administration of the irreversible tryptophan hydroxylase inhibitor 4-chloro-DL-phenylalanine methyl ester HCl (PCPA; 100 mg/kg/day, s.c., 4 days). Memory performance was assessed in novel object recognition (NOR) and spontaneous alternation (SA) tasks after acute administration of vehicle or drug. **Experiment 1:** PCPA-treated females were administered either vehicle or 1mg/kg carbidopa + 50mg/kg of the 5-HT precursor, 5-hydroxytryptophan (5-HTP). **Experiment 2:** PCPA-treated females were administered vehicle, 10mg/kg Lu AA21004 or 0.50mg/kg escitalopram (s.c.) and compared to control rats. **Experiment 3:** A dose-response curve was generated by administering vehicle, 0.1, 3, or 10mg/kg Lu AA21004 to PCPA-treated animals. **Results:** Experiment 1: PCPA treatment significantly impaired memory performance in NOR ( $F(2,22)=9.6, p<0.01$ ) and SA tasks ( $F(2,19)=10.8, p<0.001$ ). Restoring central 5-HT levels with acute 5-HTP treatment normalized cognitive performance. **Experiment 2:** PCPA-treated females were significantly impaired in NOR ( $F(3,28)=13.7, p<0.0001$ ) and SA performance ( $F(3,27)=19.2, p<0.0001$ ). Treatment with Lu AA21004 improved PCPA-induced memory deficits, while escitalopram had no effect. These differences were found despite similar SERT occupancies. **Experiment 3:** Lu AA21004 improved memory compared to PCPA alone in NOR ( $F(4,45)=6.5, p<0.001$ ) and SA ( $F(4,47)=4.8, p<0.01$ ) performance at all doses tested. **Conclusions:** The current study demonstrates that 5-HT depletion induced with PCPA leads to robust and reliable deficits in memory, as assessed by NOR and SA performance. Treatment with the 5-HT precursor 5-HTP or Lu AA21004, but not escitalopram normalized cognitive function. These data imply that Lu AA21004's actions at targets other than SERT have pro-cognitive effects that may prove important in treating depression. **Funding:** This study was jointly sponsored by H. Lundbeck A/S and the

Takeda Pharmaceutical Company.

#### NR4-35

### EFFECT OF MONITORING DEPRESSION SEVERITY ON PATIENT BEHAVIOR IN THE CLINICAL OUTCOMES IN MEASUREMENT-BASED TREATMENT (COMET) TRIAL

*Chair: Trina Chang M.D.; Author(s): Yonghua Jing, Ph.D., Albert S Yeung, M.D., Susan K Brennehan, Ph.D., Iftekhar Kalsekar, Ph.D., Tony Hebden, Ph.D., Robert McQuade, Ph.D., Lee Baer, Ph.D., Jonathan L Kurlander, MS, Angela K Watkins, MA, Jean A Siebenaler, M.D., Maurizio Fava, M.D.*

#### SUMMARY:

The COMET trial results demonstrated that patients whose primary care physician received monthly feedback regarding their depression severity had more favorable clinical outcomes than usual care patients after statistical adjustment, although no significant differences in prescribing practices were observed. In this secondary analysis, patient behaviors that might mediate clinical outcomes were examined. Patients with major depressive disorder were recruited by primary care physicians who had been assigned to either the intervention or usual care arm. Intervention-cohort patients completed the Patient Health Questionnaire (PHQ-9) during a telephone interview each month and results were faxed to their physician. Usual care patients were interviewed at 3 and 6 months and PHQ-9 results were sent at study end. Both patient cohorts were asked about medication-taking, psychotherapy/counseling, and depression support group participation at 3 and 6 months. Multivariate regression analyses were used to assess the impact of study arm assignment on patient behaviors while adjusting for demographic and baseline clinical characteristics. Of the 915 enrolled patients, 73% completed the month 6 interview (284 usual care; 380 intervention). At 3 months, adjusted odds of current antidepressant use were approximately 70% greater for intervention patients (OR 1.69; 95% CI 1.14-2.52;  $P=.010$ ) and at 6 months adjusted odds were 85% greater (OR 1.85; 95% CI 1.15-2.97;  $P=.011$ ). Regardless of intervention or usual care cohort status, at 3 and 6 months, respectively, 13% and 15% of patients reported choosing at least once in the past month to skip medication because they were feeling better. Approximately half reported never forgetting to take their medication. Intervention cohort status did not significantly affect the odds of forgetting or skipping medication. A significantly greater percentage of intervention patients reported support group participation at 3 (4% vs. 0.4%;  $P=.001$ ) and 6 (4% vs. 1%;  $P=.006$ ) months; adjusted odds

were also significantly greater for the intervention group (OR 2.98; 95% CI 1.35-6.57;  $P=.007$ ). Psychotherapy/counseling participation did not differ significantly between the cohorts. The mean number of physician-reported office visits per patient (2.9 SD 2.1) did not differ significantly between the cohorts, and no significant intervention effect was detected in multivariate analysis. In conclusion, of the variables studied, only current medication use and support group participation were found to be significantly more frequent for patients in the intervention arm. It is therefore reasonable to speculate that the improved outcomes observed in those depressed patients who had more frequent symptom measurement might have been due, at least in part, to greater medication persistence or support group participation. Funded by Bristol-Myers Squibb and Otsuka Pharmaceutical Co, Ltd.

#### NR4-36

### DIFFERENTIAL REGULATION OF 5-HT<sub>1B</sub> RECEPTORS BY ESCITALOPRAM AND THE MULTIMODAL ANTIDEPRESSANT LU AA21004

*Chair: Todd Hillhouse M.S.; Author(s): Alan L Pebrson Ph.D., David Budac Ph.D., Connie Sanchez DSc*

#### SUMMARY:

Background: Lu AA21004 is a multimodal antidepressant that functions as a 5-HT<sub>3</sub> and 5-HT<sub>7</sub> receptor antagonist, 5-HT<sub>1B</sub> receptor partial agonist, 5-HT<sub>1A</sub> receptor agonist and inhibitor of the 5-HT transporter (SERT) in vitro. Lu AA21004 induces larger extracellular [5-HT] increases in the ventral hippocampus (vHC) than escitalopram [1]. We hypothesized that this difference is mediated via differential actions at 5-HT<sub>1B</sub> receptors. Methods: Experiment 1: vHC 5-HT was evaluated using microdialysis as the 5-HT<sub>1B</sub> agonist CP94253 was locally perfused at 30, 300, and 3000 nM. Experiment 2: LuAA21004 10 mg/kg s.c. or escitalopram 1.6 mg/kg s.c. was administered in the presence or absence of a sub-effective CP94253 concentration. Experiment 3: A dose-occupancy curve was developed for Lu AA21004 (0, 2.5, 5.0, 10.0 mg/kg, 1 h s.c.) and escitalopram (0, 0.49, 1.6, 4.9 mg/kg, 1 h s.c.) at the SERT and 5-HT<sub>1B</sub> receptors using ex vivo autoradiography. Results: Local CP94253 administration had no effect on vHC [5-HT] at 30 or 300 nM, but significantly increased [5-HT] at 3000 nM ( $F(3,20)=23.87$ ,  $p<0.0001$ ). Lu AA21004 increased [5-HT] to a greater extent than escitalopram ( $F(4,22)=23.78$ ,  $p<0.0001$ ). Co-administration of 300 nM CP94253 to Lu AA21004 or escitalopram significantly reduced [5-HT] compared to systemic administration alone. Although [5-HT] was comparable in

LuAA21004+CP94253 and escitalopram alone groups, CP94253 reduced [5-HT] by a similar proportion in Lu AA21004- (26%) and escitalopram-treated (33%) rats. Occupancy experiments found that Lu AA21004 10 mg/kg and escitalopram 1.6 mg/kg occupied a similar proportion of the SERT (95% and 94%, respectively). At the 5-HT<sub>1B</sub> receptor, Lu AA21004 10 mg/kg reduced 5-HT<sub>1B</sub> receptor-specific radioactivity in a manner consistent with 79% occupancy, but escitalopram significantly increased 5-HT<sub>1B</sub> receptor specific radioactivity ( $F(4,10)=10.4$ ,  $p<0.01$ ). There was a significant positive correlation between escitalopram brain exposure and 5-HT<sub>1B</sub> receptor-specific radioactivity ( $r=0.84$ ,  $p<0.001$ ). Conclusions: Although local activation of 5-HT<sub>1B</sub> receptors using a 5-HT<sub>1B</sub> receptor agonist counteracted the increased extracellular [5-HT] produced by Lu AA21004 and escitalopram to a similar degree, these compounds interact differently with 5-HT<sub>1B</sub> receptors. Escitalopram, which does not have an affinity for the 5-HT<sub>1B</sub> receptor, unexpectedly generated a dose-dependent increase of 5-HT<sub>1B</sub> receptor binding. This effect may be interpreted as an increased cell membrane expression or an increased affinity state. However, the functional impact and the underlying molecular mechanism of this interaction remain to be investigated. Consistent with its in vitro 5-HT<sub>1B</sub> receptor affinity, Lu AA21004 dose-dependently occupied these receptors, and the effect of 5-HT<sub>1B</sub> receptor activation in reducing extracellular [5-HT] may be compatible with Lu AA21004 exerting a 5-HT<sub>1B</sub> receptor antagonistic effect in vivo. Funding: This study was sponsored

#### NR4-37

### MATERNAL, BUT NOT PATERNAL, MOOD AND ANXIETY DISORDERS ARE ASSOCIATED WITH PSYCHIATRIC DISORDERS IN YOUNG ADULTS

*Chair: Nancy Low M.D.; Author(s): Erika Dugas, MSc, Evelyn Constantin, M.D., MSc, Igor Karp, M.D., M.P.H., Ph.D., Daniel Rodriguez, Ph.D., Jennifer O'Loughlin, Ph.D.*

#### SUMMARY:

Background: Mood/anxiety disorders affect up to 15-20% of adolescents/young adults and are associated with academic failure, employment difficulties, interpersonal problems, substance misuse, and suicide. Despite early onset of symptoms of mood and anxiety disorders during childhood and adolescence, diagnosis and treatment may not occur until up to 14 years later for mood disorders, and 30 years later for anxiety disorders. Parental history of mood and anxiety disorders is the strongest risk factor for the development of these disorders in offspring. This study

tested if maternal or paternal history of mood/anxiety disorders increases the risk of mood disorders, anxiety disorders, or symptoms of specific anxiety disorders, in offspring. Methods: Data were drawn from the Nicotine Dependence in Teens Study, a prospective population-based cohort investigation of 1293 grade 7 students. Data were collected in post-secondary school in mailed self-report questionnaires when participants were aged 20.4 (0.7) years. Parental data were collected in mailed self-report questionnaires. This current analysis pertains to 565 participants with maternal and/or paternal data. The association between maternal and paternal history and each of diagnosed anxiety disorder, diagnosed mood disorder, and specific anxiety disorder symptoms in offspring was studied in multivariate logistic regression. Results: More mothers than father had been diagnosed with a mood/anxiety disorder (23% versus 12%). 14% of female offspring had a diagnosed mood/anxiety disorder, compared to 6% of male offspring. The adjusted OR (95% CI) for maternal history was 2.1 (1.0, 4.2) for diagnosed mood disorders, 3.8 (2.0, 7.4) for diagnosed anxiety disorders, 2.0 (1.2, 3.3) for panic disorder symptoms, and 2.6 (1.4, 4.7) for generalized anxiety disorder symptoms. There was no association between maternal history and social phobia or agoraphobia symptoms. Paternal history was not associated with any of the mental health outcomes in offspring. Conclusion: Maternal disorders were associated with diagnosed psychiatric disorders, as well as symptoms of specific anxiety disorders, in offspring. Efforts to detect offspring at risk due to maternal history in the general population should be encouraged.

#### NR4-38

### MIXED DEPRESSION: A STUDY OF ITS PHENOMENOLOGY AND RELATION TO TREATMENT RESPONSE

*Chair: Chi-Un Pae M.D.; Author(s): Paul A. Vöhringer M.D., Niki Holtzman, Antony loebel M.D., Sairah B. Thommi, Ashwin Patkar M.D., William Gilmer M.D., S. Nassir Ghaemi M.D., M.P.H.*

#### SUMMARY:

Mixed depression reflects the occurrence of a major depressive episode with subsyndromal manic symptoms. Not recognized in DSM-IV, it is included in proposed changes for DSM-5. Observational and cross-sectional studies have suggested that mixed depression is present in up to one-half of major depressive episodes, whether in M.D.D or bipolar disorder. Based on observational studies, antidepressants appear to be less effective, and neuroleptics more effective, in mixed than pure depression (major depressive episodes with no manic symptoms). In this report, we examine the specific manic

symptoms that are most present in mixed depression, especially as they correlate with prospectively assessed treatment response. In 72 patients treated in a randomized clinical trial (ziprasidone versus placebo), we assessed the phenomenology of manic symptom type at study entry and their influence as predictors of treatment response. The most common symptom presentation was a clinical triad of flight of ideas (60%), distractibility (58%), and irritable mood (55%). Irritable mood was the major predictor of treatment response. DSM-based diagnostic distinctions between M.D.D and bipolar disorder (type II) did not predict treatment response. In this prospective study, mixed depression seems to be most commonly associated with irritable mood, flight of ideas, and distractibility, with irritability being an important predictor of treatment outcome with neuroleptic agents. If these data are correct, in the presence of mixed depression, the DSM-based dichotomy between M.D.D and bipolar disorder does not appear to influence treatment response.

**NR4-39**  
**ASSOCIATION OF THE 5-HTTLPR WITH TREATMENT RESPONSE TO ESCITALOPRAM IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER**

*Chair: Min-Soo Lee M.D.; Author(s): Hun Soo Chang, Ph.D.*

**SUMMARY:**

Among polymorphisms of the serotonin transporter (5-HTT) gene, 5-HTTLPR has been replicated in many studies to be associated with treatment response to antidepressants. The aims of this study were to determine the relationship between the 5-HTTLPR polymorphism and the response to escitalopram in patients with major depressive disorder (M.D.D). One hundred fifteen Korean patients were examined using the Structured Clinical Interview for DSM-IV Axis I disorders, and took escitalopram at a daily dose of 5–40 mg. Clinical symptoms were evaluated using the 21-item Hamilton Depression Rating (HAM.D.21) scale during 12 weeks of treatment. The genotypes of 5-HTTLPR of the subjects were analyzed using polymerase chain reaction (PCR). The distributions of gender, age, age of onset, gender, family history of depression of other psychotic disease, suicide attempter and baseline HAM.D.21 scores did not differ according to the 5-HTTLPR genotype (ss, sl and ll). The proportion of s allele carriers in responders was higher than that in non-responders at 8 (96.6% vs. 85.7%) and 12 weeks (96.8% vs. 84.9%) of escitalopram treatment (odds ratio = 6.24 and 6.79 with  $P = 0.026$  and  $0.020$ ). However, the frequencies of genotypes in remitters

and in non-remitters were comparable ( $P > 0.05$ ). The percentile decline of HAM.D.21 in patients possessing s allele ( $64.53 \pm 3.57$ ) was larger than that in l allele homozygotes at 12 weeks of escitalopram treatment ( $33.03 \pm 16.47\%$ ,  $P = 0.029$ ). In conclusion, the genotype of 5-HTTLPR was associated with treatment response to escitalopram at 12 weeks, which suggests that the genotype may be a marker for predicting long-term response to escitalopram treatment in patients with M.D.D.

**NR4-40**  
**APPARENT RATES OF BIPOLAR DISORDER IN PATIENTS WITH COMBAT-RELATED POST TRAUMATIC STRESS DISORDER: A SITUATION OF POSSIBLE FALSE POSITIVES**

*Chair: Robert McLay M.D.; Author(s): Vasudha Ram, M.D. Jennifer Webb-Murphy, Ph.D. Scott Johnston, Ph.D.*

**SUMMARY:**

**Background:** The current definition of a manic episode excludes symptoms if they are accounted for by a substance or medical condition, but does not include stressors that might induce similar symptoms. In situations of extreme stress, such as combat, manic-like symptoms may occur, perhaps in the absence of Bipolar Disorder. **Aims:** To identify the rate of Bipolar Disorder, as assessed by structured clinical interview, in participants who enrolled in a study of PTSD, and in which the clinical providers treating the patients did not diagnose the participants with bipolar disorder. **Methods:** Data were taken from two studies of exposure therapy for PTSD, both of which started in 2005. In both studies, participants were screened by a research technician using the Mini-International Neuropsychiatric Interview (MINI) including questions about a Major Depressive Episode (M.D.E), a Manic Episode (ME), or a Hypomanic Episode (HE). At the end of the structured interview, a clinician met with the participant and determined, using his or her own clinical judgment, if the participant was accurately diagnosed. The clinician and the MINI had to agree on the diagnosis of PTSD for a participant to be included in the study. If the clinician felt participants had bipolar disorder, they were excluded. For this report, we examined the results on the MINI for those who qualified for the study. **Results:** Data from 39 participants were examined. Of these, 25 (64%) endorsed a history of a M.D.E, 15 (38%) endorsed a history of ME, and 9 (23%) endorsed a history of a HE. Thus, according to the questions on the MINI, 51% of participants suffered from Bipolar Disorder, including 38% who suffered from Bipolar Disorder Type I. Clinicians felt, however, that none of these

participants should be accurately diagnosed with Bipolar Disorder, and this did not change for any participant during the period of treatment or follow-on observation. Conclusions: Either there is an unusually high, and clinically non-obvious, rate of Bipolar Disorder in individuals with combat PTSD, or else reactions in combat produce false-positive responses for ME and HE.

**NR4-41**  
**HYPONATREMIA INDUCED PSYCHOSIS IN A 38 YEAR OLD MALE ON CITALOPRAM**

*Chair: Jamsheed Khan, M.D.; Author(s): Jessica M. Cunningham, MSIII; Ayme Frometa, M.D.; Amel Bader, M.D.*

**SUMMARY:**

The patient is a 38 year old Indian male, unemployed with a 6 month psychiatric history of Anxiety Disorder NOS and Major Depressive Disorder. He has been following up with his psychiatrist. Began experiencing symptoms of anxiety and depression, and thus sought treatment. At that time his psychiatrist started him on Citalopram 20mg PO daily and Klonopin 0.5mg PO BID. Despite compliance with his medication and weekly therapy sessions, the patient experienced increased anhedonia, sleep disturbances, intense guilt, and weight loss of 35 pounds over the course of six months. Eventually, the Celexa was increased to 40 mg. Presented with disheveled appearance, internal preoccupation, disorganized behavior and persecutory delusions for 1 day. Additionally, the patient had been non-compliant with his medication for past 4 days, he was also experiencing auditory hallucinations telling him that he had done wrong and deserved to be punished. On admission, urine tox screen and BAL were negative. The only abnormality was hyponatremia, with Na<sup>+</sup> of 125mmol/l. His urine osmolarity was within normal limits at 503 mOsm/L. Although polydipsia, intermittent hyponatremia, and psychosis (PIP syndrome) is a documented phenomenon associated with schizophrenia<sup>6</sup>, the patient's urine osmolarity rules out water intoxication or SIADH<sup>5</sup>. Psychosis and depression can also be the presenting symptoms of an Addisonian crisis<sup>7</sup>, but with a normal cortisol level of 10.1µg/dL, this differential diagnosis was also excluded. His TSH was 4.94 mIU/L, with T4 within normal limits, indicating subclinical hypothyroidism. A head CT did not reveal any acute pathology. All other lab work was within normal limits. Based on his lab work and clinical presentation it was determined that the patient's psychosis was induced by his hyponatremia. The patient was restarted on Celexa 40mg PO daily and Klonopin 0.5mg PO BID. Additionally, he was started on

Risperdal 2mg BID to manage his psychotic symptoms, and placed in group and individual therapy sessions. After four days, his Risperdal was increased to 3 mg BID and Cogentin was added. On the sixth day of admission, Risperdal was discontinued and Perphenazine was given to reduce extrapyramidal symptoms that the patient had been experiencing. Nothing was done to correct the sodium levels other than nutritional support, by day seven his Na<sup>+</sup> as 136 mmol/l and his feelings of guilt and persecutory delusions had lessened significantly. Discussion It seemed most probably that the patient's poor nutritional status, which had resulted in a 35 pound weight loss, was responsible for the disturbance in his sodium level<sup>6</sup>. Conclusion When patients report loss of weight or when the physician notices a decrease in the patient's weight, instead of changing the antidepressants physicians should also include the factors like less fluid intake as a possible cause of electrolyte imbalance and therefore electrolyte panels should be obtained at regular intervals

**NR4-42**  
**THE ASSOCIATION OF PROOPIOMELANOCORTIN POLYMORPHISM WITH THE RISK OF MAJOR DEPRESSIVE DISORDER AND WITH RESPONSES TO ANTIDEPRESSANTS**

*Chair: Min-Soo Lee M.D.; Author(s): Hun Soo Chang, Ph.D.*

**SUMMARY:**

As a response to stress, the HPA system modulates levels of cortisol and other important stress related hormones including corticotropin (ACTH), one of 6 hormones encoded by proopiomelanocortin (POMC) gene located in chromosome 2p23.3. Because pathogenesis of major depressive disorder (M.D.D) is known to be associated with an impairment of negative feedback mechanisms of the HPA system, we evaluated the association of POMC gene polymorphisms both with the risk of M.D.D and with the response to treatment with antidepressants. One hundred seventy five Korean patients with M.D.D and 193 Korean control subjects were enrolled. The M.D.D subjects were examined using the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I) and only subjects with a minimum score of 18 on the 17-item Hamilton Depression Rating (HAM.D.17) scale were included. The control subjects were less than 9 point of The Beck Depression Inventory. Clinical symptoms were assessed using the HAM.D.17 scale at baseline and after 1, 2, 4, 8 and 12 weeks of treatment with one of the antidepressants escitalopram and mirtazapine at a daily dose of 5 – 40 mg or 15–60 mg, respectively. Genotypes of the subjects

were determined using SNaPshot method. Among 39 polymorphisms on POMC gene listed in dbSNP, four polymorphisms showed higher frequencies than 0.05, of which two were on promoter region and others were synonymous polymorphisms. Among them, a promoter polymorphism, POMC -5613A>G, was associated with the risk of M.D.D; GG genotype frequency was lower in M.D.D than that in control subjects (49.1% vs 60.6%, respectively.  $P = 0.018$  and odd ratio = 0.67 [0.48 – 0.93]). Although not associated with baseline HAM.D.17 score, the polymorphism showed significant associations with the response and remission status; proportion of patients with M.D.D possessing the A allele was higher in responders (67.7%) than in non-responders (46.9%) to antidepressant treatment at 1 weeks ( $P = 0.026$  and odd ratio = 2.13 [1.10 – 4.13]). These results suggest that POMC -5613A>G affects the pathogenesis of M.D.D and may be involved in outcome of antidepressant treatment in patients with M.D.D.

#### NR4-43

### ASSESSMENT OF EXECUTIVE DYSFUNCTION IN ADULTS WITH MAJOR DEPRESSIVE DISORDER RECEIVING LISDEXAMFETAMINE DIMESYLATE AUGMENTATION OF ESCITALOPRAM

*Chair: Philip Harvey Ph.D.; Author(s): Robert M. Roth, Ph.D., Robert M. Bilder, Ph.D., Cynthia Richards, M.D., Robert Lasser, M.D., Brooke Geibel, BA, Joseph Gao, Ph.D., Brian Scheckner, Phar M.D., Madbukar Trivedi, M.D.*

#### SUMMARY:

**Objective:** Improvement of cognitive impairment, particularly executive dysfunction, is an important treatment objective in major depressive disorder (M.D.D) because it can affect everyday functioning, including the ability to return to work. We describe the effects of lisdexamfetamine dimesylate (LDX) on executive function based on subjective self-reports from the Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A). **Method:** Men and women (18–55 y) with nonpsychotic M.D.D were eligible for the study. After 8 weeks of open-label escitalopram (10 mg/d at wk 1; 20 mg/d thereafter), participants with residual M.D.D symptoms (17-item Hamilton Rating Scale for Depression scores  $\geq 4$ ) were randomized to 6 weeks of double-blind LDX (wk 9: 20 mg/d; wk 10: 20 or 30 mg/d; wks 11–14: 20, 30, or 50 mg/d) or placebo as augmentation to escitalopram. Executive function was assessed on the BRIEF A self-report using normatively derived T-scores based on the BRIEF-A standardization sample ( $N=100$ ). The BRIEF-A provides a Behavioral Regulation Index (BRI) consisting of 4 subscales, a Metacognition Index

(MI) consisting of 5 subscales, and an overall Global Executive Composite score. Statistical analyses were conducted using analysis of covariance in all participants taking  $\geq 1$  dose of randomized study drug and having  $\geq 1$  postrandomization MADRS assessment. Observed case data are reported for participants considered escitalopram nonremitters (i.e., those with MADRS total scores  $>10$  at augmentation baseline [LDX,  $n=65$ ; placebo,  $n=64$ ]). **Results:** Of 177 participants randomized to double-blind augmentation (LDX,  $n=89$ ; placebo,  $n=88$ ); 157 (LDX, 78 [87.6%]; placebo 79 [89.8%]) completed the study. For escitalopram nonremitters, the least squares (LS) mean (90% CI) change from augmentation baseline to visit 13 (observed cases) in the self-reported BRIEF-A Global Executive Composite T-score was  $-4.7$  ( $-6.4, -3.0$ ) for LDX and  $-1.7$  ( $-3.5, 0.0$ ) for placebo. The LS mean (90% CI) difference between treatments significantly favored LDX ( $-3.0$  [ $-5.4, -0.5$ ],  $P=0.0463$ ), with an approximately 3-fold score reduction from augmentation baseline for LDX versus placebo. The BRIEF-A self-report MI subscales of initiate, plan/organize, and organization of materials and the MI showed unadjusted P values of less than 0.05 while other subscales did not. During double-blind treatment, 60.2% of participants on LDX and 49.4% on placebo had a treatment-emergent adverse event (TEAE); 1 serious TEAE occurred during randomized treatment in a participant receiving placebo. **Conclusions:** Augmentation therapy with LDX improved executive function in participants with residual symptoms of M.D.D in this placebo-controlled trial. As executive function is a cognitive ability consistently linked to real-world functional outcome, these findings suggest LDX is a promising treatment for reducing executive dysfunction and associated impairments in individuals with M.D.D. Supported by Shire Development Inc.

#### NR4-44

### ADJUNCTIVE ARIPIPRAZOLE DOUBLES THE RATE OF EARLY AND SUSTAINED RESPONSE IN M.D.D PATIENTS WITH AN INADEQUATE RESPONSE TO ANTIDEPRESSANT MONOTHERAPY

*Chair: Daniel Casey M.D.; Author(s): Kimberly K. Laubmeier, Ph.D.; James M. Eudicone, M.S., M.B.A.; Ross A. Baker, Ph.D., M.B.A.; Jack Sheehan, Ph.D.*

#### SUMMARY:

**Objective:** The goal of treating major depressive disorder (M.D.D) is sustained remission of symptoms, ideally beginning early in the course of therapy. However, antidepressant therapy (ADT) often requires 6–8 weeks to determine if it has reached its intended effect, and this delay may impede the successful clinical

use of ADT. This post-hoc analysis investigated if adjunctive aripiprazole results in an early and sustained response (ESusR) compared with ADT alone. ESusR is a particularly rigorous efficacy measure because patients must respond early and at all subsequent time points. Methods: Data from three similar studies were pooled.<sup>1,2</sup> All patients had to have an inadequate response to one to three trials of ADT. Each study included an 8-week prospective ADT phase (Phase B), followed by a 6-week randomized phase of adjunctive aripiprazole versus adjunctive placebo (Phase C). ESusR was defined as a patient who had a response (=50% improvement in Montgomery–Asberg Depression Rating Scale [MADRS] total score during Phase C) to treatment at Week 2 and who sustained that response at all subsequent visits (Weeks 3, 4, 5 and 6) from among those patients who attended all visits. Results: The rate of ESusR in the adjunctive aripiprazole group was 11.6% (45/387) vs. 5.4% (21/387) in the adjunctive placebo group ( $P=0.002$ ; odds ratio [OR]=2.3, 95% confidence interval [CI]: 1.3, 3.9). Out of the overall population, 22.7% (88/387) of adjunctive-aripiprazole treated patients and 10.9% (42/387) of adjunctive placebo recipients responded at Week 2. Of those who had an early response, 51.1% (45/88) of patients in the adjunctive aripiprazole group and 50.0% (21/42) of patients in the adjunctive placebo group attained ESusR ( $P=0.904$ ). Among patients who achieved ESusR on adjunctive aripiprazole, the most common adverse events were akathisia (20.0%), restlessness (17.8%), fatigue (13.3%), insomnia (13.3%), and blurred vision (11.1%), which are similar to the general aripiprazole population.<sup>1,2</sup> The mean weekly ending dose of aripiprazole in those who achieved ESusR was 8.5 mg/day, compared with 11.8 mg with adjunctive placebo. Conclusions: Adjunctive aripiprazole treatment resulted in ESusR more than twice as often compared with ADT monotherapy. These rates compare favorably with published rates for selective serotonin reuptake inhibitors (SSRIs). The early onset of adjunctive aripiprazole efficacy may be clinically valuable as it allows for earlier identification for response and better patient management.

#### NR4-45

### LONG-TERM SAFETY AND TOLERABILITY OF LU AA21004 IN SUBJECTS WITH MAJOR DEPRESSIVE DISORDER

*Chair: Mohammed Alam M.D.; Author(s): Paula Jacobsen, MS; Yinzhong Chen, Ph.D.; Michael Serenko, M.D.; Atul Mahableshwarkar, M.D.*

#### SUMMARY:

Objective: Lu AA21004 is a multimodal antidepressant

that functions as a 5-HT<sub>3</sub> and 5-HT<sub>7</sub> receptor antagonist, 5-HT<sub>1B</sub> receptor partial agonist, 5-HT<sub>1A</sub> receptor agonist, and inhibitor of the 5-HT transporter in vitro. The goal of this study was to evaluate the long-term safety and tolerability of Lu AA21004 in subjects with major depressive disorder (M.D.D). Methods: This was a 52-week open-label extension study of subjects who completed 1 of 2 previous short-term M.D.D efficacy studies of Lu AA21004. Regardless of dose at the completion of previous study, all subjects were switched to Lu AA21004 5 mg/day for the first week of the extension study. Thereafter, the dose was adjusted (2.5, 5, or 10 mg/day) as needed. Safety and tolerability were assessed by adverse events (AEs), vital signs and weight, electrocardiograms, clinical laboratory values, physical examination findings, and the Columbia–Suicide Severity Rating Scale (C-SSRS). A safety follow-up call was made 4 weeks after completion of the study (or withdrawal). Efficacy assessments included the Hamilton Depression Scale-24 Items (HAM-D24), Montgomery Åsberg Depression Rating Scale (MADRS), Hamilton Anxiety Scale (HAM-A), and Clinical Global Impression Scale–Severity of Illness Scale (CGI-S). Results: A total of 836 subjects were enrolled and 834 (mean age 45.5 years, 62.9% women) were treated with open-label Lu AA21004; 526 (62.9%) completed the study. Of the 310 subjects who withdrew early, 49 (5.9%) withdrew due to AEs. A total of 589 subjects (70.6%) experienced at least 1 treatment-emergent AE (38 AEs in 29 [3.5%] subjects were considered serious). No deaths occurred during the study. The most common AEs from the combined population of subjects in the extension study were nausea (15.2%), headache (12.4%), nasopharyngitis (9.8%), diarrhea (7.2%), dizziness (6.8%), and upper respiratory tract infection (6.4%). Laboratory, vital signs, physical examinations (e.g., weight), and C-SSRS results revealed no trends of clinical concern. Mean HAM-D24 total score was 31.2 before the start of the initial double-blind studies, 17.6 at the start of the open-label extension and 9.7 after 52 weeks of open-label treatment. Maintenance of improvement was also seen in mean MADRS total score, MADRS response and remission rates, HAM-D24 response rate, HAM-A total score, and CGI-S score. Conclusions: In this 52-week open-label extension study, Lu AA21004 up to 10 mg/day was well tolerated with no indication of safety concerns. Lu AA21004 maintained improvement of depressive symptoms throughout the treatment period in this population of subjects with M.D.D. Funding: This study was sponsored by the Takeda Pharmaceutical Company as part of a joint clinical development program with H. Lundbeck A/S. Educational Objective: At the conclusion of this session, the participant should

understand the long-term safety and tolerability profile of Lu AA21004.

#### NR4-46

### EFFICACY OF LISDEXAMFETAMINE DIMESYLATE AUGMENTATION FOR EXECUTIVE DYSFUNCTION IN ADULTS WITH FULLY OR PARTIALLY REMITTED MAJOR DEPRESSIVE DISORDER

*Chair: Robert Roth Ph.D.; Author(s): Richard S. E. Keefe, Ph.D., Angelo Sambunaris, M.D., Manisha Madhoo, M.D., James Wu, Ph.D., Madhukar Trivedi, M.D., Colleen S. Anderson, MEd, Robert Lasser, M.D.*

#### SUMMARY:

**Objective:** A randomized placebo (PBO)–controlled trial showed lisdexamfetamine dimesylate (LDX) augmentation of selective serotonin reuptake inhibitor (SSRI) monotherapy improved executive dysfunction measured on the Behavior Rating Inventory of Executive Function–Adult Version [BRIEF-A] self-report in participants with major depressive disorder (M.D.D). We further describe LDX effects on executive function using BRIEF-A self- and informant-reports. **Method:** Men and women (18–55 y) with mild M.D.D (Montgomery-Asberg Depression Rating Scale score  $\leq 18$ ) and executive dysfunction (BRIEF-A Global Executive Composite [GEC] T-score  $\geq 60$ ) on stable SSRI monotherapy for  $\geq 8$  weeks were eligible for the study. After a 2-week screening period for stability of executive dysfunction and depressive symptoms, participants were randomized to 9 weeks of double-blind LDX (wk 1: 20 mg/d; wks 2–6: maintain or increase LDX in 10-mg increments weekly to 70 mg/d; wks 7–9: maintain optimized dose) or PBO augmentation. The primary endpoint was change on self-report BRIEF-A GEC T-score; secondary endpoints included changes on the informant-report BRIEF-A GEC T-score and on self- and informant-report BRIEF-A Behavioral Regulation Index (BRI) and Metacognition Index (MI) T-scores. Data from randomized participants who took  $\geq 1$  study drug dose and had  $\geq 1$  post baseline BRIEF-A assessment were analyzed using ANCOVA, with last observation carried forward for missing data. **Results:** Of 143 randomized participants (LDX, 71; PBO, 72), 119 completed double-blind treatment (LDX, 60; PBO 59). Mean $\pm$ SD self-report BRIEF-A GEC T-scores improved from baseline (LDX, 76.8 $\pm$ 9.66; PBO, 74.2 $\pm$ 8.88) to study endpoint (LDX, 55.2 $\pm$ 16.15; PBO, 61.4 $\pm$ 14.61); the least squares (LS) mean (95% CI) treatment difference significantly favored LDX (-8.0 [-12.7, -3.3];  $P=0.0009$ ). Mean self-report BRIEF-A GEC T-score reductions from baseline at study endpoint were -28.1% with LDX and -17.0%

with PBO. Mean $\pm$ SD informant-report BRIEF-A GEC T-scores improved from baseline (LDX, 63.9 $\pm$ 10.81; PBO, 63.1 $\pm$ 11.01) to study endpoint (LDX, 54.8 $\pm$ 11.85; PBO, 59.6 $\pm$ 10.71); the LS mean (95% CI) treatment difference at study endpoint significantly favored LDX (-5.9 [-9.3, -2.6];  $P=0.0006$ ). Consistent with GEC T-score findings, statistically significant LS mean (95% CI) treatment differences favoring LDX were observed for the BRI (self-report: -5.1 [-9.4, -0.9],  $P=0.0181$ ; informant report: -5.0 [-8.1, -1.8],  $P=0.0023$ ) and MI (self-report: -9.0 [-13.7, -4.3],  $P=0.0002$ ; informant report: -6.1 [-9.6, -2.7];  $P=0.0006$ ) at study endpoint. **Conclusions:** These findings support the potential utility of LDX augmentation for executive dysfunction in M.D.D and show that patients and knowledgeable informants observe improved executive function in everyday life with LDX. Further, changes on the informant report indicate that self-reported improvement in executive function is not simply the result of a PBO effect. Supported by Shire Development, Inc.

#### NR4-47

### LONG-TERM SAFETY AND TOLERABILITY OF ONCE-MONTHLY ARIPIPRAZOLE INTRAMUSCULAR DEPOT (ARI-IM-DEPOT) FOR MAINTENANCE TREATMENT IN SCHIZOPHRENIA

*Chair: Wolfgang Fleischhacker M.D.; Author(s): Raymond Sanchez, M.D.; Pamela Perry, M.S.; Na Jin, M.S.; Brian Johnson, M.S.; Robert A. Forbes, Ph.D.; Robert D. McQuade, Ph.D.; William H. Carson, M.D.; John Kane, M.D.*

#### SUMMARY:

**Objective:** To understand the safety and tolerability profile of aripiprazole intramuscular depot (ARI-IM depot) during maintenance treatment of schizophrenia. **Methods:** Subjects requiring chronic treatment with an antipsychotic were eligible and subjects not already on aripiprazole monotherapy were cross-titrated during weekly visits from other antipsychotic(s) to oral aripiprazole monotherapy during the 4–6 weeks oral conversion phase (Phase 1). All subjects requiring chronic treatment with an antipsychotic entered a 4–12-week oral stabilization phase (Phase 2) and received oral aripiprazole (10–30 mg/day). Subjects meeting stability criteria for 4 weeks then entered an intramuscular depot stabilization phase (Phase 3), wherein they received ARI-IM-depot injections every 4 weeks (400 mg, single decrease to 300 mg permitted) with co-administration of aripiprazole oral tablets in the first 2 weeks. Subjects meeting stability criteria for 12 consecutive weeks were randomized (2:1) to ARI-IM-depot or placebo during a 52-week,

double-blind maintenance phase (Phase 4). Safety of treatment was assessed across the study phases by time of first onset of adverse events (AEs), changes in movement disorder rating scales and changes in weight and metabolic parameters. Results: The study was stopped early because efficacy was demonstrated by the pre-planned interim analysis (conducted after 64 relapses). ARI-IM-depot was well tolerated with similar rates of AEs across all phases. Discontinuations due to treatment-emergent AEs were: Phase 1, 3.8% (24/632); Phase 2, 3.0% (21/709); Phase 3, 4.9% (n=28/576); Phase 4, 7.1% (n=19/269). Most AEs were mild or moderate; severe AEs were rare (<5.0% incidence in all phases). AEs >5% incidence in any phase were: insomnia (all phases), headache (Phases 1, 3 and 4), anxiety, akathisia, weight increase (Phase 3 and 4) and injection site pain (Phase 3) and tremor (Phase 4). The majority of AEs (headache, somnolence, nausea) had a peak first onset within the first 4 weeks of treatment. The incidence of treatment-emergent EPS and EPS-related events was similar in all phases (Phase 4 ARI-IM-depot 14.9% vs. placebo 9.7%). Mean baseline weight in each phase was similar (range 80.4–84.8 kg). Mean changes in weight from baseline were Phase 1: –0.2 kg; Phase 2: 0.1 kg; Phase 3: –0.2 kg; and Phase 4 (ARI-IM-depot vs. placebo): –0.2 vs. –0.4 kg. There were no unusual shifts in laboratory values or fasting metabolic parameters across all study phases. Shifts from normal to high metabolic values occurred at similar low rates between ARI-IM and placebo in the double blind phase. Discussion: No unexpected AEs emerged during the transition to IM depot, or with long-term ARI-IM-depot. Rates of AEs in Phase 1 were no different than rates in Phase 2, suggesting that the study switch strategy was useful. These data suggest that ARI-IM-depot offers a new option with a different risk–benefit profile than currently available treatments.

**NR4-48**  
**EFFICACY AND SAFETY OF**  
**DESVENLAFAXINE 50 MG/D FOR**  
**PREVENTION OF RELAPSE IN ADULT**  
**OUTPATIENTS TREATED FOR MAJOR**  
**DEPRESSIVE DISORDER**

*Chair: Joshua Rosenthal M.D.; Author(s): Patrice Boyer M.D., Ph.D., Cécile Vialet, Eunbee Hwang Ph.D., Karen A. Tourian M.D.*

**SUMMARY:**

Objective: Desvenlafaxine (administered as desvenlafaxine succinate) has demonstrated efficacy for the prevention of relapse of depressive symptoms in patients with major depressive disorder (M.D.D) in a long-term study using doses of 200 to 400

mg/d. The objective of this study was to evaluate the long-term efficacy and safety of desvenlafaxine at the recommended dose of 50 mg/d compared with placebo for long-term relapse prevention. Method: Adult outpatients (=18 years) who were generally healthy with a diagnosis of M.D.D (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition–Text Revision) and 17-item Hamilton Rating Scale for Depression (HAM-D17) total score =20 at screening and baseline were enrolled in a multicenter, double-blind (DB), placebo-controlled, randomized withdrawal trial. Patients who responded to 8-week open-label (OL) treatment with desvenlafaxine 50 mg/d and had continuing stable response through week 20 were randomly assigned to receive placebo or desvenlafaxine 50 mg/d (1:1) in a 6-month, DB, randomized withdrawal phase. [The primary efficacy endpoint was the time to relapse following randomization to the DB (defined as HAM-D17 total score =16, discontinuation due to unsatisfactory efficacy, hospitalization for depression, suicide, or suicide attempt), compared between groups using the log-rank test. Safety data were collected throughout the trial. Results: A total of 874 patients were enrolled in the study; 548 patients were randomly assigned to receive placebo (n=276) or desvenlafaxine 50 mg/d (n=272) in the DB withdrawal phase. During the DB phase, 28.3% of placebo-treated patients relapsed compared with 13.6% of desvenlafaxine-treated patients. Time to relapse was significantly shorter for placebo vs desvenlafaxine (P<0.001). At the end of the 6-month DB treatment, the estimated probability of relapse was 30.2% for placebo compared with 14.3% for desvenlafaxine 50 mg/d. Sensitivity analyses that excluded the first 2 and 4 weeks of DB treatment resulted in findings consistent with primary analysis. Treatment-emergent adverse events were similar to prior short term studies for the initial OL phase, and in the DB phase were consistent with discontinuation from desvenlafaxine or relapse of depression for the group switched to placebo. [A larger percentage of patients on placebo in DB (8.3%) discontinued DB treatment due to adverse events compared with patients continued on desvenlafaxine (3.3%). Conclusions: Long-term treatment with desvenlafaxine at the recommended dose of 50 mg/d was effective and generally well tolerated in this relapse prevention trial. Desvenlafaxine 50 mg/d significantly increased time to relapse compared with placebo in patients stabilized after 20 weeks of OL desvenlafaxine treatment. Research supported by Pfizer Inc.

**NR4-49**  
**EFFICACY AND SAFETY OF**  
**DESVENLAFAXINE 50 MG/D IN A**  
**RANDOMIZED, PLACEBO-CONTROLLED**

**STUDY OF PERI/POSTMENOPAUSAL WOMEN WITH MAJOR DEPRESSIVE DISORDER**

*Chair: Anita Clayton M.D.; Author(s): Susan G. Kornstein, M.D., Boadie W. Dunlop, M.D., Kristen Focht, M.B.A., Jeff Musgnung, MS, Tanya Ramey, M.D., Ph.D., Weibang Bao, Ph.D., Philip T. Ninan, M.D.*

**SUMMARY:**

**Objective:** Desvenlafaxine (administered as desvenlafaxine succinate) has demonstrated short-term efficacy for treating major depressive disorder (M.D.D) in peri- and postmenopausal women at doses of 100 to 200 mg/d. The objective of this study was to evaluate the short-term efficacy and safety of desvenlafaxine at the current recommended dose of 50 mg/d compared with placebo in this population. **Method:** Peri- and postmenopausal women (40 to 70 years) with a primary diagnosis of M.D.D (Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition–Text Revision) were randomly assigned to receive placebo or desvenlafaxine 50 mg/d in a 10-week, multicenter, double-blind, placebo-controlled trial. The primary efficacy endpoint was change from baseline in the 17-item Hamilton Depression Rating Scale (HAM-D17) total score at week 8, analyzed using an analysis of covariance with baseline HAM-D17 score as the covariate and site and treatment as fixed factors. Safety data were collected throughout the trial. **Results:** A total of 434 patients took at least 1 dose of study drug and 432 patients (desvenlafaxine, n=216; placebo, n=216) provided data for the primary efficacy analysis (took =1 dose of study drug and had =1 post baseline HAM-D17 evaluation). Reduction in adjusted HAM-D17 total score from baseline to week 8 was significantly greater for desvenlafaxine (–9.9) compared with placebo (–8.1; P=0.004). Desvenlafaxine-treated patients achieved significant reductions in HAM-D17 total scores vs placebo in both the perimenopausal (P=0.008) and postmenopausal (P=0.016) subgroups. Response (=50% decrease from baseline on HAM-D17 total score) and remission (HAM-D17 total score =7) rates were numerically higher for desvenlafaxine (response: 41.2%; remission: 23.6%) compared with placebo (response: 33.3%; remission: 17.1%), but neither difference was statistically significant. Desvenlafaxine-treated patients achieved significant functional improvement compared with placebo based on week 8 Sheehan Disability Scale scores (–9.13 vs –8.12; P=0.038). Improvement from baseline to week 8 in Menopause Rating Scale total scores with desvenlafaxine treatment (–6.88) vs placebo (–5.61) approached significance (P=0.051). Treatment-emergent adverse events (TEAEs) were reported by 155/217 (71%) patients administered desvenlafaxine and 148/217 (68%) patients administered

placebo. In all, 5.5% of desvenlafaxine-treated patients discontinued the study due to adverse events compared with 2.3% for placebo. Nausea was the most common TEAE reported by desvenlafaxine-treated patients (11%; placebo 7%), no TEAE that was the primary reason for withdrawal occurred in more than 1 subject in either treatment group. **Conclusions:** Short-term treatment with desvenlafaxine at the current recommended dose of 50 mg/d was effective and generally well tolerated in this placebo-controlled study of peri- and postmenopausal women with M.D.D. Research supported by Pfizer Inc.

**NR4-50****ABRUPT DISCONTINUATION COMPARED WITH A 1-WEEK TAPER REGIMEN IN DEPRESSED OUTPATIENTS TREATED FOR 24 WEEKS WITH DESVENLAFAXINE 50 MG/D**

*Chair: Arif Khan M.D.; Author(s): Philip T. Ninan, M.D., Tanya Ramey, M.D., Ph.D., Michael Messig, Ph.D., Gina Buckley, MT, MS, Jeff Musgnung, MS*

**SUMMARY:**

**Objective:** To determine whether the occurrence of discontinuation symptoms was equivalent for abrupt discontinuation vs 1-week taper to desvenlafaxine 25 mg/d following 24-week treatment with desvenlafaxine 50 mg/d (administered as desvenlafaxine succinate) for major depressive disorder (M.D.D). **Method:** Adult outpatients (aged =18 years) with M.D.D who completed 24-week, open-label treatment with desvenlafaxine 50 mg/d were randomly assigned to 1 of 3 groups (1:2:2 ratio) for the double-blind taper phase: desvenlafaxine 50 mg/d for 4 weeks (no discontinuation); desvenlafaxine 25 mg/d for 1 week followed by placebo for 3 weeks (taper); or placebo for 4 weeks (abrupt discontinuation). The primary endpoint was Discontinuation Signs and Symptoms Scale (DESS) total score over the first 2 weeks of the double-blind taper phase. Secondary endpoints included incidence of taper-emergent adverse events (AEs). The null hypothesis that the absolute difference in DESS total scores between taper and abrupt discontinuation groups >2.5 was tested by calculating the 95% 2-sided confidence interval (CI) on the mean difference between the 2 groups and declaring the regimens equivalent if the CI was completely contained within the prespecified margins of (–2.5 to 2.5). DESS total scores were analyzed using analysis of covariance. **Results:** A total of 480 patients enrolled in the open-label phase; 357 had =1 postrandomization DESS record and were included in the primary analysis. The adjusted mean DESS score was 4.1 for the no discontinuation group (n=72), 4.8 for the taper group (n=139), and 5.3 for the abrupt-discontinuation group (n=146). The difference

in adjusted mean DESS total scores between the abrupt-discontinuation and taper groups was 0.50, and the 95% CI (-0.88 to 1.89) fell completely within the prespecified range. Taper-emergent AEs were reported by 54 patients (38.8%) in the taper group compared with 75 patients (51.4%) in the abrupt-discontinuation group; 26 patients (36.1%) in the no discontinuation group reported AEs during the double-blind period. The number of patients who discontinued due to AEs or discontinuation symptoms during the double-blind period was similar between taper (4 [2.8%]) and abrupt-discontinuation groups (3 [2.1%]). Conclusions: This study demonstrated that abrupt discontinuation of desvenlafaxine 50 mg/d produced statistically equivalent DESS scores compared with the 1-week taper using 25 mg/d. Research supported by Pfizer Inc.

#### NR4-51

### LEVOMILNACIPRAN IN THE TREATMENT OF MAJOR DEPRESSIVE DISORDER: FUNCTIONAL HEALTH AND WELL-BEING EFFICACY RESULTS FROM A PHASE III CLINICAL TRIAL

*Chair: Steve Blum M.B.A.; Author(s): Stavros Tourkodimitris, Ph.D., Adam Ruth, Ph.D.*

#### SUMMARY:

**Objective:** Levomilnacipran (1S, 2R-milnacipran) is a potent and selective serotonin and norepinephrine reuptake inhibitor (SNRI) in clinical development for the treatment of major depressive disorder (M.D.D) in adults. Primary and post hoc analyses were conducted on data from a positive Phase III trial (NCT00969709) to evaluate the functional health and wellbeing of patients with M.D.D treated with sustained released (SR) levomilnacipran. **Methods:** An 11-week, double-blind, multicenter, parallel-group, placebo-controlled, fixed-dose study in patients (age range, 18-65 years) who met DSM-IV-TR criteria for M.D.D. Patients had a current major depressive episode  $\geq 8$  weeks and a score  $\geq 30$  on the Montgomery-Asberg Depression Rating Scale-Clinician Rated (MADRS-CR). Study comprised a 1-week single-blind, placebo lead-in, 8-week double-blind treatment, and 2-week double-blind down-taper. Patients were randomized to placebo (PBO; n=175) or once-daily levomilnacipran (LVM; n=529) 40 mg, 80 mg, or 120 mg (titrated-up from an initial dose of 20 mg). Functional health and wellbeing were measured using the SF-36v2 acute (1-week recall) health survey. The SF-36 was scored using norm-based methods that standardize the scores to a mean of 50 and a standard deviation of 10 in the general US population, with higher scores indicative of better health. Changes from baseline to Week 8 in

the individual health dimensions [Physical Functioning (PF), Role Physical (RP), Bodily Pain (BP), General Health (GH), Vitality (VT), Social Functioning (SF), Role Emotional (RE), Mental Health (MH)], and the physical (PCS) and mental (MCS) component summary scores were computed based on the ITT population. Treatment comparison between LVM and PBO were performed using the least squares mean differences (LSM.D.) from an ANCOVA model, adjusting for treatment group, pooled study site and baseline value of the underlying score. **Results:** Patients in both treatment groups had significant deficits in mental-health based on baseline scores for the MCS (PBO: 17.2 $\pm$ 9.2; LVM: 18.2 $\pm$ 8.5); conversely, baseline scores for the PCS (PBO: 52.6 $\pm$ 11.1; LVM: 51.1 $\pm$ 11.1) were slightly higher than the population norm. Following 8 weeks of randomized double-blind treatment, patients in the LVM treatment arms compared with PBO-treated patients demonstrated significantly greater improvement in MCS (LSM.D. = 4.4 $\pm$ 1.36; P=.0013) and in individual dimensions for GH (2.3 $\pm$ 0.69; P=.0007), VT (2.4 $\pm$ 1.05, P=.0228), SF (3.1 $\pm$ 1.17; P=.0086), RE (3.1 $\pm$ 1.20; P=.0097) and MH (4.3 $\pm$ 1.16; P=.0003). Nonsignificant changes were noted for the PCS and the other SF-36 dimension scores (PF, RP, BP). **Conclusions:** M.D.D patients treated with levomilnacipran experienced statistically significant and clinically meaningful improvements in functional health and wellbeing as measured by the SF-36 MCS and associated individual dimensions. This study was funded by Forest Laboratories, Inc.

#### NR4-52

### ADJUNCTIVE USE OF ARIPIPRAZOLE OR BUPROPION?

*Chair: Suhayl Nasr M.D.; Author(s): Anand Popli, M.D., John Crayton, M.D., Burdette Wendt*

#### SUMMARY:

**Objective:** To compare the effectiveness of using Aripiprazole or Bupropion as an adjunct to other antidepressants. **Method:** A chart review was performed on all patients who began treatment in the past 5 years at a private, outpatient psychiatric clinic. Data collected include demographic information, diagnoses, medication history, and QIDS depression scores at each visit. Patients were included if they had not taken either Aripiprazole or Bupropion but had it added to their medication regimen during the course of their treatment at the clinic. **Results:** Adjunctive treatment was observed with Bupropion in 83 patients and with Aripiprazole in 70 patients. Both groups of patients had their QIDS score significantly lowered by their first visit after having the medication added. Bupropion users lowered their score from 11.7 to 9.6 (p<.01) at the first

visit, and had an average of 8.6 for their 5 visits after beginning Bupropion. Aripiprazole patients lowered their score from 12.4 to 10.2 ( $p < .01$ ) at the first visit and had an average of 10.0 for their first 5 visits. 66% of Bupropion users lowered their score at the first visit, with 23% achieving remission, compared with 70% of Aripiprazole patients, with 17% achieving remission. During the observation period 56% of Bupropion patients achieved remission compared to 50% of Aripiprazole patients. At the end of the observation period 33% of Bupropion patients were in remission compared to 50% of patients on Aripiprazole. Both groups of patients had significant reductions to their score on the symptoms of sadness, concentration, and general interest. In addition, Bupropion patients had significant decrease in the low energy score while Aripiprazole patients had a significant decrease in the thoughts of death and suicide score. None of the differences between Aripiprazole and Bupropion patients were statistically significant. Conclusion: Bupropion and Aripiprazole were comparable in significantly lowering patients' QIDS scores and helping half the patients or more achieve remission. One area of difference between the two medications is that Bupropion significantly helped patients with their energy while Aripiprazole decreased patients' preoccupation with death and suicide. References: 1) Rush AJ, Trivedi MH, Wisniewski SR, et al. Bupropion-SR, sertraline, or venlafaxine-XR after failure of SSRIs for depression. *N Engl J Med.* 2006 Mar 23;354(12):1231-42. 2) Berman RM, Marcus RN, Swanink R, et al. The efficacy and safety of aripiprazole as adjunctive therapy in major depressive disorder: a multicenter, randomized, double-blind, placebo-controlled study. *J Clin Psychiatry.* 2007 Jun;68(6):843-53.

#### NR4-53

### KETAMINE SAFETY: A DESCRIPTION OF PHYSIOLOGICAL & PSYCHOLOGICAL EVENT MONITORING DURING ADMINISTRATION OF LOW-DOSE INTRAVENOUS KETAMINE IN TREATMENT

*Chair: Nora Finnegan B.S.N.; Author(s): Sarah Szymkiewicz, MS Roman Dale, M.D.*

#### SUMMARY:

The glutamatergic system has increasingly become the focus of research in Major Depressive and Bipolar Disorders. Medications that target this system, particularly low-dose intravenous ketamine, have been investigated as a treatment modality for treatment-resistant depression. Compared to traditional antidepressant strategies and augmenting techniques, ketamine infusions have been shown to be relatively

safe, efficacious, and fast-acting. The published safety data is based on six infusions, or less. This study further investigates the safety of repeat (range of 2-34) low-dose intravenous ketamine infusions in seventeen patients over 16 months. Patients aged between 18-79 who had failed adequate treatment trials of antidepressant monotherapy, augmentation strategies, mood stabilizers, and electroconvulsive therapy were referred for ketamine therapy. Ketamine was administered at 0.5 mg/kg of ideal body weight over 40 minutes. Dosages ranged between 27 to 35 mg. The infusions were then followed by 500 cc of normal saline at 250 cc/hr until discharge. Infusions were administered by an Advanced Cardiac Life Support certified registered nurse with equipment capable of monitoring blood pressure, pulse, respiration, saturated oxygen, and electrocardiogram. Patients were monitored at 5 minute intervals throughout the infusion and 15 minute intervals post infusion until discharge. Average values for the vital signs were then determined at baseline and at 10 minute intervals until discharge. Vital signs from 210 infusions were reviewed, with 2,521 sets being analyzed. Results indicate that vital signs remained stable at  $\pm 20\%$  of the baseline values. Transient treatment-emergent side-effects included nausea, paresthesia, visual changes, dissociation, anxiety, paranoia, and euphoria. No infusion needed to be terminated. Two bipolar patients switched into mania and four patients developed persistent insomnia. No drug-seeking or cognitive side-effects were noted. These results demonstrate that repeat low-dose intravenous ketamine infusions for treatment-resistant depression can be administered safely with mostly mild transient physiological and psychological side-effects.

#### NR4-54

### IMPROVING METABOLIC HEALTH AND QUALITY OF LIFE IN MENTAL HEALTH CONSUMERS WITH THE CHUQ-IUSMQ MIEUX-ÊTRE WELLNESS PROGRAM: A FIVE-YEAR NATURALISTIC STUDY

*Chair: Christian Sbriqui M.D.; Author(s): Isabelle Lachance, ps.ed., M.Sc.; Sophie Bonneville, M.Sc. and the CHUQ-IUSMQ Mieux-Être Wellness Program Collaborative Group*

#### SUMMARY:

Presented is a five-year, ongoing, naturalistic evaluation of the Centre hospitalier universitaire de Québec (CHUQ)- Institut universitaire en santé mentale de Québec (IUSMQ) Mieux-Être Wellness program in Québec City, Canada. The program, offered at no cost to adult mental health consumers living in the community, includes a range of group and individual activities aimed at increasing physical and mental health,

quality of life and treatment compliance. Entry criteria are flexible so as to allow participants presenting a metabolic risk who are motivated to initiate lifestyle changes. Three groups of about 15 consumers each, referred by either their GP's, psychiatrists or internists are begun each year. So far, over 200 participants have entered the program which is of one year duration with subsequent yearly follow-ups. The initial 12 weeks are intensive with participants attending two to three weekly activities which are aimed to foster empowerment. These include nutritional counseling, cooking and relaxation workshops, a physical exercise program and weekly walking club. Afterwards, group and individual sessions occur every three months for up to one year. An adapted 8-week MBSR training, Qi-Gong and art therapy workshops are offered after the first 3 months. Metabolic health parameters, CGI severity of illness score, BPRS total score, WHOQOL quality of life and ROMI treatment compliance measures are conducted at baseline and every three months for up to one year. Of 207 participants, 32.4% presented with major depression, 20.8% bipolar disorder, 13.5% schizophrenia, 10.6% schizoaffective disorder, 9.2% anxiety disorder and 13.5% other psychiatric disorder. 69% of participants were females. The mean age of participants was 45.0 + 10.6 years. 77.3% of participants received an antipsychotic, 70% an antidepressant and 43% a mood stabilizer. Partial results following 3 and 12 months of the program using descriptive statistics and SPSS 14.0 for repeated measures ANOVA between baseline and following 3 and 12 months will be presented. Our results indicate modest yet statistically significant improvements in several metabolic health parameters in this at-risk population. Limitations of this naturalistic program evaluation (diagnostic heterogeneity, uncontrolled use of psychotropic medications) are to be balanced with the "real world" conditions of this ongoing program evaluation.

#### NR4-55

### THE MINI MENTAL STATUS EXAMINATION AND GLOBAL ASSESSMENT OF FUNCTIONING AS DETERMINANTS OF MEDICAL DECISION MAKING CAPACITY

*Chair: Gaurav Jain M.D.; Author(s): Pravesh Basnet, M.D.; Mary E. Royce, ACNP-BC; Lokesh Shabani, M.D.; Kristina Dzara, Ph.D.; and David S. Resch, M.D.*

#### SUMMARY:

Background: The Mini-Mental State Exam (MMSE) is a measure of overall cognitive ability. The Global Assessment of Functioning (GAF) score is the clinician's judgment of an overall level of functioning based on psychiatric evaluation. Both are frequently utilized

in Medical Decision Making Capacity (M.D.MC) evaluations.; Authors assessed the utility of these measures as an aid to the determination of M.D.MC by the psychiatry consultation team in the medical and surgical inpatient facilities of an academic medical center. Method: All patients referred to psychiatry consultation for M.D.MC determination during a one-year retrospective period were included (n=51). The initial consultation and follow-up notes were reviewed. Sociodemographic and clinical data were recorded and patients were grouped by final M.D.MC assessment. The study was IRB approved. Results: The consultation team agreed with the referring physician (M.D.MC absent) 48% of the time (n=24), although final M.D.MC was not documented in one chart. Most individuals (62.7%; n=32) had one or more axis I disorders. In the M.D.MC absent group, 75% (n=18) had any axis I disorder, compared to 50% (n=13) for the M.D.MC present group (p=.086). Cognitive disorders (including dementia and delirium) were present in 54.2% (n=13) of the M.D.MC absent group, compared to 19.2% (n=5) of the M.D.MC present group (p=.018). MMSE was attempted on 26 patients (50.9%), but could only be conducted on 20 (39.2%). GAF scores were available for 33 patients (64.7%). Those with and without M.D.MC did not vary by sociodemographic characteristics. MMSE and GAF scores between groups with and without M.D.MC were significant (p=.05 and p=.037, respectively). A MMSE score of = 23 had 56% sensitivity and 91% specificity and a GAF score of = 50 had 94% sensitivity and 44% specificity to detect M.D.MC. Pearson's correlation between the MMSE and GAF was 0.668 (p=.009). Conclusions: The use of MMSE and GAF together may be helpful in the determination of M.D.MC. Documentation of these measures needs improvement. These are meant to aid clinical evaluation, but not replace clinical judgment. Presence of Axis I psychiatric diagnosis did not significantly predict absence of M.D.MC, although cognitive disorders were significantly higher in the M.D.MC absent group.

#### NR4-56

### ANHEDONIA IN STROKE PATIENTS: NEUROANATOMICAL AND ENDOCRINOLOGICAL CORRELATES

*Chair: Luisa Terroni Ph.D.; Author(s): Patricia F. Matos, M.D. Edson Amaro Jr., M.D., Ph.D. Claudia C. Leite, M.D., Ph.D. Fabio Yamamoto, M.D. Gisela Tinone, M.D., Ph.D. Matildes F. M. Sobreiro, Psychologist. Valeri G. Delgado, Psychologist. Lucila E. Kabaogue, M.D., Ph.D.. Dan V Iosifescu, M.D. Mara C. S. Lucia, Ph.D. Ayrton C Moreira, M.D., Ph.D. Milberto Scaf, M.D., Ph.D. Renerio Fraguas, M.D., Ph.D.*

**SUMMARY:**

Background: Anhedonia has been associated with increased cortisol levels and neurobiological changes in depressed and nondepressed subjects. However little is known about this relationship in stroke patients. This study aimed to investigate the association of anhedonia with salivary cortisol levels and the location of stroke in cortical areas of the limbic-cortico-striatal-pallidal-thalamic circuit. Method: We investigated 36 patients in a neurology clinic in the first month after a first-ever supratentorial ischemic stroke. Anhedonia was diagnosed by a psychiatrist administering the SCID-I/P for DSM-IV. Salivary cortisol levels were measured in the morning, evening and after dexametasone challenge. We used MRI acquisitions in a 1.5-Tesla System and a semi-automated brain morphology method to assess stroke location. The quantification of lesion volume was done according to the Brodmann Map in the MRIcro program. Prevalence of anhedonia was compared in patients with cortisol levels in the upper tertile versus the other two tertiles. Result: The whole sample showed a significant decrease from morning to evening cortisol levels ( $p < 0.001$ ). Prevalence of anhedonia was 71.4% in patients with morning cortisol levels in the upper tertile versus 28.6% for patients the lower two tertiles of cortisol level ( $p = 0.029$ ). Anhedonic patients had greater lesions in the parahippocampal cortex compared with patients without anhedonia (10.14 voxels;  $sd = 17.72$  versus 0.86 voxels;  $sd = 4.64$ ;  $p = 0.027$ ). The lesions in hippocampal and parahippocampal region significantly correlated with cortisol levels in patients with anhedonia ( $\rho = -0.845$ ;  $p = 0.034$ ). Conclusion: Anhedonia in early stroke patients may be related to disruption of the LCSPT circuit via lesion in the parahippocampal cortex and mediated by increased levels of morning cortisol. References Brouwer, J. P., B. C. Appelhof, et al. (2006). "Prediction of treatment response by HPA-axis and glucocorticoid receptor polymorphisms in major depression." *Psychoneuroendocrinology* 31(10): 1154-63. Putnam, K. M., D. A. Pizzagalli, et al. (2008). "Neural activity and diurnal variation of cortisol: evidence from brain electrical tomography analysis and relevance to anhedonia." *Psychophysiology* 45(6): 886-95. Terroni, L., E. Amaro, et al. "Stroke lesion in cortical neural circuits and post-stroke incidence of major depressive episode: A 4-month prospective study." *World J Biol Psychiatry* Treadway, M. T. and D. H. Zald "Reconsidering anhedonia in depression: lessons from translational neuroscience." *Neurosci Biobehav Rev* 35(3): 537-55.

**NR4-57****A NOVEL TREATMENT OF HALLUCINOGEN PERSISTING PERCEPTION DISORDER***Chair: Henry Abraham M.D.***SUMMARY:**

Hallucinogen persisting perception disorder (HPPD) is a poorly understood chronic disorder arising from the use of hallucinogenic drugs. It is characterized by continuous visual disturbances including geometric pseudohallucinations, "visual snow," trails of moving objects through the visual field halos around objects, and afterimages. This drug-induced visual disorder is continuous and lifelong in approximately half the cases. There is no known effective pharmacological treatment. Studies of HPPD patients with electrophysiological brain mapping show that the disorder is represented by widespread disinhibition in the portions of the cerebral cortex processing visual information. Recently it was discovered that the medication tolcapone, an antiparkinsonian agent operating at the level of the enzyme COMT, was found to increase certain inhibitory sensory processes in subjects with a specific genetic variant of the enzyme. Based on this finding an open label trial of tolcapone and Sinemet was performed in 15 consecutive patients suffering from chronic HPPD. We now report that this combination of medications is effective in one third of the sample, with a 53% reduction in symptom intensity in responders. A two tailed, paired predrug and postdrug T-Test across the entire sample was statistically significant for a medication effect at the  $P < 0.001$  level. This constitutes a novel potential treatment for HPPD.

**MONDAY MAY 07, 2012****New Research Young Investigator Session 2****NR5-01****SEVERITY OF DEPRESSIVE SYMPTOMS IN LATE PREGNANCY DEPENDS ON THE INTERACTION BETWEEN CIRCADIAN RHYTHM AND SLEEP DISTURBANCES***Chair: William Simpson B.S.C.; Author(s): Benicio N. Frey, M.D., Ph.D Meir Steiner, M.D., Ph.D, FRCPC***SUMMARY:**

Objective: Depression is highly prevalent during pregnancy and the postpartum period. Up to 80% of women experience perinatal depressive symptoms, with 10-15% developing clinically significant depressive illness. Circadian rhythm disruptions such as changes in sleep quality, eating patterns, day to day and social activities, are commonly seen during late pregnancy. Research has shown that circadian/

biological rhythm disruptions are strongly tied to changes in mood. Sleep changes are of particular interest as sleep deprivation studies indicate significant neuropsychological and cognitive changes, even when sleep is only mildly disrupted. Poor sleep quality during pregnancy is significantly correlated with depressive symptoms, however no study to date has investigated the relationship between sleep quality, biological rhythm disruption and symptoms of depression during this time period. Methods: Twenty medication-free women were investigated between 30 and 37 weeks gestation. Circadian rhythm functioning, sleep quality and depressive symptoms were assessed via self-rated questionnaires. Circadian rhythm was assessed using the Biological Rhythm Interview of Assessment in Neuropsychiatry (BRIAN), sleep using the Pittsburgh Sleep Quality Index (PSQI) and depression using the Edinburgh Perinatal Depression Scale (EPDS). Results: Correlations were strong between PSQI and BRIAN ( $rP=0.76$ ,  $p<0.001$ ), BRIAN and EPDS ( $rP=0.83$ ;  $p<0.001$ ) and PSQI and EPDS ( $rP=0.64$ ;  $p=0.003$ ). Both the EPDS and BRIAN contain items pertaining to sleep. To further assess the correlation between these variables, while controlling for overlapping sleep items, we eliminated all sleep sub-scores from the EPDS and the BRIAN. This manipulation slightly reduced the correlation between PSQI and BRIAN ( $rP=0.65$ ;  $p=0.002$ ), but did not alter the strong association between EPDS and PSQI ( $rP=0.65$ ;  $p=0.002$ ) or EPDS and BRIAN ( $rP=0.84$ ;  $p<0.001$ ). Subsequent multiple regression analysis was conducted to model the effect of the PSQI and BRIAN on EPDS scores. This analysis revealed a significant interaction between the PSQI and BRIAN ( $t=2.57$ ;  $p=0.02$ ) and accounted for 78% of the variance in the sample. Conclusions: The severity of depressive symptoms in late pregnancy appears to be highly correlated with variations in circadian rhythm and sleep disturbances. The interaction between sleep and circadian rhythm in the multiple regression analysis suggests that a combination of these factors, rather than either factor alone, is associated with depressive symptoms during pregnancy. Given that depressive symptoms during pregnancy is one of the strongest predictors of subsequent postpartum depression, investigating factors which modulate the biological clock could aid in the development of new treatment and prevention strategies.

#### NR5-02

### A CLINICAL COMPARISON BETWEEN YOUNGER AND OLDER PSYCHIATRIC OUTPATIENTS WITH DEPRESSION

*Chair: Reshmi Saranga M.D.; Author(s): Elizabeth C. Penick, Ph. D, Elizabeth J. Nickel, M.A., Ekkehard Othmer,*

*M.D., Ph. D, Barry Liskow, M.D., Edward N. Hunter, Ph.D., William F. Gabrielli, M.D., Ph.D.*

#### SUMMARY:

**Objective:** The controversy continues about whether the depressions commonly found among older people are sufficiently different from those found among young people to warrant its own diagnostic classification. This study uses a comprehensive database to address that question. **Method:** During a five-year period, 1,002 consecutively admitted outpatients in a University Psychiatric Outpatient Clinic met diagnostic criteria for major depression (29% male). Patients were administered a structured psychiatric interview, a psycho-social survey that included family history, treatment history, ratings of a current and past functioning, and the Symptom Checklist-90-R. The youngest 10% of depressed patients (= 23 years; N=115) and the oldest 10% of depressed patients (>60 years; N=97) were selected for study. **Results:** The young and old depressive groups did not differ by gender. Despite the almost four decade difference, younger patients endorsed a significantly greater number of lifetime depressive symptoms; younger patients were more likely to report hypersomnia, increased appetite/weight gain, decreased libido, loss of confidence and suicidal behavior, including a suicide attempt (37% vs. 15%). Most striking was the enormous increase in comorbid psychiatric syndromes among the younger depressive patients. All of the syndromes reviewed, except for cognitive impairment, were more than doubled in the younger patient group. Similarly, although a family history of depression did not distinguish the younger from older groups, psychiatric comorbidity in biological relatives was uniformly higher in the families of young patients. On the SCL-90-R, younger females (but not males) with depression indicated higher levels of current distress than older females when first seen. **Conclusion:** Compared to older patients with depression, younger depressed patients demonstrated a strikingly greater degree of psychiatric comorbidity for themselves and among biological relatives that clearly should be a major focus in the clinical management of young depressed patients. However, these findings do not support the suggestion that depression in younger and older patients represent distinctly different clinical syndromes.

#### NR5-03

### PLASMA ASS LEVELS, DEMENTIA, AND DEPRESSION IN ELDERLY PERSONS: THE ROTTERDAM STUDY

*Chair: Nese Direk M.D.; Author(s): Elisabeth M.C. Schrijvers, Albert Hofman, M. Arfan Ikram, Henning Tiemeier*

**SUMMARY:**

Objectives: Two soluble forms of amyloid  $\beta$ -peptides, amyloid  $\beta$ 1-40 (A $\beta$ 1-40) and amyloid  $\beta$ 1-42 (A $\beta$ 1-42), have been associated with the risk of Alzheimer's disease (AD). Based on the observation that depression occurs commonly before the onset of AD, a few studies tested the association of amyloid  $\beta$  levels with depression in older adults. However, the findings of these cross-sectional studies are incongruous and the role of dementia in this association has not been tested formally. Therefore, we tested the cross-sectional and longitudinal associations between amyloid  $\beta$  levels and depression in community-dwelling older adults controlling for incident dementia. Methods: Within the Rotterdam Study, 924 persons with A $\beta$ 1-40 or A $\beta$ 1-42 assessments and free of dementia and free of depressive symptoms at baseline participated. Participants were evaluated for depressive symptoms with a Centre for Epidemiological Studies-Depression scale at baseline (1997-1999) and two follow-up visits (2002-2004 and 2009-2011). We investigated the cross-sectional and longitudinal association between amyloid  $\beta$  levels and depression. Additional analyses were conducted stratifying for the occurrence of dementia during follow-up. Results: In the cross-sectional analyses, A $\beta$ 1-40 and A $\beta$ 1-42 levels were positively associated with depressive symptoms in participants who would later develop dementia. In the longitudinal analyses, lower levels of A $\beta$ 1-40, A $\beta$ 1-42 predicted higher depression scores at follow-up in those who remained free of dementia. Conclusions: These findings suggest that the association of amyloid  $\beta$ -proteins and depressive symptoms in the cross-sectional evaluation is due to the subsequent dementia. However, the longitudinal findings in a cohort free of dementia during follow-up suggest that amyloid  $\beta$ -proteins may play a distinct role in the etiology of depression.

**NR5-04**  
**EMOTIONAL PROCESSING DEFICITS IN**  
**PATIENTS WITH A FIRST EPISODE OF**  
**MAJOR DEPRESSIVE DISORDER: AN FMRI**  
**STUDY**

*Chair: Jianying Li M.Med.; Author(s): Xiaohua Cao, Ph.D., Zhifen Liu, M.M., Ning Sun, M.M., Yong Xu, M.D., Kerang Zhang, M.D.*

**SUMMARY:**

Objective: To investigate the neural mechanisms underlying emotional processing deficits in patients with major depressive disorder (M.D.D) by comparing the differences between subjects with and without M.D.D at the behavioral and brain functional level. Methods: 26

patients with M.D.D and 20 age and gender-matched normal adults were recruited. All of the participants were assessed by the 17-item Hamilton Depressive rating scale (HAM.D.). The subjects were scanned when performing an event-related emotional processing task, in which three types of pictures (positive, neutral and negative pictures) appeared randomly. The subjects were required to concentrate on the pictures and push the corresponding button to judge the nature of each picture. Behavioral data were analyzed using the PASW statistics 18 software, and the average response time and accuracy were calculated and compared between groups. Imaging data were analysed using the DAPRSE, SPM and Xjview software, and one-sample t-tests and independent two-sample t-tests were done. Results: 1. The patients showed longer reaction time than the controls ( $791.51 \pm 203.20$  and  $659.77 \pm 151.20$  ms respectively). The differences in reaction time were mainly caused by the differences when observing negative pictures, with  $780.15 \pm 196.04$  ms in M.D.D and  $645.54 \pm 185.79$  ms in the controls. No significant difference in accuracy were found between groups, but the M.D.D group showed significantly lower accuracy when exposed to positive pictures relative to the controls, with  $0.84 \pm 0.27$  and  $1.11 \pm 0.22$  respectively after arcsine square root transformation. 2. When looking at the positive and neutral pictures, the patient group exhibited more activation in the superior frontal gyrus than the control group. When looking at the negative picture stimuli, the patient group showed more activation in the superior frontal gyrus and middle frontal gyrus than the healthy subjects. 3. Correlation analysis showed significant positive correlations between HAM.D. score and the reaction time when observing the positive, negative and neutral pictures. That is, the greater the HAM.D. scores, the longer the reaction time. Significant negative correlations were seen between the HAM.D. score and the accuracy of neutral pictures, with the greater the HAM.D. scores, the lower accuracy when looking at the neutral pictures. Conclusions: Compared with the controls, patients with M.D.D showed impaired brain function abnormalities, with more regions activated when performing an emotional task (superior frontal gyrus and middle frontal gyrus), slower response (longer mean reaction time), and numbness when looking at the positive pictures. A negative cognitive bias were observed in M.D.D, with longer reaction times relative to the controls when exposed to the negative stimuli.

**NR5-05**  
**THE EFFECT OF ANTIDEPRESSANT**  
**ADMINISTRATION ON AWAKENING**  
**CORTISOL LEVEL**

*Chair: Wonwoo Kim M.D.; Author(s): Jong-Taek Choi, M.D., Young-Jun Kwon, M.D., Ph.D., Hwa-Young Lee, M.D., Ph.D.*

#### SUMMARY:

**Background:** Dysfunction of hypothalamic-pituitary-adrenal(HPA) system is assumed to be involved in the pathophysiology of major depressive disorder. Depressive patients have shown significantly increased levels of awakening cortisol level. Antidepressant treatments have an effect on abnormal HPA axis and it also on cortisol level. Many clinical studies have suggested that a restoration of HPA-axis hyperactivity is associated with antidepressant treatment. We aimed to investigate the effect of antidepressant administration on awakening cortisol level according to the class of antidepressant. **Methods:** The total number of subjects were thirty-one depressive inpatients. Awakening blood cortisol level(6 am) and Hamilton depression rating scale were measured at the beginning of treatment, and after 4weeks of treatment with antidepressants. Three antidepressants were used mirtazapine (13 patients), venlafaxine (10 patients) and escitalopram(8 patients). **Results:** Overall awakening cortisol level was significantly decreased after antidepressant treatment ( 16.53±6.33 pg/ml to 13.55±5.68 pg/ml, p=0.039). Mirtazapine(18.74±5.64 pg/ml to 13.58±6.14 pg/ml, p=0.033) and escitalopram(15.54±6.29 pg/ml to 11.35±5.60 pg/ml, p=0.008) decreased awakening cortisol level. In contrast, venlafaxine(14.44±6.91 pg/ml to 15.29±5.04 pg/ml, p=0.776) did not attenuate awakening cortisol level. **Conclusions:** The effects of antidepressant on cortisol level are different according to the class of antidepressant.  $\beta$ 1-adrenoreceptor and 5-HT<sub>2A/C</sub> mediated mechanisms may lead to an activation of the HPA system during treatment with serotonin and noradrenaline reuptake inhibitors. These effects may explain why venlafaxine did not lead to an attenuation of HPA system activity within 4 weeks of treatment. The effects of antidepressant administration on cortisol level might provide the information about selection of antidepressant according to the awakening cortisol level before antidepressant administration .

#### NR5-06

#### AN UNUSUAL CASE OF CPAP-INDUCED MANIA

*Chair: Richa Aggarwal M.D.; Author(s): Saunders, E. M.D.; Baweja, R. M.D.; Singareddy, R. M.D.*

#### SUMMARY:

**Introduction/case:** Obstructive sleep apnea (OSA) affects 4-7 %of the general population. OSA patients have

recurrent episodes of complete or partial cessations in breathing with associated oxygen desaturations and/or arousals. Bipolar disorder is a severely disabling mood disorder characterized by the presence of recurrent episodes of abnormally elevated energy levels, cognition and mood (DSM-IV TR). Here we present a case of a 51 year-old man, Mr. H, with stable, asymptomatic bipolar disorder, who developed a manic episode after he was started on CPAP for OSA for the first time. Mr. H's apnea/hypopnea index was high at 94.6, indicating very severe OSA. His SaO<sub>2</sub> was below 90% for 18.4% of the total sleep time in the laboratory. On CPAP, his apnea/hypopnea was eliminated, and his minimum oxygen saturation improved to 93% during REM and 94% during NREM sleep. After 3 weeks of CPAP treatment, Mr. H developed manic symptoms including euphoria with increased energy, physical aggression, motor hyperactivity, racing thoughts, pressured speech and visual hallucinations. He was treated pharmacologically and his manic symptoms resolved despite continued use of CPAP. **Discussion:** A clear mechanism for development of mania due to CPAP treatment of OSA is unknown. One hypothesis is the induction of affective symptoms due to sudden alterations in the concentration of gaseous elements in the blood, which in turn may affect the CNS. **Conclusion:** Clinicians should be vigilant for the development of manic episodes in bipolar patients who are treated with CPAP for their OSA, and should be aware of the possibility of development of a new mania in a patient with major depressive disorder.

#### NR5-07

#### THE INTERNATIONAL MOOD NETWORK (IMN): PRELIMINARY FEASIBILITY AND FINDINGS. DATA FROM THE INTERNATIONAL MOOD NETWORK (IMN)

*Chair: Paul Vöbringer M.D.; Author(s): Paul A. Vöbringer, Homayoun Amini, Sergio Barroilhet, Serge Beaulieu, Marcelo Cetkovich-Bakmas, Jagan Chilakamarri, Rodrigo Cordoba, Eduardo Correa, Nick Craddock, Jürgen De Fruyt, Rif El-Mallakh, Xenia Gonda, Oscar Heeren, Gerhard Heinze, Luis Herbst, Ingrid Vargas Huicochea, Flavio Kapczinski, Tadafumi Kato, Tammas Kelly, Beny Lafer, Carlos Loyola, Marcia Marinelli, Sivan Mauer, Lorenzo Mazzarini, Sonia Medina, Philip Mitchell, Adel Omrani, Chi-Un Pae, Gordon Parker, Jim Phelps, Jeffrey Rakofsky, Luis Risco, Janusa Rybakowski, Joseph Sadek, Ihsan Salloum, Paula Salvatore, Gabriele Sani, Richard Shelton, Daniel Smith, Sergio Strejilevich, Alan Swann, Tomasz Szafranski, Leonardo Tondo, Gustavo Vazquez, Eric Youngstrom, Rodolfo Zaratiegui, S. Nassir Ghaemi.*

#### SUMMARY:

Introduction: The International Mood Network (IMN) is a multicenter international collaboration created to answer some of the most pressing research questions that require hundreds or thousands of patients to have adequate statistical power. Without several years of patient enrollment, such sample sizes are beyond the reach of most individual institutions. Since its inception in June of 2011, 48 sites have agreed to contribute anonymous patient data. The present study analyzes the preliminary IMN data for clinical and demographic characteristics. Methods: The IMN establishes a joint international research database, accessible to all participating sites. The entry of anonymous patient data is based on a common core set of variables. The data was pooled from multiple sites using a centralized online system developed by the Tufts Clinical and Translational Science Institute (CTSI) and then analyzed in the Mood Disorders Program at Tufts Medical Center. This study outlines the preliminary clinical and demographic characteristics of the first 85 patients submitted to the IMN. Results: We will present data on an estimated sample of 300 subjects or more. Here we present an interim analysis of an initial sample of 85 patients. The sample was 53% female, with mean age  $37.7 \pm 12.7$  years. Bipolar disorder was diagnosed in 85% of the sample (Type I 56%, Type II 25%, NOS 2%) and major depressive disorder (M.D.D) in 15%. 28% had a rapid-cycling course. Family history of mental illness was present in 81%, past substance abuse in 27%, past psychosis in 30%, and past suicidal ideation in 40%. The sample had a mean of 1.3 hospitalizations, and had a moderate to severe lifetime CGI severity of illness. 60% of the sample was clinically judged to be responsive to mood stabilizers, 52% to antidepressants, and 42% to neuroleptics. Past antidepressant-induced mania was present in 25%. Conclusions: These data provide evidence of feasibility of an international database for mood disorders. Clinical and demographic characteristics of this cohort are consistent with prior studies and extend those findings. This new cohort will be used for prospective research. Such large cohorts are needed to advance clinical research in psychiatry.

**NR5-08**  
**UNDERDIAGNOSIS OF BIPOLAR DISORDERS: AN INTERNATIONAL REALITY DATA FROM THE INTERNATIONAL MOOD NETWORK (IMN)**

*Chair: Niki Holtzman B.A.; Author(s): Niki S. Holtzman, BA; Paul A. Vöbringer, M.D.; Matthew C. Sullivan, BA; S. Nassir Ghaemi, M.D., M.P.H., for the IMN investigators.*

**SUMMARY:**

Introduction: Data from the International Mood

Network (IMN) aid in answering research questions through collaboration of multiple international research sites. Previous studies have shown that bipolar disorder (BD) is underdiagnosed, often mistaken as unipolar depression. Recently, some have claimed that this condition is overdiagnosed. The present study examines the issue of misdiagnosis of BD in a cross-cultural, international sample with data from the IMN. Methods: The IMN is a joint international research database. The entry of anonymous patient data is based on a common core set of variables and supplemented with optional additional data required for specific projects. The data was pooled from multiple sites using a centralized online system developed by the Tufts Clinical and Translational Science Institute (CTSI) and then analyzed in the Mood Disorders Program at Tufts Medical Center. Misdiagnosis was defined as diagnosis of non-BD conditions after the first manic episode. Results: We will present data on an estimated sample of 300 subjects or more. Here we present an interim analysis of an initial sample of 85 patients, of whom 84% were diagnosed with bipolar disorder. Of the BD sample, 21 patients (29.6%) were misdiagnosed with other psychiatric conditions before receiving the correct diagnosis of BD. In the BD sample, mean age was  $37.3 \pm 12.5$  years, mean age of onset of a mood disorder was 19, the age patients first experienced a major depressive episode (M.D.E) was 20, and the age of patients' first manic episode was 23. Patients first received MH treatment at age 23. Amount of time misdiagnosed was  $14.05 \pm 10.95$  years. Conclusions: Misdiagnosis of BD represents an unresolved international public health issue. Consistent with numerous misdiagnosis studies, recently and from a decade ago, BD continues to be underdiagnosed in about one-third of the patients who have the condition; these data extend those results to an international level. In those misdiagnosed, about 14 years elapse before the correct diagnosis is made, leading to much unnecessary morbidity. These IMN findings support the notion that further measures to improve early detection of BD are needed.

**NR5-09**  
**CLINICAL PREDICTIVE FEATURES OF MIXED DEPRESSION: AN INTERNATIONAL STUDY DATA FROM THE INTERNATIONAL MOOD NETWORK**

*Chair: Matthew Sullivan B.A.; Author(s): Matthew C. Sullivan, BA; Paul A. Vöbringer, M.D.; Niki S. Holtzman, BA; S. Nassir Ghaemi, M.D., M.P.H. for the IMN Investigators.*

**SUMMARY:**

Introduction: Data from the International Mood

Network (IMN) aid in answering research questions through collaboration of multiple international research sites. The depressive mixed state is of research interest because it is the most common mood state in bipolar disorder (BD) patients. The DSM-IV definition of the depressive mixed state is narrow and may exclude many instances of this mood state. Koukopoulos has delineated criteria that define the mixed state more broadly, emphasizing irritability, agitation, and mood lability, during a clinical depressive episode. Method: Data for the present study were obtained from the IMN, a joint international research database. The data was pooled from multiple sites using a centralized online system developed by the Tufts Clinical and Translational Science Institute (CTSI) and then analyzed in the Mood Disorders Program at Tufts Medical Center. We examine the presence of the depressive mixed state as defined by DSM-IV and Koukopoulos mixed criteria and compare the respective frequencies of the depressive mixed state. Predictors of fulfillment of Koukopoulos criteria are examined using logistic regressions. Results: We will present data on an estimated sample of 300 subjects or more. Here we present an interim analysis of an initial sample of 85 patients. The mean age was  $37.7 \pm 12.7$  years, and 53% of subjects were female. Diagnostic breakdown of the sample was bipolar disorder - Type I 56%, Type II 25%, NOS 2%; unipolar depression 15%. Of these subjects, 21% met Koukopoulos mixed state criteria and 6% met full DSM-IV mixed state criteria. Two factors were identified as clinical predictors of Koukopoulos mixed state criteria: younger age of first mental health treatment (OR 0.73; 95% CI [0.17, 0.99]) and greater lifetime illness severity (OR 1.03; 95% CI [1.05, 1.92]). Conclusions: These results indicate that while relatively few people are diagnosable with mood disorders meet full DSM-IV criteria for mixed states, a broader definition identifies this condition in 21% of an unselected international mood disorder sample. Younger age of initial treatment and greater severity of illness were predictors of mixed states.

**NR5-10**  
**CLINICAL PREDICTIVE FEATURES OF**  
**SUBSTANCE ABUSE IN MOOD DISORDERS:**  
**AN INTERNATIONAL STUDY DATA FROM**  
**THE INTERNATIONAL MOOD NETWORK**  
**(IMN)**

*Chair: Derick Vergne M.D.; Author(s): Derick E. Vergne M.D., Paul A. Vöbringer, M.D.; Niki S. Holtzman, BA; Matthew C. Sullivan, BA; S. Nassir Ghaemi, M.D., M.P.H., for the IMN Investigators.*

**SUMMARY:**

Introduction: Data from the International Mood

Network (IMN) aid in answering research questions through collaboration of multiple international research sites. Substance abuse is of research interest because it is a common comorbidity in mood disorder patients, and is associated with poor outcomes. Method: Data for the present study were obtained from the IMN, a joint international research database. The data was pooled from multiple sites using a centralized online system developed by the Tufts Clinical and Translational Science Institute (CTSI) and then analyzed in the Mood Disorders Program at Tufts Medical Center. We examined correlations with substance abuse in this a subsample of patients with past substance abuse by using multivariate logistic regression modeling. Results: We will present data on an estimated sample of 300 subjects or more. Here we present an interim analysis of an initial sample of 85 patients, of whom 84% were diagnosed with bipolar disorder and 28% of whom had past substance abuse. In the past substance abuse subsample, the mean age was  $43.75 \pm 6.84$  years, patients had a mean of  $2.0 \pm 0.8$  hospitalizations, and mean age of onset of the first mood episode was  $30.0 \pm 8.0$  years. The age of first mental health treatment was  $30.0 \pm 3.9$  years, with bipolar diagnosis occurring at age  $36.0 \pm 5.5$  years. Two factors were identified as strong predictors of substance abuse: older current age (OR 1.07; 95% CI [1.00, 1.14]) and history of past suicide attempts (OR 16.9; 95% CI [2.37, 120.3]). Conclusions: Substance abuse was present in 28% of an international, unselected mood disorder sample. Substance abuse was highly correlated with suicidality, supporting the importance of this clinical variable in addressing the most dangerous outcome of mood disorders. This subset of patients had an older age of onset than is standard for bipolar disorder, and experienced a six-year delay from first psychiatric treatment to correct bipolar diagnosis.

**NR5-11**  
**ASSOCIATION OF SUBJECTIVE DEPRESSION**  
**AND COGNITIVE FUNCTIONS IN**  
**TRAUMATIC BRAIN INJURY**

*Chair: Heesung Hwang M.D.; Author(s): Hyun-Jung Park, M.D., Han Yong Jung, M.D., Ph.D., Soyoung Irene Lee, M.D., Ph.D., Shin Gyum Kim, M.D., Kyung-Se Na, M.D.*

**SUMMARY:**

Objective: Depression and cognitive dysfunction are common neuropsychiatric sequelae in patients with traumatic brain injury (TBI). Because depression could influence on the cognitive function, it is important to evaluate the association of depression and other cognitive functions. We aimed to investigate whether subjective depression is associated with memory impairment and executive dysfunction in TBI. Methods:

A retrospective chart review study was conducted from January 2003 to December 2010. Charts of patients with mental retardation were not assessed. Memory functions were represented as memory quotient (MQ) with Rey-Kim memory test. Executive functions were assessed with Kim's executive function test (EXIT) and represented as executive intelligence quotient (EIQ). Subjective depression was measured by the Beck Depression Inventory (BDI). Patients with TBI were divided into four groups according to quartile of the BDI scores. Differences in MQ, EIQ, and BDI scores were compared by analysis of variance with Bonferroni correction for multiple comparison. Correlation between BDI scores and cognitive variables were also investigated. Results: A total of 129 TBI patients' chart was assessed. There were no differences in age, gender, education, and intelligent quotient (IQ) among four groups. Each cut-off point for the quartile of the BDI was 22, 30, and 38. The lowest quartile (0 - 25%) group had significantly lower scores on the EIQ compared to the highest quartile (76 - 100%) group. MQ was not significantly different among the four groups. There were no differences in MQ and EIQ regarding second (26 - 50%) and third (51 - 75%) quartile group. Both the MQ ( $r = -.201$ ) and EIQ ( $r = -.311$ ) had negative correlation with BDI scores in a total sample. Conclusion: Our results suggest that clinicians should consider level of subjective depression in interpreting cognitive functions, especially executive functions in patients with TBI.

**NR5-12****A COMPARISON STUDY BETWEEN VISUAL INTERPRETATION AND STATISTICAL PARAMETRIC MAPPING (SPM) ANALYSIS OF SPECT IMAGES IN TRAUMATIC BRAIN INJURY PATIENTS**

*Chair: Hyun Jin Jung, M.D.; Author(s): Seongjin Cho, M.D., Cheongyub Cheong, M.D., Yongchon Park, M.D., Ph.D.*

**SUMMARY:**

**Objectives :** The first objective of this study was to examine the extent to which the results of visual interpretation of brain single photon emission computed tomography (SPECT) images correspond with those of SPM analysis in patients with traumatic brain injury (TBI). The second objective was to examine the association between brain lesions appearing in the SPM analysis and neuropsychiatric symptoms of which the patients complained. **Methods :** SPECT images from 10 TBI patients (all male, mean age  $46.8 \pm 12.32$ ) and age- and sex-matched 10 control subjects were interpreted by an experienced radiologist. Their

SPECT images were also analyzed by SPM2 software for comparing the individual images with the controls. **Results :** Generally, the results of visual interpretation of SPECT images corresponded with those of SPM analysis in 5 of 10 TBI cases. In the remaining cases, brain lesions not identified from visual interpretation were found through SPM analysis. The location of these lesions included the cingulate gyrus, caudate nucleus, thalamus, and subcallosal area. SPM analysis also made it easy to identify an association between TBI patients' neuropsychiatric symptoms brain damage region **Conclusion :** This study suggested the possibility of clinical applications of SPM analysis of SPECT data from patients with TBI.

**NR5-13****A SYSTEMATIC REVIEW OF THE MANAGEMENT OF IMPULSE CONTROL DISORDERS IN PARKINSON'S DISEASE PATIENTS**

*Chair: Robini Ravindran M.D.*

**SUMMARY:**

Impulse Control Disorders have been seen primarily in Parkinson's patients who are being treated with dopamine agonist drugs. However it has also been noted in patients taking levodopa-carbidopa and other agents. The patients were seen to gamble pathologically, shop excessively, engage in risky sexual practices etc. Clinicians would stop the offending agent and these behaviours would resolve. This poses another problem because the disabling motor symptoms from Parkinson's disease would return. The explanation for these impulse control disorder is there is likely an overstimulation of the mesolimbic pathway in addition to the nigrostriatal pathway linked to Parkinson's disease. It should be noted that one study has shown that patients developing ICDs have been known to display some degree of impulsivity prior to starting the agent. The overall prevalence of ICDs in Parkinson's patients is 5% with an additional 5-10% experiencing this disorder at one point during their illness. This systematic review is looking at alternative management strategies that have emerged in practice. One study shows use of quetiapine or clozapine is helpful. Another study shows deep brain stimulation is an useful option but different studies show that this too can lead to impulse control disorders. Amantadine has been shown to be free of this side effect.

**NR5-14****CASE REPORT OF A YOUNG FEMALE WITH CATATONIA AND PNEUMONIA RESPONDING RAPIDLY TO RIGHT UNILATERAL ULTRA-BRIEF PULSE ELECTROCONVULSIVE**

**THERAPY**

*Chair: Kevin Holleman D.O.; Author(s): Marc A Capobianco, M.D.*

**SUMMARY:**

**Abstract Objective:** Bilateral ECT is a known effective treatment for catatonia but can cause significant memory loss. Right Unilateral Ultra-Brief Pulse Electroconvulsive Therapy (RUL UBP ECT) has been shown to be efficacious with minimal cognitive adverse effects in adult patients with major depression. Few published reports exist demonstrating the effectiveness of Right Unilateral Ultra-Brief Pulse ECT for catatonia. We describe one such case. **Methods:** S is a 27 year old African American female with a past psychiatric history of postpartum psychosis and three previous admissions for presumptive schizophrenia, catatonic type which had been responsive to risperidone 3mg qhs. She was brought into the hospital by her mother who reported that S had not been eating, drinking, or speaking for two days. She was noted to be poorly compliant with medications and after care following three previous admissions. **Results:** Examination on admission revealed the patient to be verbally unresponsive, cataleptic, with waxy flexibility, fixed staring, akinetic, withdrawn, with minimal PO intake and incontinent of bowel and bladder. Medical and neurologic work up was normal. She was started on Lorazepam and titrated to 8mg QID and maintained on Risperidone 3mg QHS. Shortly afterwards, the patient experienced an increased leukocytosis, became febrile and was found to have a left lower lobe pneumonia which was effectively treated with IV Levofloxacin. Risperidone was discontinued due to concern of neuroleptic malignant syndrome. Because there was not much change in her condition with high dose benzodiazepines, the court approved 15 ECT treatments in 30 days. Dramatic improvement was seen after one right unilateral ECT. She continued to improve with three subsequent treatments over the course of one week as evidenced by serial Bush-Francis catatonia scores of 17, 8, 0 and 0. ECT was then held for observation whereby she subsequently regressed (Bush-Francis Score of 9); thus ECT was re-initiated and she received three additional treatments with good effect (Bush Francis Scores of 0, 0, 0). Risperidone was also titrated up to 4mg qhs. At time of discharge the patient was noted to be socializing well on the ward with complete return to baseline functioning. **Conclusion:** This case describes a patient presenting with acute catatonia secondary to underlying psychosis. While the current literature supports the use of bilateral ECT as the primary treatment modality if benzodiazepines fail; side effects such as memory impairment and cognitive deficits may limit its utilization. Right unilateral

ultra-brief pulse ECT has a significantly lower incidence of memory loss and should be considered as an effective alternative.

**NR5-15****COMBINED USE OF SUICIDE INTENT SCALE AND KAROLINSKA INTERPERSONAL VIOLENCE SCALE IN THE PREDICTION OF SUICIDE**

*Chair: Jon Stefansson M.D.; Author(s): Peter Nordström (M.D., Ph.D., Adj. Ass. Professor); Bo Runeson (Professor, M.D., Ph.D.); Jussi Jokinen (M.D., Ph.D., Senior researcher)*

**SUMMARY:**

Over the past 30 years, Beck's Suicide Intent Scale (SIS) has been the prevailing psychometric scale for assessing suicide intent in suicide attempters (Freedenthal, 2008). In a recent review article, five out of 13 studies showed a positive relationship between high SIS scores and suicide over a follow-up period ranging from 10 months to 20 years (Freedenthal, 2008). We have recently reported that the Suicide Intent Scale is a valuable tool in clinical suicide risk assessment (Stefansson et al., 2012). Karolinska Interpersonal Violence Scale (KIVS) measures both the exposure to violence and expressed violent behaviour (Jokinen et al., 2010). Two subscales: exposure to violence as a child and expressed violent behaviour as an adult were predictive for subsequent suicide in suicide attempters. The aim of this study was to investigate if the combined use of Suicide Intent Scale and Karolinska Interpersonal Violence Scale will offer a better prediction of suicide risk than use of only one clinical rating scale. This is a cohort study involving 81 suicide attempters included to the study between 1993 and 1998. Patients were assessed with both SIS and KIVS. By use of the unique personal identification number patients were linked to the Cause of Death register, maintained by the National Board of Health and Welfare in Sweden. Seven patients had committed suicide before April 2011; suicides were ascertained from the death certificates. Positive predictive value for Suicide intent scale alone was 16.7 % with area under the curve of 0.74. Combined assessment with KIVS gave higher specificity and a positive predictive value of 26% with AUC of 0.85. A combined use of the Karolinska Interpersonal Violence Scale (KIVS) and Suicide Intent Scale (SIS) showed a better predictive value in suicide prediction indicating that they measure different components of risks.

**NR5-16****PARENTAL BONDING AND SUICIDE IN ADOLESCENTS AND ADULTS**

*Chair: Simona Goschin M.D.*

**SUMMARY:**

Abstract Objective: Lack of parental bonding or overprotection are known risk factors for adult mental disorders including anxiety and depression. Although both anxiety and depression are associated with suicidality, the literature is inconsistent about the role of parental bonding deficiencies in suicidal behavior. This review presents the current state of knowledge of the relationship between parental bonding and suicidality. Method: Computerized databases Medline, PubMed, Psycinfo, Psychlit, and Google Scholar were searched for key words suicidality, suicide, suicide attempt, suicidal behavior, parental bonding, and parental bonding instrument. Of these, reports on the relationship between suicidality and parental bonding as measured by validated parental binding instruments were reviewed. Results: Ten papers were analyzed. Of these, all used the Parental Bonding Instrument (PBI) and one used both PBI and the Object Representation Inventory. Of these, seven differentiated between suicidal attempts and suicidal behavior, and three did not. All but one reported that both lack of maternal care and maternal overprotectiveness were associated with increase in suicidal behavior. The papers were split with regard to the effects on suicidality of deficient paternal bonding, although low paternal care appeared to be more pernicious. Common methodological problems included low subject numbers and lack of a uniform definition of various aspects of suicidality. Conclusion: The data indicates that neglectful parental care and overprotective behavior on the part of mothers are associated with an increase in suicidal behavior in adults. Future studies with larger sample sizes and standardized definition of types of suicidal behavior are needed to confirm these findings. Early intervention aimed at improving parenting style in families with a history of affective disorders could be effective in reducing suicidal behavior in their offspring.

**NR5-17**

**CORRELATION BETWEEN SLEEP DISTURBANCE, QUALITY OF LIFE IMPAIRMENT AND INCREASED SUICIDE RISK AMONG HEMODIALYSIS PATIENTS**

*Chair: Valfrido De-Melo-Neto M.D.; Author(s): Duarte, Daniella Bezerra. M.D.. Brandão, Susana. MS. Lisboa, Diego. MS. Pinheiro, Maria Eliete. Ph.D.. (Nardi, Antonio Egidio. Ph.D.. (*

**Summary:**

Background: Depression, anxiety and sleep disturbance

represent three of the most common psychiatric features in hemodialysis patients. They can impair quality of life of these patients. Objectives: To investigate the prevalence of Axis I Psychiatric Disorders among End Stage Renal Disease (ESRD) patients submitted to hemodialysis treatment, according to DSM-IV criteria. To measure quality of sleep and quality of life scores and to correlate quality of sleep scores with psychiatric data and quality of life scores. Methods: This is a cross-sectional study with 50 ESRD patients treated in 2 public hemodialysis services of Maceió, Brazil. The patients were evaluated with Mini International Neuropsychiatric Interview 5.0.0 (MINI 5.0.0) to determine the prevalence of axis I DSM-IV diagnosis. The Pittsburgh Quality of Sleep Index (PQSI) was used to determine the quality of sleep and the Short Form Health Survey (SF-36) was used to investigate quality of life characteristics of the sample. Beck Depression Inventory (BDI) was used to measure the intensity of depressive symptoms. Results: The mean age was 41,86 years old (SD=14,24). 54% were male. 80% were afro-descendent patients. The mean of schooling was 7.32 years ( $\pm 4,5$ ). 60% were married. 86% did not work but received benefits from the government. 56% had hypertension (HTN), 9.4% had HTN plus diabetes mellitus. 22% of the patients had Major Depression (M.D.), 6% had dysthymia, 18% had increased risk of suicide (10% mild and 8% severe risk). 6% had panic disorder (PD) and 4% had GAD. The mean PQSI was 7.04 ( $\pm 3.58$ ). According to Pearson Correlation Coefficient (PCC) there was significant correlation ( $p < 0,05$ ) between lower PQSI scores and the following domains of SF-36: functional capacity, physical aspects, pain, vitality, social aspects and mental health. Lower PQSI scores were also correlated with higher BDI scores ( $p < 0.01$ ). X2 results correlated worse quality of sleep with M.D. diagnosis ( $p = 0.02$ ) and with increased suicide risk ( $p < 0.01$ ). Among patients that scored higher than 5 PQSI points, there was relationship between M.D. and increased suicide risk. But no relationship was found between the latter and poorer quality of life or BDI scores. Discussion: The sample was composed by poorer schooled people, with occupational problems. Major Depression was the main psychiatric diagnosis and it was correlated with worse quality of sleep and increased suicide risk. Lower quality of sleep scores correlated with worse quality of life scores. Conclusion: This study was able to show that ESRD patients submitted to hemodialysis treatment present high prevalence of psychiatric disorder, increased suicide risk and worse quality of life and quality of sleep. The latter was correlated with Major Depression and with increased suicide risk, proving that is of great importance to investigate psychiatric conditions among this population.

### NR5-18 SUICIDE RISK IN A CARDIOLOGY OUTPATIENT SERVICE

*Chair: Valfrido De-Melo-Neto, M.D.; Author(s): Leutenegger, Ignacio, MS. Melo, Dieggo, MS. Murta, Gustavo MS, Amorim, Edla Cavalcanti, MS. Nardi, Antonio Egidio, Ph.D..*

#### Summary:

**Background:** Suicide is a public health problem worldwide. Each year about 1 million people commit suicide in the world. Psychiatric problems such as anxiety and mood disorders may contribute to increase these rates. **Objectives:** To identify the prevalence of Axis I Psychiatric Diagnosis according to DSM-IV criteria and to determinate the suicide risk among a cardiology sample. Correlate psychiatric diagnosis with increased risk of suicide and with heart illnesses. To correlate quality of life (QOL) scores with psychiatric diagnosis and increased suicide risk. **Methods:** It is a cross-sectional study with 50 cardiology outpatients of the Hospital of the Federal University of Alagoas, Brazil. The Mini International Neuropsychiatric Interview (MINI 5.0.0) was used to investigate the suicide risk, and to screen the main Axis I disorders according to DSM-IV criteria. QOL scores were measured by the World Health Quality of Life (WHOQOL) bref version questionnaire. Hamilton Depression Rating Scale and Hamilton Anxiety Rating Scale were used to measure the intensity of depressive and anxious symptoms. **Results:** The mean age was 53.86 ( $\pm 12.93$ ) years old. 76% were female. 70% were afro-descendent, 66% were married, 70% referred good family relationship. The mean schooling was 4.66 ( $\pm 14.41$ ) years. 84% had Arterial Hypertension (HTN), 16% Chagas Disease (American Trypanosomiasis) and 18% coronariopathy. 14% had Major Depression (M.D.), 10% Recurrent M.D., 14% dysthymia, 26% increased suicide risk, 6% had panic disorder (PD), 12% agoraphobia and another 12% had GAD. According to Pearson Chi-square ( $p < 0.01$ ): GAD, Dysthymia, Recurrent Major Depression, and Major Depression at the moment of the interview ( $p < 0.05$ ) were statistically correlated with suicide risk. Female gender, living alone, unsatisfying sleep pattern and Chagas Disease were also correlated with increased risk for suicide. From the 8 patients who presented Chagas Disease, 4 had dysthymia, 3 had GAD and 6 presented suicide risk according to MINI 5.0.0. Nor HTN nor Coronariopathy were correlated with increased suicide risk. The patients with increased suicide risk also presented higher scores at the Hamilton Scales for depression and anxiety ( $p < 0.05$ ) and lower QOL scores in the WHOQOL-bref physical domain ( $p < 0,01$ ). GAD was also correlated with lower physical

domain scores ( $p < 0.01$ ). Recurrent M.D. was correlated with lower scores at the physical, psychological and environmental WHOQOL domains. Unsatisfying sleep pattern was correlated with higher anxiety and depression ratings and with lower levels of QOL in all WHOQOL domains ( $p < 0.05$ ). **Conclusion:** Anxiety and mood disorders, female sex and sleep disturbance may contribute to increase suicide risk among cardiopathy patients. As far as we know, this is the first time that a correlation between Chagas disease and suicide risk was identified and additional data must be obtained to better understand this relationship.

### NR5-19 RELATIONSHIP OF SIPP-118 PERSONALITY DIMENSIONS TO DSM IV AXIS II DIAGNOSES

*Chair: Thachell Tanis B.A.; Author(s): Thachell Tanis, Dilini Herath, Reetuparna Bhattacharjee, Azra Qizilbash, Irina Kopeykina, Igor Galynker, M.D., Ph.D., Lisa J. Cohen, Ph.D.*

#### SUMMARY:

**EDUCATIONAL OBJECTIVES:** At the conclusion of this session, the participant should be able to: 1) Identify the relationship between SIPP personality dimensions and Axis II diagnoses. 2) Recognize the deficits in personality functioning which significantly contribute to specific personality disorders. **ABSTRACT:OBJECTIVE:** It is well known that the American Psychiatric Association's revision of the Diagnostic and Statistical Manual of Mental Disorders (DSM-V) personality section is moving toward a dimensional approach. However, many still debate the validity of using a dimensional approach over a categorical approach for evaluating personality pathology. In the present study we seek to compare dimensional and categorical measures of personality pathology. Specifically we look at the 5 axis II diagnoses that are provisionally to be retained in DSM-V. **METHODS:** Personality pathology was assessed in 92 non-psychotic psychiatric patients (age 18-65) in treatment at an urban hospital. To measure personality pathology categorically we administered the Personality Diagnostic Questionnaire (PDQ-4) a 100 item self report questionnaire which provides personality diagnoses consistent with the DSM-IV diagnostic criteria for Axis II disorders. To measure personality pathology dimensionally we administered the Severity Indices of Personality Problems (SIPP-118), a 118 item self report questionnaire which measures sixteen facets of adaptive functioning which make up five core domains of personality: self-control, identity integration, responsibility, relational functioning, and social concordance. **RESULTS:** The 16 personality facets of the SIPP were entered into 5 backwards

elimination linear regression analyses with borderline, antisocial, obsessive-compulsive, avoidant and schizotypal personality disorder PDQ-4 scales listed as dependent variables. The final model for borderline yielded frustration tolerance, aggression regulation and self-respect as significant predictors. Emotional regulation, aggression regulation, self-respect and responsible industry were significant predictors of antisocial personality disorder. Emotion regulation, aggression regulation, and cooperation were significant predictors for OCPD. Frustration tolerance, self-respect, and cooperation were significant predictors for Avoidant personality disorder. Lastly, effortful control, feeling recognized and cooperation were significant predictors for schizotypal personality disorders. **CONCLUSION:** These results suggest that the 5 personality diagnoses proposed for DSM-V are associated with specific personality dimensions, several of which overlap across personality disorder diagnoses. As the DSM-V moves towards a dimensional approach to personality pathology, it is important to identify relevant deficits in personality functioning and investigate how they relate to established personality disorder diagnoses.

#### **NR5-20 ASENAPINE IN DEVELOPMENTALLY DISABLED ADULTS**

*Chair: Sridhar Reddy B.S.; Author(s): Jason Crawford, BS; Lee S. Cohen, M.D.*

##### **SUMMARY:**

This is the first clinical report of the use of Asenapine, a second-generation sublingual administered atypical antipsychotic compound, in adults with developmental disability. Risperidone and aripiprazole have been studied in developmentally disabled and autistic children and are FDA-approved for the treatment of irritability associated with autism in children, but studies are limited in adults. We studied six adults with developmental disability, all of whom have concomitant intellectual disability and severe behavioral issues characterized by aggression, impulsivity, and self-injurious behavior. One case was comorbid for Moebius syndrome, and two cases were comorbid for seizure disorder. The sample included two female and four male cases. Mean patient age of the sample is 34 years old (range 25 to 58 years old). Mean length of time on Asenapine is 14.5 months (range 9 to 19 months). One patient was discontinued on Asenapine after 9 months due to no improvement. Mean titrated total daily dose was 15 mg daily (range 10 to 20 mg daily). Cases were retrospectively chart-reviewed for Clinical Global Impression Severity Scale (CGI-S) before initiating Asenapine and Clinical Global Impression

Improvement Scale (CGI-I) after initiating Asenapine. Mean CGI-S of the sample is 6 (range 6 to 7), which correlates with severe illness, and mean CGI-I of the sample is 3 (range 2 to 4), which correlates with minimal improvement. Two patients were much improved (2), two patients were minimally improved (3) and two patients showed no change (4) after clinical review by a board certified adult psychiatrist. Overall, 67% of patients treated with Asenapine showed improvement in clinical functioning. Asenapine may present as an alternative compound for impulsivity-aggression in the treatment of developmental disability in adults for those patients unable to swallow pills.

#### **NR5-21 THE IMPACT OF THE 2003 DUTY HOURS REGULATIONS ON NATIONAL PSYCHIATRY BOARD PASS RATES**

*Chair: Gaurav Jain M.D.; Author(s): Kristina Dzara, Ph.D., Mir Nadeem Mazhar, M.D., Manisha Punwani, M.D.*

##### **SUMMARY:**

**Background:** In July 2003, the Accreditation Council for Graduate Medical Education (ACGME) initially mandated nationwide duty hours restrictions (DHR). While the aims of these changes were to improve working conditions and patient safety, there are concerns about potential adverse effects on graduate medical education (GME). The authors assessed the impact of the 2003 DHR on GME quality by using national psychiatry board pass rates as a measure of quality and competency. **Methods:** Authors obtained the national psychiatry board pass rates for part I and part II of the American Board of Psychiatry and Neurology for years 2000 to 2010. Data were divided into two groups: pre-DHR (2000–2003), and post-DHR (2007–2010). Chi-square, odds ratios, and 95% confidence intervals were calculated. **Results:** Pre-DHR, the part I total, first, and multiple attempt pass rates were 64.0%, 80.7%, and 39.0%, which increased post-DHR to 76.8%, 89.7%, and 39.1%, respectively. For part II, pre-DHR total, first, and multiple attempt pass rates were 53.5%, 60.2%, and 43.5%, respectively. Post-DHR, rates increased to 71.8%, 78.7%, and 53.8%. For part I, authors noted increases in the likelihood of total pass [OR=1.865] and first attempt pass [OR=2.093] ( $p<.0001$ ). There was no change for part I multiple attempters. Post-DHR, for part II total [OR=2.203], first attempt [OR=2.435], and multiple attempt [OR=1.514] pass rates increased ( $p<.0001$ ). **Conclusions:** There is a significant increase in the total and first attempt candidates pass rates for psychiatry part I and part II examinations. Multiple attempt candidates did not benefit as strongly.

The results suggest a positive impact of the 2003 DHR changes on the quality of GME.

#### NR5-22

### EFFICACY OF HALOPERIDOL VS LEVOSULPIRIDE INJECTION IN PATIENTS WITH ACUTE PSYCHOSIS: A RANDOMIZED DOUBLE-BLIND STUDY

*Chair: Sagar Lavania M.D.; Author(s): Samir Kumar Prabaraj (M.D.), Harinder Singh Bains (MRCPsych), Vishal Sinha (M.D.).*

#### SUMMARY:

**BACKGROUND:** With growth in the knowledge of psychopharmacology, we have evolved from typical to atypical antipsychotic agents. Yet, typical antipsychotics remain the first choice in treating acute psychotic symptoms, whereas atypical ones are considered alternatives. The present study was designed to compare the efficacy of Haloperidol with Levosulpiride in patients with acute psychosis. **METHODS:** This was a prospective, double-blind, parallel-group clinical study, involving 60 drug-naïve acute psychotic patients. Patients were randomly assigned into two groups, 'A' and 'B', of 30 patients each, and received either intramuscular Haloperidol injection (10-20 mg/day) or Levosulpiride injection (25-50 mg/day), for initial 5 days. A blinded rater assessed the subjects using socio-demographic pro-forma, Brief Psychiatric Rating Scale (BPRS), Overt Agitation Severity Scale (OASS), Overt Aggression scale – Modified (OAS-M), Simpson Angus Scale (SAS) and Barnes Akathisia Rating Scale (BARS) at baseline and daily for next 5 days. Intent to treat (ITT) analysis was carried out with last observation carried forward (LOCF). **RESULTS:** Repeated measures ANOVA for BPRS scores showed significant effects of time ( $F=79.2$ ,  $df=1.62/93.97$ ,  $p<.001$ ,  $\eta^2=0.577$ , Greenhouse-Geisser corrected), and a trend towards greater reduction in scores in Haloperidol group as shown by group  $\times$  time interaction ( $F=2.81$ ,  $df=1.62/93.97$ ,  $p=.076$ , Greenhouse-Geisser corrected) with small effect size ( $\eta^2=0.046$ ). For OASS, repeated measures ANOVA showed significant effects of time ( $F=43.87$ ,  $df=1.64/95.16$ ,  $p<.001$ ,  $\eta^2=0.431$ , Greenhouse-Geisser corrected), but no group  $\times$  time interaction. Repeated measures ANOVA for OAS-M scores showed significant effects of time ( $F=66.01$ ,  $df=1/58$ ,  $p<.001$ ,  $\eta^2=0.532$ , Greenhouse-Geisser corrected), and greater reduction in scores in Haloperidol group as shown by group  $\times$  time interaction ( $F=4.83$ ,  $df=1/58$ ,  $p=.032$ , Greenhouse-Geisser corrected) with small effect size ( $\eta^2=0.077$ ). Higher rates of akathisia as well as extrapyramidal symptoms were noted in the Haloperidol group. **Discussion:** Both

Haloperidol and Levosulpiride injection were equally efficacious for controlling severity of agitation in acute psychosis; whereas Haloperidol was found to be superior to Levosulpiride injection for overt aggression, and possibly for psychotic symptoms. Extrapyramidal adverse effects were more frequent in Haloperidol group as compared to those receiving Levosulpiride.

#### NR5-23

### POLYSOMNOGRAPHIC PREDICTORS OF RESPONSE TO MILNACIPRAN IN DEPRESSION

*Chair: Sagar Lavania M.D.; Author(s): Amrit Pattojoshi (M.D.), Samsuel Haque Nizamie (M.D.), Basudeb Das (M.D.)*

#### SUMMARY:

**OBJECTIVE:** Milnacipran has shown clinical improvement in patients of depression which was accompanied by an improvement of disturbed sleep parameters with regard to increased total sleep time, increase in sleep efficiency. In this study, the authors sought to study and compare the polysomnographic predictors of Milnacipran on sleep architecture and its response in drug naïve/free patients with depression. **METHOD:** In this study, patients ( $N=15$ ) with ICD-10 clinical diagnosis of unipolar depression ( $N=7$ ) or recurrent depressive disorder ( $N=8$ ) and normal controls ( $N=15$ ) were enrolled. Three consecutive night PSG were done for patients and two consecutive nights for control, and the first night was used as an adaptation night while the second night was used for recording and scoring for sleep parameters. After two consecutive night PSG recording patients were administered 25mg of milnacipran 4 hour prior to PSG recording on day 3. One week after starting milnacipran at a dose of 25mg BD, the dose of milnacipran was hiked to 50mg twice daily. Patients were assessed with Hamilton depression rating scale (HAM-D)\* and Hamilton anxiety rating scale (HAM-A)\*\* and WHO QOL- BREF\*\*\* (Field trial version) at four and eight weeks after starting milnacipran. **RESULTS:** Of the 15 patients who completed the study 13 were responders to a 8 weeks trial of milnacipran in a fixed dosage schedule. Analysis of the sleep parameters at baseline and 4 hours after milnacipran treatment revealed significant increase in REM latency from a mean value of 72.03 minutes to 103.73 minutes ( $p=0.000$ ). Post medication analysis of the stage 2 sleep power spectral values shows an increase in power in the delta region in the left frontal region ( $p=.010$ ); left parietal region ( $p=.033$ ); and left temporal region ( $p=.018$ ). Post medication analysis of the REM sleep power spectral values revealed an increase in the left parietal delta band ( $p=.043$ ); left

parietal theta; right parietal delta band ( $p=.037$ ); and left temporal theta band ( $p=.043$ ). Of the 15 patients who completed the study, 13 were responders to 8 weeks trial of milnacipran in a fixed dosage schedule. Significant changes were found in terms of improvement in both HAM-D as well as HAM-A scores post treatment with very good effect size (For HAM-A; Pillai's trace  $F=265.8$ , Effect size- $0.978$ ). Significant changes were also found in all the four domains of WHO-QOL-BREF. CONCLUSIONS: The present study revealed that an increase in REM latency, and increased hyperactivation of cortical areas like left frontal, parietal and temporal as shown by increase in power spectral values, may predict acute antidepressant effect of Milnacipran.

**NR5-24**  
**ANTIPSYCHOTIC USE AND INPATIENT ADMISSIONS AT THE VA: WHAT IS THE RELATIONSHIP?**

*Chair: Stephanie Peglow D.O.; Author(s): Abigail Dwiggin M.D., Martin Cruz Ph.D., Gregory Briscoe M.D., Kathleen Stack M.D..*

**SUMMARY:**

**Objective:** The electronic records (CPRS) of patients discharged from Hampton VAMC inpatient psychiatric ward in 2008 were reviewed. Those prescribed antipsychotics were examined for variables which might be related to treatment outcomes. **Method:** After IRB approval, gender, race, period of service, diagnostic category and tobacco use was recorded. Outcomes were measured by time to re-hospitalization, unscheduled and planned outpatient visits. The length of index hospitalization, subsequent hospitalizations, homeless, co-occurring substance use disorders (SUD) were recorded as these variables may impact service use and treatment compliance. **Results:** One hundred seventy-three of 364 (48%) were prescribed antipsychotics. Of these, 35% were homeless, 68% were Black and 29% White. Ninety-one percent were male, 97% were admitted voluntarily. Forty-three percent were Vietnam Era, 22% Post-Vietnam Era and 31% were Persian Gulf War and 53% had PTSD. The primary discharge diagnosis was a psychotic illness 38%, mood disorder 30%, and anxiety disorder 17%. Atypical antipsychotics were used in 99% of patients with typicals almost exclusively used as in dual-therapy. Most frequently prescribed was quetiapine (40%), aripiprazole (26%) and then risperidone (16%). Those prescribed quetiapine had the longest time to re-admission, 112 days, with aripiprazole 83 days to re-admission. Length of stay did not vary by type of antipsychotic. Twenty-two of 24 (91%) on dual-antipsychotic therapy had a schizophrenia diagnosis which was associated with

longer length of stay and shorter time to readmission. SUD was present in 74% of veterans on antipsychotics yet this was not associated with time to readmission. However as the number of substances used increased, the length of in-hospital stay decreased as did attendance at outpatient appointments. Nicotine dependence was associated with a longer length of stay (14 and 10 days respectively) and shorter time to readmission (78 and 100 days respectively). **Conclusion:** Most veterans that were prescribed antipsychotic medication had a diagnosis of a psychotic disorder. Quetiapine was the most frequently prescribed antipsychotic and was associated with longer time to readmission. Typical antipsychotics were primarily used in combination with atypical and in those who had schizophrenia, a longer length of stay and shorter time to readmission. Lastly, this data suggests patients on antipsychotics that smoke are higher users of inpatient services.

**NR5-25**  
**MULTIPLE EPISODES OF RHABDOMYOLYSIS IN A PATIENT WITH SCHIZOAFFECTIVE DISORDER, INDUCED BY PALIPERIDONE, ZIPRASIDONE, QUETIAPINE AND HALOPERIDONE**

*Chair: Kapila Marambage M.D.; Author(s): Eileen Zhivago, M.D.; Rashi Aggarwal, M.D.*

**SUMMARY:**

**Objective –** Rhabdomyolysis is a potentially lethal clinical syndrome that comprises of acute, diffuse breakdown of muscle tissue due to many causes, and usually produces myoglobinuria, acute renal failure and leads to death in about 10% of cases. The pathogenesis of Rhabdomyolysis has been described as a disturbance in the Calcium homeostasis of the myocyte leading to cell breakdown and enzyme leakage to occur. This patient developed Rhabdomyolysis related to Antipsychotic use on multiple occasions, without Neuroleptic Malignant Syndrome. **Case Summary -** A 23 year old African American male with Schizoaffective Disorder, who was initially on Risperidone. About a year later he was switched to Paliperidone. Two weeks later he was admitted with a two day history of generalized body aches, back ache, and rigidity on passive extension of limbs. His CK was elevated at 23614. Following discharge he was started on Ziprasidone and was asked to take Ziprasidone with meals to increase bioavailability. The next day he was admitted to hospital with soreness of legs / arms and back. His CK increased to 8411. After being antipsychotic free for two months, he was started on Haloperidol, which gave rise to soreness of limbs again with a CK of 994. Haloperidol was discontinued and Quetiapine was started without

any improvement. One month later he was started on Olanzapine and maintained for the next two months without any report of Rhabdomyolysis. In summary he developed two episodes of frank Rhabdomyolysis, in response to Paliperidone and Geodon and showed clinical and laboratory features compatible with early stages of Rhabdomyolysis, while on Haldol and Seroquel. He made a full recovery, following withdrawal of the offending agent, without any evidence of Neuroleptic malignant syndrome. Discussion - There have been case reports of Rhabdomyolysis caused by different Antipsychotics in the absence of Neuroleptic Malignant Syndrome (NMS), especially Ziprasidone, Haloperidol, Quetiapine, Risperidone and Olanzapine. One suggested mechanism of Rhabdomyolysis in the absence of NMS is an increase of skeletal muscle cell membrane permeability in vulnerable subjects. Therefore, Antipsychotics can cause acute rhabdomyolysis as part of a Neuroleptic Malignant Syndrome or via direct toxic effect on myocytes. The degree of Rhabdomyolysis that can manifest ranges from a subclinical rise of Creatine Kinase (CK) to a medical emergency comprising of compartment syndrome, and pigment-induced acute Renal failure. It is not known whether it is dose or duration dependent. Some patients, like ours, might be predisposed to this side effect. Conclusion - A specific protocol for prevention of Rhabdomyolysis has not been described. Currently there are no clear guidelines on how to restart Antipsychotics after a lapse, due to Rhabdomyolysis. In a patient who has had Rhabdomyolysis once, restarting antipsychotics should be done with caution.

#### **NR5-26 HAIR LOSS ASSOCIATED WITH SSRIS**

*Chair: Sadia Gbaffar M.D.; Author(s): Sadia Gbaffar, M.D.; Gbulam Bajwa, M.D.; Deepa Hasija, M.D.; Sree latha Jadapalle, M.D..*

#### **SUMMARY:**

Drug induced alopecia is a transient, reversible disorder, manifests as diffuse, nonscarring loss of hair which resolves after discontinuation of the drug. Gender difference is noticed showing higher occurrence in women probably due to the hormonal alterations. The pathophysiology of drug induced alopecia is not clear, but many theories were discussed in the literature. Psychotropic medications like anxiolytics, dopaminergic agents, mood stabilizers and antidepressants are known to cause hair loss. Selective serotonin reuptake inhibitors (SSRIs) became the first-line agents to treat clinical depression. SSRIs are the most extensively used antidepressants, as they have improved adverse reaction profile and a superior safety margin in overdoses when

compared with other antidepressants. During SSRI treatment drug-induced alopecia has been reported commonly affecting the scalp. Ghanizadeh also reported a case of drug induced alopecia with sertraline. Literature shows case reports on drug induced alopecia with the following antidepressants: among SSRIs sertraline, paroxetine, fluvoxamine and fluoxetine, among the SNRIs venlafaxine and other antidepressants like nefazodone, trazodone and mirtazapine treatment. We reported a case of a patient who had alopecia with almost all the SSRIs including escitalopram which to our knowledge is the first case reported. Our patient had no hair loss with duloxetine which is an SNRI. Both anagen and telogen effluvium were proposed as possible etiology behind this medication-related alopecia. [4] Alopecia may contribute to noncompliance. Experimental studies demonstrate that drug-induced alopecia is due to the conversion of growing hair follicles into resting hair follicles and shedding of the hair shaft takes place up to 3 months after the initial insult. Literature shows that alopecia being a rare adverse reaction to SSRIs and the risk of alopecia seems to differ between the different SSRIs. Hedenmalm et al conducted a study to evaluate the association of alopecia and SSRIs by using the SWEDIS (the national Swedish database for spontaneously reported ADRs), and Vigibase, (the international ADR database of the World Health Organization). The results displayed that sertraline showed a statistically significant association with alopecia in both SWEDIS and Vigibase and citalopram was next significantly associated with alopecia in Vigibase, but not in SWEDIS. [5] Zalsman et al reported a case of drug induced alopecia due to paroxetine. [7] Conclusion: Antidepressant induced alopecia is a very traumatizing side effect and its increased occurrence in women itself demands extensive research on pathophysiology. Our case was selected to highlight the necessity of additional information to improve the safety of usage of the antidepressants.

#### **NR5-27 EFFICACY OF ADJUNCTIVE TREATMENT OF SCHIZOPHRENIA WITH CELECOXIB: A SYSTEMATIC REVIEW**

*Chair: Pamela Ramos M.D.; Author(s): Joshua Chiappelli M.D., Carol Vidal M.D., Carla Reese M.D., Seth Himelbock M.D. M.P.H.*

#### **SUMMARY:**

Context: Currently established treatments for schizophrenia are often ineffective or do not improve important symptom domains such as negative or cognitive symptoms. Based on a possible role of inflammatory processes in the pathophysiology of

schizophrenia, Celecoxib has been used as an adjunctive treatment, but the efficacy of this medication is unclear. Objective: This systematic review aims to assess the quality and results of clinical studies on the efficacy of adjunctive treatment with Celecoxib in persons with schizophrenia. Data Sources: PubMed, Cochrane Library, and the Clinical Trials Registry were searched in October 2010. Study Selection: Clinical studies in the English language that were randomized, placebo-controlled, had clinical subjects diagnosed with schizophrenia, and measured clinical outcomes with the PANSS were included in the review. Data Extraction: Independent observers extracted data and evaluated each study for bias using Cochrane guidelines. Results: Five studies meeting inclusion criteria were found, including a total of 385 patients. Insufficient data were reported to conduct a meta-analysis. Although three studies showed a positive effect of adjunctive treatment with celecoxib, the largest study, which included 190 patients, showed no effect. All five studies were randomized and placebo-controlled, but insufficient details were reported to fully assess risk of bias. Conclusions: There is insufficient evidence to support the efficacy of celecoxib as an adjunctive treatment in schizophrenia.

**NR5-28**  
**VALPROATE SERUM CONCENTRATIONS**  
**FOLLOWING A SINGLE 500 MG TEST DOSE**

*Chair: Aarti Gupta M.B.B.S Author(s): Dr. Adel Wassef*

**SUMMARY:**

Background: Calculating valproic acid dose based on body weight (15-20mg/kg) has been found to produce significant variability in interpatient valproic acid level, which questions its reliability. In this study, the authors hypothesized that valproic acid steady state concentration on a dose of 2000mg (L2000) correlate better with serum concentration following a single 500 mg test dose (L500) than with the valproate dose expressed in mg/kg. The study was conducted to test if the required dose of valproic acid can be more effectively based on levels following a test dose of 500mg than mg/kg. Method: The study enrolled 44 consenting adult inpatients. They received a single dose of divalproex sodium 500mg, followed by drawing serum to measure total and free valproate concentrations 13hrs later (L500). The dose was then increased to 2000mg and trough valproate concentrations were then collected at steady state after three days ( L2000). Valproate concentrations were measured using fluorescence polarization. Results: As hypothesized, the L2000 concentrations correlated better with L500 concentrations than with the valproate dose calculated as mg/kg weight. In fact, the mg/kg dose did not correlate

significantly with total and free valproate concentrations at L2000 (n= 44). The L2000/L500 ratio was 3.338 ( $\pm 0.760$ , n= 44, 99% confidence limits= 3.024- 3.643) for total valproate concentrations, and 6.995 ( $\pm 2.737$ , n= 44, 99% confidence limits= 5.789-8.200) for free valproate. Conclusions: There is significant correlation between serum levels of Valproate dose calculated on the basis of levels of a test dose of Valproate 500mg. The study demonstrated that basing Valproate dose on the traditional mg/kg weight is not an effective choice. A rough estimate of total valproate concentration on 2000mg/day can be made by multiplying L500 by 3.0-3.6, though it is advisable to confirm the estimate by laboratory measurement. Using L500 levels to estimate L2000 levels offers advantage by allowing faster dose escalation and reaching therapeutic valproate levels sooner. This would specially help by stabilizing the patient faster and cutting down the length of hospital stay.

**NR5-29**  
**RAPID TREATMENT OF DEPRESSION IN**  
**PATIENTS RECEIVING HOSPICE CARE WITH**  
**METHYLPHENIDATE AND KETAMINE**

*Chair: Steve Koh M.D.; Author(s): A Iglewicz, M.D., JY Lo, BSN, MSBA, CH Carr, NP, MSN, RA Nelesen, Ph.D., SD Romero, LS Lloyd, DrPH, CF von Gunten, M.D., Ph.D., DV Jeste, M.D., and SA Irwin, M.D., Ph.D.*

**SUMMARY:**

Psychiatric morbidity in patients receiving hospice care is highly prevalent, under-recognized, under-treated, and/or mistreated. Current interventions for depression do not work fast enough for patients enrolled in hospice care. Quick acting, safe and effective depression treatment is needed in this population to achieve high quality end-of-life experience. Research has suggested use of methylphenidate and ketamine as potential agents for rapid treatment of depression. Open label trials using methylphenidate and oral ketamine in hospice patients with depression are being conducted; we have previously shown use of oral ketamine in hospice patients. Methylphenidate was dosed starting at 5mg twice a day to maximum dose of 20mg twice a day. Oral ketamine was dosed at 0.5mg/kg nightly. Patients were evaluated at set intervals by the research team. Primary outcome measured was Hospital Anxiety and Depression Scale and second outcome was Adverse Symptom Frequency Scale. Pilot data of at least three patients treated with methylphenidate and eight patients treated with oral ketamine will be presented which demonstrates efficacy, safety, and rapid depression treatment. In this small study, no adverse events were recorded except for increase in anxiety with methylphenidate use. The

study shows potential utility of methylphenidate and oral ketamine in safe, rapid treatment of depression in hospice patients.

### NR5-30

#### **HYPONATREMIA DIRECTLY CAUSED BY ATYPICAL ANTIPSYCHOTICS: A RETROSPECTIVE STUDY AND LITERATURE REVIEW FOR QUALITY IMPROVEMENT**

*Chair: Mebnaz Waseem M.D.; Author(s): Carolina Mercader, DO; Marek Belz M.D.; Medical students: Erin Livingston, Thao Tong; Amel Badr M.D..*

#### **SUMMARY:**

**Background:** Hyponatremia is seen in about 4% of patients with chronic Schizophrenia and occasionally in patients with Bipolar Disorder, Depression, and Mental Retardation. Hyponatremia is a state of imbalance in water-electrolyte homeostasis, generally defined as a lowered serum sodium level of <136 mmol/L. Case reports of drug-induced Hyponatremia suggest that atypical antipsychotics can induce hyponatremia.

**Methods:** We conducted both a retrospective study and a literature review. For the retrospective study, we analyzed serum sodium lab values of 72 patients in our outpatient clinic between ages 18-65 with Psychotic Disorders who were taking atypical antipsychotics. Patients with Axis III comorbidity were excluded from this study. We also conducted a literature review of cases of Hyponatremia caused by atypical antipsychotics.

**Results:** In our retrospective study, of the 72 patients analyzed, 5 patients had abnormal serum sodium levels below 136 mEq/L. Of those 5 patients, 3 patients were taking Risperidone, 1 patient was taking Paliperidone, and 1 was taking Olanzapine. In our literature review, we obtained findings that suggest Hyponatremia can be directly due to several commonly used atypical antipsychotic including Olanzapine, Risperidone, Aripiprazole, and Ziprasidone. One 34 year old patient with Schizophrenia was found to have developed Hyponatremia 8 weeks after initiation of Olanzapine 20 mg PO daily (115 mmol/l). One 32yo Schizophrenic male patient started on Ziprasidone therapy was admitted into the ER with Hyponatremia (122 mEq/L ) 20 days after initiation with Ziprasidone. Another case involved a 60 Schizophrenic male who was started on Aripiprazole, and after 2 weeks had a decrease in serum sodium from baseline of 142 mEq/L to 120mEq/L. Another case of Hyponatremia also occurred in a 48yo Schizophrenic male taking Risperidone, whom was initially stable on Risperidone with baseline sodium 136 mEq/L but two weeks after initiation presented to ER with generalized seizure and was later diagnosed with Hyponatremia with a serum sodium 110mEq/L.

**Conclusion:** Though our own retrospective study does not show statistically significant results, we found incidences of Hyponatremia in patients on atypical antipsychotics. Our literature study indicates that Hyponatremia can be caused by several commonly used atypical antipsychotics including Aripiprazole, Ziprasidone, as well as Olanzapine, and Risperidone. These results suggest the importance of Panel 14 laboratory workups. Even if a patient's initial workup is unremarkable, consecutive workups should be done as development of Hyponatremia can vary anywhere between 1 to 8 weeks. We suggest routine workups of patients every 2 weeks in order to closely monitor serum sodium level. More frequent monitoring will help the clinician prevent the development of electrolyte imbalance and will thus help improve patient quality of care.

### NR5-31

#### **THE IMPACT OF THE PSYCHIATRIC CONSULTATION/LIAISON SERVICE ON HEALTHCARE OUTCOMES**

*Chair: Lance Feldman M.D.; Author(s): Mark Rapp, M.D.; Amanda Pearl, Ph.D.; Sanjay Yadav, M.D.*

#### **SUMMARY:**

**Objective:** To evaluate the impact of the psychiatric consultation/liaison service on healthcare outcomes. **Method:** IRB approval was obtained to complete a retrospective, case-control analysis for a recent 5 year period including approximately 15,000 patients at a large, university based hospital. All medically hospitalized patients who received a psychiatric consultation during their hospital stay were compared to a group of similar patients based on medical diagnoses without a psychiatric history and a group of similar patients based on medical diagnoses with a known previous major psychiatric disorder who did not receive a psychiatric consultation during their hospitalization. **Results:** The authors anticipate determining that psychiatric consultations will significantly decrease the average amount of pain medication utilized, average length of stay and average overall cost of hospitalization. **Conclusions:** The authors anticipate concluding that the psychiatric consultation/liaison service is a valuable, cost-effective tool which improves overall patient and healthcare outcomes. We will also report on any particular subsets of patients who particularly benefit from the service provided.

### NR5-32

#### **DELIRIUM IN CENTENARIANS: A TWO CASE SERIES**

*Chair: Antonio Nascimento M.D.; Author(s): Marcos Muniz Moreira, M.D., Maria Luisa Bertino Guimaraes, M.D. and Markus Salomão Miguel, M.D.*

#### SUMMARY:

Introduction: Delirium is a highly prevalent mental disorder in patients hospitalized for a general medical condition. Its prevalence is higher among special populations as elderly patients or patients with dementia. This disorder is associated with longer hospitalizations, higher hospitalization costs and increased mortality. The world's population is aging steadily and the number of centenarians is growing faster than other segments of the population. In the United States and other industrialized nations, centenarians occur at a prevalence rate of about 1 per 6,000. In 1994, the prevalence rate was one per 10,000, making centenarians one of, if not the fastest growing segments of the population (the United States currently has the greatest number of centenarians in the world estimated at 70,490). Centenarians present a different pattern of clinical comorbidities than other groups of elderly people. Currently, no studies on delirium in centenarians have been published, as revealed by a systematic revision on PubMed, ISI Web of Knowledge and SCOPUS databases with the keywords delirium and centenarians. Objective: to study clinical, sociodemographic and epidemiologic features of delirium in centenarians in a private general hospital. Method: Patients aged 100 and older treated for delirium by the consultation-liaison psychiatry team in a private general hospital during a three year period were included in this case series. Sociodemographic (gender, age, marital status) and epidemiologic data (cause of hospitalization, clinical comorbidities and treatments) have been collected and analyzed using descriptive statistics methods. Results: Two patients have fulfilled inclusion criteria. Both (100%) were widowed Caucasian females. Their mean age was 101.5±0.7 years. Both hospitalizations have been caused by infectious diseases (urinary tract infection for one patient and pneumonia for the other). Both patients presented a high number of clinical comorbidities (5 and 4) and both presented hypertension and dementia (comorbidities which have been listed as risk factors for delirium in persons aged 85 and older). Both patients have been treated with antipsychotics (quetiapine 12,5mg/day for one patient, haloperidol 0,4mg/day for the other) with successful results (CGI=2). Conclusion: Risk factors for delirium previously identified for the elderly in general (high number of comorbidities and infections) and for the oldest-old (hypertension and dementia) were present in the centenarians with delirium. Larger populational studies of delirium in centenarians are necessary to identify risk factors in

this population and the most adequate treatment for delirium in these patients.

#### NR5-33 PSYCHIATRIC MANIFESTATIONS OF H.PYLORI: A CASE REPORT

*Chair: Sadia Ghaffar M.D.; Author(s): Sadia Ghaffar, M.D. ; Sara Sheikh, M.D..*

#### SUMMARY:

H. Pylori infection is a common bacterial infection for humans, and the organism is the most prevalent gastric microbial pathogen. It has been associated with the development of extra digestive disorders such as, respiratory disorders, vascular disorders and Parkinson's disease. A link between chronic anxiety and peptic ulcer disease is also suggested. Over the last years the focus of research on the causes and treatments for PUD has been on psychosomatic/psychological arena, along with and immunologic/inflammatory pathways and genetic approaches. Nearly all PUD patients have H.pylori, only a small percentage of individuals with H. Pylori develop ulceration. Recent laboratory-based studies suggest that another possible pathway for this association could be related to the hypothesis that stress, which is associated with generalized anxiety disorder (GAD) and PUD, is immunomodulatory and may cause a shift in inflammatory reactions to infections with organisms normally controlled by TH1 lymphocytes/cytokines, such as H. Pylori. Moreover, GAD has a relatively early onset, suggesting that GAD may be a long-standing stressor that precedes the onset of PUD. GAD as a representative of chronic anxiety, is associated with a significantly increased odds of self – reported PUD among adults in the community. Each mental disorder, with the exception of dysthymia, was associated with significantly increased odds of PUD after adjusting for differences in socio- demographic characteristics. GAD is associated with an almost five-fold increase in likelihood of PUD compared with that among patients without GAD. Also, bipolar disorder was associated with an eight-fold increase in odds, and those with agoraphobia reported more than four times higher than that among without agoraphobia. Female gender is associated with increased GAD, whereas higher income was associated with lower odds of GAD. GAD is associated with increased reporting of physical symptoms and is frequently characterized by physiologic anxiety symptoms, over reporting of medical problems, and associated with psychosocial distress. GAD should be treated when it co –occurs with PUD as it may play a role in the etiology of PUD. We report the case of a 52 year old female diagnosed and treated for H.Pylori who was referred to the psychiatrist with wide array

of psychosomatic complaints including insomnia, generalized anxiety, fibromyalgia, and attention deficit hyperactivity disorder. In conclusion, clinically an increased awareness of the likelihood that patients seeking help for PUD may be at increased risk for concurrent GAD may improve rates of identification and treatment of this common yet frequently unrecognized anxiety disorder. Antidepressant treatment is associated with improvement among patients with other gastrointestinal problems.

**NR5-34**  
**DOSE-RELATED EFFECT OF ACCULTURATION ON SUICIDAL IDEATION AND ATTEMPTS AMONG HISPANICS LIVING IN THE US**

*Chair: M. Mercedes Perez Rodriguez M.D.; Author(s): Enrique Baca-Garcia, M.D., Ph.D.; Maria A. Oquendo, M.D.; Shuai Wang, Ph.D.; Carlos Blanco, M.D., Ph.D.*

**SUMMARY:**

**Background:** Acculturation is a multi-dimensional construct. Measuring different facets of acculturation may yield better results than a single measure. Only one nationally representative survey has examined the effect of acculturation on suicidal ideation and attempts among Hispanics in the US, and found that different facets of acculturation increased lifetime suicidal ideation and attempts. We aimed to examine the impact of five complementary measures of acculturation (age at migration, time in the US, language preference, social network composition, race/ethnic orientation) on suicidal ideation and attempts among Hispanics in the US. We aimed to extend prior findings by demonstrating a linear, dose-related effect of acculturation on suicidal ideation and attempts. **Method:** Subjects: Hispanics living in the US (N=6,359) from wave 2 of the National Epidemiologic Survey of Alcohol and Related Conditions (n=34,653, 2004-2005). We used descriptive statistics, linear chi-square tests and multinomial regression logistic models to analyze the effect of acculturation on risk of lifetime suicidal ideation and attempts. **Results:** The older the age at the time of migration, the lower the lifetime risk for suicidal ideation and attempts compared to those younger at the time of migration or US-born. Lifetime suicidal ideation increased with time spent in the US. As the degree of English language orientation increased, there was a dose-related increase in the risk for suicidal ideation and attempts. As the Hispanic/Latino social network and Hispanic/Latino race-ethnic identification decreased, risk for suicidal ideation and attempts increased. **Conclusions:** Acculturation is a multi-dimensional construct. Multiple facets of acculturation were

significant correlates of lifetime suicidal ideation/attempts, with a linear, dose-related effect (i.e., higher levels of acculturation were correlated with increased risk for suicidal ideation and attempts). Hispanics living in the US are diverse in terms of level of acculturation. This is a key factor for tailoring interventions and providing personalized mental health care.

**NR5-35**  
**IS THERE AN ASSOCIATION BETWEEN FIRST EPISODE OF PSYCHOSIS AND POLYCYTHEMIA VERA: A CASE REPORT**

*Chair: Syed Hussaini M.D.; Author(s): Bharat Nandu, M.D., Neha Kulkarni, MS III, Mohsin Khan, MS III*

**SUMMARY:**

Leukocytosis, a hematological response, should be suspected in response to bacterial, fungal or parasitic infection, cancer, hemorrhage and exposure to certain medications or chemicals. An excessive white blood cell response associated with a cause outside the bone marrow is termed as "leukemoid reaction". Literature review shows that clinical signs associated with leukocytosis are fever, weight loss, bruising or bleeding, liver or spleen enlargement. However, limited information is available about the psychiatric manifestations associated with leukocytosis. In this case report we report a case of 62 year old Caucasian female with no past psychiatric history was brought to the ER with a chief complaint disorganized behavior, unable to care for self, and having auditory hallucinations for the past 6 months. Her laboratory workup displayed elevated white blood cell count of 21,000. After discharge, patient underwent a complete workup for a possible myelodysplastic syndrome. CT of the brain, and a bone marrow performed demonstrated no T- or B-cell lymphoma but Patient was positive for a JAK2 kinase mutation. Patient was given a diagnosis of Polycythemia Vera, however the cause of first episode of psychosis remained under the investigation.

**NR5-36**  
**A CASE REPORT OF A 47 YEAR-OLD WOMAN WITH MYXEDEMA MADNESS STATUS POST RADIOIODIDE ABLATION FOR GRAVE'S DISEASE**

*Chair: David Edgcomb M.D.; Author(s): Cornell West, MS-IV, Nancy Maruyama, M.D.*

**SUMMARY:**

**Introduction:** Myxedema Madness was coined in 1949 by Richard Asher to describe non-pitting edema with psychosis in the setting of hypothyroidism.

Hypothyroidism secondary to radioiodide ablation for Grave's Disease can cause acute psychosis and personality changes.(1)The neuropsychiatric manifestations of hypothyroidism are variable and occur in 5-15% of patients(2). Publications on this topic have been scarce in recent years. We report a case of Myxedema Madness in a 47 year-old nurse admitted with acute paranoia secondary to hypothyroidism occurring several months after radioiodide ablation therapy for Grave's Disease. The classical and atypical clinical manifestations of this case are discussed. Case report: Ms. Z is a 47 year-old nurse with Insulin Dependent Diabetes Mellitus (IDDM). In April 2010 Grave's Disease was diagnosed and initially managed with methimazole. By February 2011, radioiodide ablation was required. The week prior to admission she was more paranoid. She had abusive command auditory hallucinations (CAH), suicidal and homicidal ideation, goiter, and constipation. Admission TSH was elevated at 104 and T4 was low (1.3) The patient had a history of hearing a male voice in her head for 15 years. She never told her family and was highly functional without psychiatric intervention. Admission medications were insulin and methimazole 10 mg daily. On exam she had exophthalmos and was weeping, anxious, guarded, and mildly disheveled. She was paranoid with CAH instructing her to harm herself and others. There was no evidence of cognitive deficits. In the ED, she received lorazepam and levothyroxine. The first night on the medical unit she had an acute episode of CAH telling her to hang herself. She tied a sheet around her neck and then received haloperidol 5 mg, lorazepam 2 mg, and diphenhydramine 50 mg. During the hospitalization she received a total of three doses of levothyroxine at 125 mcg, four doses of liothyronine 50 mcg, and one dose of aripiprazole 2 mg, after which she denied psychotic symptoms and suicidal ideation, and had no other behavioral disturbances. Neurological exam, brain imaging, and EEG were unremarkable. Following the hospitalization she took levothyroxine but refused aripiprazole. Nevertheless her paranoia, anxiety, sleep patterns, and grooming continually improved. The paranoia worsened on returning to work, but the symptoms resolved rapidly without antipsychotics. Discussion: We review the literature on Myxedema Madness, describe its phenomenology and course, and discuss the controversy over whether to use antipsychotics in treatment. Her case demonstrates how Myxedema Madness can arise in patients with chronic, unspecified psychosis as a sudden worsening of symptoms. Hypothyroidism may exacerbate or mimic psychiatric problems and can lead to suicidal behavior without prompt diagnosis and treatment.

## WHAT PREDICTS NEUROPATHIC PAIN IN SEVERELY ALCOHOL DEPENDENT SUBJECTS?

*Chair: Tulasi Kanukuntla M.D.; Author(s): Ann M. Manzardo, Ph.D., Elizabeth C. Penick, Ph.D., Albert Poje, Ph.D., Jan Campbell, M.D.*

### SUMMARY:

**Objective:** It is known that chronic alcohol abuse is associated with the development of pain syndromes, such as peripheral neuropathy, especially in severely dependent individuals. However, many clinical correlates of pain in this population have not been characterized. The proposed study sought to investigate clinical factors that influence pain reports among a severely alcohol dependent group. **Method:** A group of 113, alcohol dependent men (N= 85) and women (N= 28) with a mean(SD) age= 47.1(7.9) were recruited from the Kansas City metropolitan area to participate in a clinical trial of alcoholism at the University of Kansas Medical Center. All research was conducted in accordance with university guidelines governing research using human subjects. All subjects were self-identified alcoholics who met DSM IV-tr criteria for current alcohol dependence. Subjects completed a series of psychiatric interviews and psychometric questionnaires at baseline that included the Symptom Checklist-90. The SCL-90 scale scores, drinking and drug abuse histories, lifetime alcoholism severity and a family history of psychiatric illness were correlated with subjective reports of past month pain that limits activities and numbness in the extremities. **Results:** Ratings of past month pain and numbness were highly correlated ( $R = 0.24$ ;  $p < 0.01$ ). Both pain and numbness ratings were associated with increased psychiatric distress as well as comorbid substance abuse, particularly abuse of psychomotor stimulants ( $OR_{pain} = 6.7$ ; 95% CI=1.5-30.6;  $OR_{numb} = 3.0$ ; 95% CI=1.1-7.8). Numbness without pain was significantly correlated with a family history of drug abuse ( $OR_{numb} = 3.2$ ; 95% CI=1.4-7.1) and depression ( $OR_{numb} = 2.9$ ; 95% CI=1.3-6.6). **Conclusions:** Both pain and numbness were associated with significantly higher levels of subjective emotional distress in this severely alcohol dependent group. Surprisingly, neither measure was correlated with the quantity and frequency of drinking or the duration of alcoholic drinking. Both measures were associated with psychomotor stimulant abuse which may be a reflection of neurotoxic effects of stimulant drugs. Our findings suggest that alcohol dependent patients who complain of pain and/or numbness should be carefully screened for other comorbid psychiatric conditions and drug use to maximize treatment options.

**NR5-38**  
**RELIGION, SPIRITUAL BELIEFS AND**  
**EXPECTATIONS OF TREATMENT**

*Chair: Matej Markota None Author(s): Bryan Balvaneda, Iveta Kysela, Abdurasul Boltaev, and C.D. Hanson, M.D.*

**SUMMARY:**

Previous research has shown that individuals reporting religious and spiritual beliefs also report more positive levels of mental health, and that positive expectations of treatment also lead to increased treatment seeking and treatment outcomes. Research on the intersection of religiosity and expectations of treatment, however, remains scant. The present study recruited 14 patients at a small psychiatric clinic in a predominantly Latino community in Massachusetts. We administered the Brief Multidimensional Measurement of Religiousness/Spirituality (MMRS) and Anticipated Benefits of Care (ABC) questionnaires. Contrary to our hypotheses, initial results indicate a strong correlation ( $r = .73$ ) between religiousness/spirituality and expectations of treatment. Religion and spiritual beliefs of treatment do not appear to influence significantly expectations of treatment.

**NR5-39**  
**STANDARDIZATION OF THE KOREAN**  
**VERSION OF THE POST-TRAUMATIC**  
**EMITTERMENT DISORDER SELF-RATING**  
**SCALE**

*Chair: Cheolmin Shin M.D.*

**SUMMARY:**

**Objectives :** This study aimed to introduce the concept of embitterment, post-traumatic embitterment disorder(PTED) and Korean version of the Post-Traumatic Embitterment Disorder Self-Rating Scale(PTED Scale). We also investigated the reliability and validity of the Korean version of the PTED Scale. **Methods :** Subjects included both male and female psychiatric outpatients, all aged 18 years or older. All subjects were diagnosed as having DSM-IV depressive disorder. To investigate the prevalence of post-traumatic embitterment disorder in Korea and investigate the reliability and validity of the Korean version of the PTED Scale, Korean version of PTED Scale, 9-item Patient Health Questionnaires(PHQ-9) and 15-item Patient Health Questionnaire(PHQ-15) were administered to Subjects **Results :** 30.4% of subjects were reported as having PTED, speaking this prevalence is similar to that presented in the first German study. The test-retest reliability of the PTED Scale was good, and the internal consistency of that was

excellent(Cronbach's  $\alpha=0.962$ ). Positive correlations were found between the PTED Scale and PHQ-9 and PHQ-15, speaking for a good convergent validity of the PTED Scale. **Conclusion :** From this study, we introduce PTED and the PTED Scale and standardize the PTED Scale to screen and diagnose PTED. The Korean version of PTED Scale is a reliable and valid measurement for embitterment as an emotional reaction to a negative life event.

**NR5-40**  
**FUTURE CHALLENGES IN PSYCHIATRY**

*Chair: Alexander Nawka M.D.; Author(s): Martina Rojnic Kuzman, M.D., Ph.D. Florian Riese, M.D. Olga Paravaya, M.D. Lucia Pacheroova, M.D. Nikolaus Bausch-Becker, M.D. Guillaume Favre, M.D. Domenico Giacco M.D.*

**SUMMARY:**

**Background:** Recently there has been increased interest on the topic of the future of psychiatry. Many challenges have been identified and discussed, e.g. questionable validity of psychiatric diagnoses and results of scientific research; lack of coherent psychiatric basis with opposing ideologies and concepts within psychiatry; mounting patient and carer criticism; negative public image of psychiatry; imperfect and obsolete postgraduate training. To find out what the trainees do think about the future challenges, Board members of the European Federation of Psychiatric Trainees ([www.efpt.eu](http://www.efpt.eu)) decided to carry out an online survey. **Methods:** The questionnaire asked the respondents to name in open ended questions the three most important future challenges to psychiatry as a profession and challenges to postgraduate psychiatric training. A qualitative analysis of the data has been performed and responses were grouped into broader thematic clusters. In total 66 trainees from 32 countries participated in this survey. 39% were male, the mean age was  $30.9(\pm 3.7)$  years, and the mean number of years of completed training was  $3.3(\pm 1.6)$ . **Results:** The three most important future challenges to psychiatry as a profession are; the negative public image of psychiatry (45.4%); questionable results of studies on psychiatric treatment (42.4%); and the lack of a coherent theoretical foundation of psychiatric disorders (34.8%). Other topics of concern were the funding of the mental health system, the role of pharmaceutical companies, client's discontent and recruitment problems to psychiatry. In regard to the question on the future of psychiatric training, trainees identified two crucial challenges; to improve the quality of educational opportunities (62.1%); and to perform international standardization of training programs (31.8%). Less frequently mentioned, but still of big concern are challenges in regards to the level of

psychotherapy training, quality of supervision, training in psychopathology, and training in general medicine skills. Conclusion: Findings of this survey are both disturbing and promising at the same time. Negative image of psychiatry, being identified by trainees as the most important challenge, might be overcome by direct actions of destigmatization, but also indirectly by tackling the other „core“ challenges. It is noteworthy that the other important challenges reflect the need for a coherent framework for psychiatric knowledge base, better definition of diagnostic criteria and improvement of the efficacy of psychiatric treatments. Recognizing and facing these challenges in a constructive way, will turn them into opportunities for a better future of our profession.

**NR5-41**  
**INFLUENCING CONTROLLED SUBSTANCE**  
**PRESCRIBING: ATTENDING AND RESIDENT**  
**PHYSICIAN USE OF A STATE PRESCRIPTION**  
**MONITORING SYSTEM**

*Chair: Lance Feldman M.D.; Author(s): Kristi Skeel Williams, M.D.; Michele Knox, Ph.D.; John Coates, M.D.*

**SUMMARY:**  
**OBJECTIVE:** The purpose of this study is to evaluate the influence of attending physician awareness and utilization of a state prescription monitoring program on resident physician behavior. **METHODS:** Twenty-five attending physicians and 70 residents in Emergency Medicine, Internal Medicine, Neurology, Pediatrics and Psychiatry at a large midwestern university-based hospital were provided an 11 item questionnaire assessing awareness and utilization of a state prescription drug monitoring program. **RESULTS:** Ninety-five of 156 physicians responded. Residents who used the system had, on average, a significantly higher proportion of attendings using the system; residents required to utilize the system had the highest proportion of attendings using the system. **CONCLUSIONS:** It appears that due to the behavioral influence of attending physicians, residents were significantly more likely to utilize the system. If system utilization is desired, attendings should use the system and require resident participation.

**NR5-42**  
**DELUSIONAL PARASITOSIS INDUCED**  
**BY METHYLENEDIOXYPYROVALERONE**  
**(M.D.PV)**

*Chair: Arlenne Shapov M.D.; Author(s): Fernando Espi Forcen M.D., Olufunke Fajobi M.D.*

**SUMMARY:**

Methylenedioxypropylamphetamine, a synthetic cathinone, is a new designer drug of abuse commonly known under the street name of “Bath Salts.” This compound is a potent dopamine and norepinephrine reuptake inhibitor with possible stimulant effects similar to cocaine, amphetamines, or ecstasy (1). To date, very little formal information describing the psychiatric effects of this drug has been published. Only few reports of paranoid psychosis are currently found in the literature. We present the case of a man with no psychiatric history that developed severe delusional parasitosis after the recreational consumption of this drug.

**NR5-43**  
**BDNF AND S100B IN SCHIZOPHRENIA**  
**SPECTRUM DISORDERS: ASSOCIATIONS**  
**WITH SYMPTOMATOLOGY AND**  
**TREATMENT RESPONSIVENESS**

*Chair: Noortje Van De Kerkhof M.D.; Author(s): D. Fekkes, MSc, Ph.D. Frank M.M.A. van der Heijden, M.D., Ph.D. Professor Willem M.A. Verhoeven, M.D., Ph.D.*

**SUMMARY:**

**Background:** Neurotrophic proteins are involved in brain plasticity processes. Brain Derived Neurotrophic Factor (BDNF) is the most abundant neurotrophic protein in the brain and is involved in synapse formation. S100B, a calcium-binding protein secreted by astrocytes, stimulates neurite outgrowth and enhances survival of developing neurons. Serum levels of these proteins were shown to be increased or decreased in schizophrenia patients. In the present study the relationship between the neurotrophic proteins BDNF and S100B and symptomatology as well as response to treatment with antipsychotics was investigated. **Methods:** Eighty patients with schizophrenia spectrum disorders were included and subsequently treated with antipsychotics. Assessments consisted of CASH, PANSS and CGI-S/CGI-I at baseline and after six weeks of treatment. At both time points, serum levels of BDNF and S100B were measured and compared to a matched control sample. Subgroups were defined according to baseline serum levels of BDNF and S100B. Associations with symptomatology and treatment response were analyzed within and between the biochemical subgroups. **Results:** Baseline BDNF and S100B levels were lower in patients compared to controls ( $p < 0.001$  and  $p = 0.015$  respectively) and did not change significantly during treatment. Age was positively correlated with S100B levels. When dividing the total group according to baseline biochemical parameters (low and high 25% and middle 50%), the low and high S100B group had higher PANSS total scores than the middle group.

After six weeks, the high subgroup showed more negative symptoms ( $p=0.01$ ) and the low subgroup had more positive symptoms ( $p<0.001$ ). No differences were found between the BDNF groups. Conclusion: Overall, BDNF and S100B levels are lower in patients with schizophrenia spectrum disorders. The observed differences between high and low subgroups suggest a relationship between neurotrophic proteins, symptom dimensions and treatment response irrespective of diagnostic categories.

#### NR5-44

### A STUDY OF HEALTH COMMUNICATIONS: HOW WELL DO PSYCHIATRISTS COMMUNICATE AT THE TIME OF INITIAL DIAGNOSIS OF SCHIZOPHRENIA?

*Chair: Gretchen Barnas M.D.; Author(s): Dale D'Mello, M.D.*

#### SUMMARY:

**Introduction:** Schizophrenia is often persistent, frequently disabling, and highly stigmatized. The initial diagnosis is a life-changing event, yet communication at first-break has not been extensively examined. **Purpose:** The purpose of the study was to examine physician reaction to diagnosing first episode schizophrenia and health communication at the initial diagnosis of schizophrenia. **Methods:** An internet survey, using the online tool Survey Monkey, was sent to two groups of individuals: a) psychiatrists and b) patients and their family members. The psychiatrists were identified using the membership roster of the Michigan Psychiatric Society (MPS). The patients and their family members were identified through participation in the Michigan chapter of National Alliance for Mental Illness (NAMI). Emails with a link to the questionnaire were sent to both groups through their affiliated organizations. Psychiatrists were asked a series of questions about personal and emotional reactions to diagnosing schizophrenia. They were then queried about perceptions of their competence at communicating at the time of initial diagnosis. The patients and their family members were asked a similar series of questions about their perceptions of the psychiatrists' communication at the time of diagnosis. **Results:** Psychiatrists acknowledged experiencing a spectrum of emotions (sadness, worry and helplessness) upon the initial diagnosis of schizophrenia. There was an inverse correlation between the years of clinical experience and intensity of worry (Pearson correlation coefficient  $p<0.05$ ). The intensity of the emotional reaction had a significant influence upon clinical decision-making (Pearson correlation coefficient  $p<0.01$ ). There was a striking and statistically significant

disparity in perception of communication between psychiatrists and patients and their family members. The psychiatrists perceived themselves as substantially more effective and thorough in providing information in all dimensions (diagnosis, symptoms, etiology, support systems, pharmacotherapy, psychosocial therapies and consequences of concurrent substance abuse) than the patient and family member respondents. Conclusion: The timing, modalities and methods of effective communication with patients and their family members at initial diagnosis of schizophrenia require further study and enhancement.

#### NR5-45

### VAPTANS: A POTENTIAL NEW APPROACH FOR TREATING CHRONIC HYPONATREMIA IN PSYCHOTIC PATIENTS

*Chair: Dawn Filmeyer M.S.; Author(s): Alex G. Geboy, M.S. Richard C. Josiassen, Ph.D. Jessica L. Curtis Rita A. Shaughnessy, M.D., Ph.D. Nina Skuban, M.D.*

#### SUMMARY:

**Background:** Hyponatremia (serum sodium concentration  $[Na^+] < 136$  mEq/L) is a potentially life-threatening condition often presenting chronically in patients with psychotic disorders. Vasopressin antagonists have recently shown in short-term studies to correct hyponatremia in diverse patient populations, including individuals with both psychosis and idiopathic hyponatremia. However, the safety and efficacy of long-term administration of vaptans is only beginning to be investigated. The objective of this study was to assess whether one of the vaptans, specifically tolvaptan, maintained its safety and efficacy over a prolonged period in patients with psychosis and chronic idiopathic hyponatremia. **Methods:** SALTWATER was a multicenter, open-label extension of the Study of Ascending Levels of Tolvaptan in Hyponatremia. Of the 111 subjects enrolled in SALTWATER, eight were male patients with both psychosis and idiopathic hyponatremia who received oral tolvaptan. All had evidence of impaired water excretion demonstrated either by persistent hyponatremia ( $< 135$  mEq/L) despite fluid-restriction or standard evidence of SIADH (i.e., urine osmolality  $> 100$  mOsmoles/Kg with  $[Na^+] < 130$  mEq/L). Study assessments occurred on Day 1 (baseline and 8 hours after first dose), Days 2 through 14 (to end of titration), and Day 31; every 8 weeks from Weeks 10 through 58; every 12 weeks from Weeks 70 through 214; and a follow-up visit 7 days after the last dose of tolvaptan. Safety was assessed at all visits. **Results:** These subjects provided a total of 7406 patient-days of exposure to tolvaptan. Mean serum  $[Na^+]$  for the eight psychotic patients increased from

131.6 mEq/L at baseline to >135 mEq/L throughout the observation period ( $P < 0.05$  versus baseline at most points). No drug-related adverse events led to study discontinuation. Conclusion: Chronic hyponatremia is known to have deleterious effects on the quality of life for many patient groups. These preliminary results suggest that oral tolvaptan provides rapid, effective, and safe treatment of chronic hyponatremia in patients with psychotic disorders and that the effect is safely sustained over long periods of time. This represents an important step forward in treating this significant unmet need in psychotic populations.

**NR5-46**  
**REDUCTIONS IN FALLS AND MEDICAL COSTS ASSOCIATED WITH VAPTAN-CORRECTED CHRONIC HYPONATREMIA IN PSYCHOTIC INPATIENTS**

*Chair: Alexander Geboy M.S.; Author(s): Dawn M. Filmyer, MS., Danielle Martin, BS., Jessica L. Curtis, Rita A. Shaughnessy, Ph.D., M.D., and Richard C. Josiassen Ph.D..*

**SUMMARY:**

Background: Chronic hyponatremia (serum sodium  $[Na^+] < 136$  mEq/liter) occurs in a significant fraction of psychotic patients, and has been associated with an increased rate of falls. Falls and fractures increase morbidity and mortality in this population and impact medical costs associated with treatment. We wondered whether the correction of abnormal serum  $[Na^+]$  with vasopressin-receptor antagonists (vaptans) might reduce the risk for falls and fractures and decrease medical costs associated with treatment. Methods: Retrospective review of hospital chart records of psychotic inpatients diagnosed with hyponatremia without polydipsia and exposed to a vaptan for a minimum of 6 months. Chart review included demographic data, pharmacy records (6 months prior to vaptan initiation and 6 months on drug consecutive), recorded medical events, daily level of nursing supervision, and untoward events. Results: Seven chronically hyponatremic cases were identified (5 males; mean age 56.6+6.2yrs; range duration of hospitalization 8-46 yrs). Significant reductions were observed between chronic hyponatremic state prior to vaptan therapy (6 months) and normonatremic state on vaptan therapy (6months): days of restricted privileges 94 to 32; aggressive/ assaultive behaviors 18 to 6; traumatic falls 4 to 0; non-traumatic falls 26 to 2; emergency room visits 11 to 5; seizures 1 to 0; days of 1:1 close observation 187 to 0; days of q-15 minute checks 2 to 0; and mean drug costs \$10,303.91+6,065.95 to \$7,992.352+ 3,581.519. Conclusions: In light of the beneficial health consequences and medical cost

reduction, the correction of chronic hyponatremia using vaptans in highly selected cases warrants serious consideration.

**NR5-47**  
**SUICIDE IN SCHIZOPHRENIA: RELATION TO DRUG TREATMENT AND SIDE EFFECTS**

*Chair: Johan Reutfors M.D.; Author(s): Shabram Babmanyar, M.D., Ph.D. Robert Bodén, M.D., Ph.D. Lena Brandt, M.Sc. Erik G. Jönsson, M.D., Ph.D. Anders Ekblom, M.D., Ph.D. Urban Ösby, M.D., Ph.D.*

**SUMMARY:**

Background: Patients with schizophrenia are at increased risk for suicide, but data from controlled studies of how pharmacotherapy and side effects are related to suicide risk is limited. The aim of the study was to explore suicide risk in relation to prescription of antipsychotics and antidepressants as well as in relation to extra-pyramidal side effects. Methods: Of all patients with a first clinical discharge diagnosis of schizophrenia or schizoaffective disorder in Stockholm County between 1984 and 2000 ( $n=4,000$ ), patients who died by suicide within five years from diagnosis were defined as cases ( $n=84$ ; 54% male). Individual matching was performed with one schizophrenia control per suicide case from the same population. Information on prescribed medication and side effects was retrieved from psychiatric records in a blinded way. Associations between exposures and suicide risk were evaluated by conditional logistic regression while adjusting for possible confounding factors (age at onset, sex, and education). Results: A lower suicide risk was found in patients who had been prescribed a second generation antipsychotic (clozapine, olanzapine, risperidone, or ziprasidone; 12 cases and 20 controls): adjusted odds ratio [AOR] 0.29 (95% confidence interval [CI], 0.09-0.97). When the 6 cases and 8 controls who had been prescribed clozapine were excluded, the AOR was 0.23 (95% CI, 0.06-0.89). No significant association was observed between suicide and having been prescribed any antidepressant (33 cases and 30 controls) or any antipsychotic (83 cases and 83 controls). A history of akathisia did not affect the suicide risk significantly: AOR 1.21 (95% CI, 0.44-3.33). However, a lower suicide risk was found in patients with other extra-pyramidal side effects: AOR 0.33 (95% CI, 0.12-0.94) Conclusions: The lower suicide risk for patients who had been prescribed second generation antipsychotics may be related to a pharmacological effect of these medications, to differences in compliance, or to differences in other characteristics associated with a lower suicide risk. Having extra-pyramidal side effects (except akathisia) appears to be associated with lower suicide risk in the

early phase of schizophrenia; a possible explanation for this might be higher antipsychotic medication adherence among these patients.

#### NR5-48

### FUNCTIONAL STATUS RATING SCALES AS PREDICTORS OF EVERYDAY FUNCTIONING IN PEOPLE WITH SCHIZOPHRENIA: GLOBAL VS SUBSCALE RATINGS

*Chair: Samir Sabbag, M.D.; Author(s): Davide Prestia, M.D.; Philip D. Harvey, Ph.D.*

#### SUMMARY:

**Background:** Disability is common in people with schizophrenia and there are deficits seen in multiple functional domains, with most patients showing impairment in functional milestones. It is not clear from current literature whether different domains of disability (vocational, residential, and social) are independent from each other or if disability reflects a global trait. In this study, we examined the level of specificity of functional status rating scales for their correlation with the achievement of functional milestones in these different domains. We examined whether global and subscale scores on two different disability scales were related to the achievement of functional milestones. **Methods:** In the VALERO study, schizophrenics (N=198) were examined with an assessment everyday functioning on six different functional status rating scales. We used two hybrid scales: the Quality-of-Life Scale (QLS) and the Specific Levels of Functioning Scale (SLOF). We examined the association between the total scores on the two functional status scales and their domain-specific subscales. Achievement of several different functional milestones (independence in residence, current vocational activities, ever having a stable long term relationship) were also taken into consideration. Ratings were generated by interviewers on the basis of a systematic assessment procedure including self-reports, informant reports and interviews with the patient. The interviewers were not aware of the achievement of functional milestones at the time of the assessments. **Results:** Total scores on the SLOF and QLS were highly correlated with each other ( $r=.56$ ,  $p<.001$ ) and the subscales measuring vocational, social, and residential functioning were all intercorrelated (all  $r>.62$ , all  $p<.001$ ). Total scores on both the QLS and the SLOF were not significantly associated with the achievement of any of the three functional milestones (all  $F<1.1$ ; all  $p>.50$ ). However, each of the specific subscales (social, residential, vocational) for both of the rating scales was significantly associated with achievement of the relevant functional milestones and not associated with achievement of other milestones. In addition, none

of the functional rating subscales was associated with achievement of other milestones. For example, current employment was significantly associated with SLOF vocational skills ratings ( $F(1,194)=10.72$ ,  $p<.001$ ), but unassociated with scores on the SLOF social ( $F=.13$ ) or residential ( $F=.40$ ) ratings. **Discussion:** Functional status rating scales yield highly valid and quite specific ratings of functional disability. Global ratings do not generate meaningful predictions of achievement of specific functional milestones, which argues against global rater bias, but also raises questions about the usefulness of total scores for inferences about specific functional achievements. For the prediction of everyday milestones, the two rating scales appeared similar in their usefulness.

#### NR5-49

### PREDICTORS OF COMMUNITY INTEGRATION IN OLDER ADULTS WITH SCHIZOPHRENIA

*Chair: Carolina Jimenez M.D.; Author(s): Helen H. Ryu, M.D., Elena F. Garcia-Aracena, M.D., Carl I. Cohen, M.D.*

#### SUMMARY:

**OBJECTIVES:** Community integration (CI) measures the extent to which people live, participate and socialize in the community. It is a multidimensional construct that covers independence, physical, social, and psychological integration. Even though, CI is considered a desirable outcome in patients with schizophrenia, few studies have looked for predictors of CI over time. This longitudinal study explores: (1) the changes in the level of CI over time; (2) clinical and social variables at baseline that predict CI on follow-up; (3) the effect of baseline CI on various clinical and social outcomes. **METHODS:** The study consisted of 254 persons with schizophrenia spectrum disorders aged 55 and over living in NYC who developed the disorder prior to age 45. Data on 102 patients followed for a mean of 51 months are presented. Mean age was 60 years, 55% were male, and 55% were white. The CI scale comprises 12 items divided in 4 dimensions: independence, psychological, physical, and social integration. The CI scale was also dichotomized into two groups (scores of  $<9$  versus 9-12) based on median scores for a non-psychiatric elderly comparison group; 59% of the latter group attained scores of 9 or above. **RESULTS:** There was no significant difference between the means of the 12-item CI scale at Time 1 ( $7.9 \pm 2.2$ ) and Time 2 ( $8.0 \pm 2.5$ ). Only 28% achieved high CI at T1 and T2, 38% never attained high CI status, and 34% fluctuated between high and low CI. Using linear regression analysis, significant predictors of CI on follow-up were: CI at T1 ( $\beta = .43$ ), depressive symptoms at T1 as assessed by Center of Epidemiologic Studies-Depression Scale (CES-D) scores ( $\beta = -.18$ ),

cognitive functioning at T1 as measured by Dementia Rating Scale ( $\beta = .20$ ), lower frequency of mental health services at T1 ( $\beta = -.26$ ), and greater financial wellbeing at T1 ( $\beta = .17$ ). Partial correlations, after adjusting for baseline level of each outcome measure, age and gender, indicated that baseline CI significantly predicted clinical remission at T2 ( $r = .32$ ), lower PANSS positive at T2 ( $r = -.34$ ), lower PANSS general psychopathology at T2 ( $r = -.39$ ), and higher quality of life index scores at T2 ( $r = .21$ ). **CONCLUSIONS:** CI of older adults with schizophrenia fluctuates substantially over time; is affected by several baseline factors, and impacts subsequent psychopathology and quality of life. Since two fifths of patients never attained high CI, it is essential to identify variables that can potentially modify this outcome. Despite the observational nature of our study, it suggests that targeting cognitive functioning, financial well-being, and depressive symptoms may improve CI over time. This study was funded by National Institute of General Medical Sciences grants SO6-GM-74923 and SO6-GM-5465.

#### **NR5-50 FROM COMMUNITY INTEGRATION TO SUCCESSFUL AGING IN SCHIZOPHRENIA**

*Chair: Carolina Jimenez M.D.; Author(s): Helen H. Ryu, M.D., Elena F. Garcia-Aracena, M.D., Carl I. Cohen, M.D.*

##### **SUMMARY:**

**INTRODUCTION:** Successful aging (SA) requires absence of disease and disability in conjunction with high cognitive, physical and social functioning. While the role of physical health should not be underestimated, in schizophrenia it may be relevant to explore other psychosocial views such as community integration (CI). CI examines the extent of independence, physical, social, and psychological integration of patients. Hence, it is considered an empirical measure of recovery. This study examines: (1) the relationship of CI and SA in older adults with schizophrenia; (2) the changes in CI and SA over time. **METHODS:** The study consisted of 254 persons with schizophrenia spectrum disorders aged 55 and over living in NYC who developed the disorder prior to age 45. Data on 102 patients followed for a mean of 51 months is presented. Mean age was 60 years, 55% were male, and 55% were white. High SA was defined as scoring 5 out of 6 on the SA Scale, and high CI as scoring 10 out of 12 on the CI Scale. **RESULTS:** At baseline, the CI and SA scales had a correlation of 0.41 (16% shared variance). There were no significant T1-T2 (time 1-time 2) differences in the scores of CI (7.9 vs. 8.0) and SA (3.4 vs. 3.3). Notably, only 13% achieved high CI at T1 and T2, 61% never attained high CI, and 24% fluctuated between high and low CI.

Similarly, only 11% achieved high SA at both times, 68% of the patients never attained high SA, and 23% fluctuated between high and low SA. **CONCLUSIONS:** There was little movement towards CI and SA in this population, with about equal numbers moving in and out of these categories, and only a small percentage remaining permanently in them. Therefore, CI and SA cannot be considered on a linear continuum; rather they assess different paradigms of positive aging. This study was funded by National Institute of General Medical Sciences grants SO6-GM-74923 and SO6-GM-5465.

#### **NR5-51 SECURITY OF ATTACHMENT ACROSS AXIS I DIAGNOSES IN PSYCHIATRIC INPATIENTS**

*Chair: Eeva Mikkola M.D.; Author(s): Reetuparna Bhattacharjee, Thachell Tanis, Azra Qizilbash, Dilini Herath, Irina Kopeykina, Igor Galynker, M.D. Ph.D., Lisa J. Cohen Ph.D.*

##### **SUMMARY:**

**Objective:** The relationship between attachment styles and treatment outcome across different psychiatric diagnoses has been supported by a robust literature. However, there is little data addressing the nature of attachment style in severe and persistent mental illness. The aim of the current study is to evaluate whether attachment style varies across four Axis I diagnoses: schizophrenia, schizoaffective, bipolar disorder and major depressive disorders. **Methods:** Attachment style was assessed among 33 psychiatric inpatients (age 18-65) in treatment at a major urban hospital. Attachment style was measured by the Relationship Style Questionnaire (RSQ), a 30 item, self-report questionnaire which measures four types of attachment: secure, dismissing, fearful and preoccupied. To determine Axis I diagnoses, we administered the Structures Clinical Interview for DSM-IV-TR Axis I disorders, Patient Version with psychotic Screen (SCID-P), a semi-structured interview for diagnosing major Axis I DSM-IV-TR disorders. **Results:** As an initial analysis ( $n=33$ ), we compared attachment style measures across diagnostic groups (schizophrenic, schizoaffective, bipolar, major depressive disorder) by MANOVA and found no significant differences across groups. However, when we compared attachment style scores for each disorder against all other disorders, we found that schizophrenic subjects had significantly higher secure attachment scores and lower preoccupied scores than the other subjects. Moreover depressed subjects had significantly higher preoccupied scores than the other subjects. **Conclusion:** Schizophrenic subjects may have less insecure attachment styles than subjects with other forms of mental illness. This may reflect the greater contribution

of nature as opposed to nurture in the development of schizophrenia vs. mood disorders. As attachment styles have been found to be associated with treatment outcome, these findings warrant greater consideration of role of attachment in the conceptualization and treatment of schizophrenic and depressed psychiatric inpatients. References: Schmitt F, Lahti I, Piha J: Does attachment theory offer new resources to the treatment of schizoaffective patients?. *Am J Psychother* 2008; 62: 35-49 Roelofs J, Lee C, Ruijten T, Lobbestael J: The mediating role of early maladaptive schemas in the relation between quality of attachment relationships and symptoms of depression in adolescents. *Behav Cogn Psychoth* 2011; 39: 471-479. Morley TE, Moran G: The origins of cognitive vulnerability in early childhood: Mechanisms linking early attachment to later depression. *Clin Psychol Rev* 2011; 31: 1071-1082.

**NR5-52****BDNF PLASMA LEVELS AND COGNITIVE FUNCTION OF SCHIZOPHRENIC PATIENTS IN TREATMENT WITH SECOND GENERATION ANTIPSYCHOTICS**

*Chair: Rodrigo Nieto M.D.; Author(s): Hernan Silva M.D. Manuel Kukuljan M.D. Ph.D. Aida Ruiz M.D. Ph.D. Alejandra Armijo M.D. Javiera Donoso M.D. Pablo Contreras M.D. Cristian Aguirre M.D. Mirko Igor M.D. Rodrigo de Marinis M.D.*

**Summary:**

Schizophrenia is characterized by positive, negative, cognitive and affective symptoms. Cognitive symptoms are important because they are significantly related to quality of life of patients and their ability to be reintegrated to society. Prediction of treatment response in schizophrenia has been studied in regard to several molecular markers, but mainly according to the improvement of positive and negative symptoms, measured by PANSS. Several studies have linked BDNF not only to the pathogenesis of schizophrenia, but also to neuronal plasticity, learning, and memory, making it a good candidate for a biomarker for cognitive improvement in schizophrenia. This is supported by a recent study that correlated an increase in BDNF plasma levels with cognitive improvement in patients who received cognitive rehabilitation techniques. However, currently there are no studies linking BDNF plasma levels with changes in cognitive functioning in schizophrenic patients secondary to treatment with second generation antipsychotics. This project examines whether BDNF can be considered a biomarker that predicts response to drug treatment for cognitive symptoms of schizophrenia. We studied a group of schizophrenic patients who started treatment with

second generation antipsychotics, in whose cognitive functioning was measured with MOCA and the MATRICS consensus cognitive battery, and plasma levels of BDNF were measured with ELISA. This will be done again after six months of treatment, to determine whether changes in cognition are correlated with changes in BDNF plasma levels in these patients. We expect that higher BDNF plasma levels significantly correlate with a higher level of improvement in cognitive functioning. We present the experimental design and preliminary results.

**NR5-53****COURSE OF DEPRESSION AMONG OLDER ADULTS WITH SCHIZOPHRENIA: A 4-YEAR FOLLOW-UP**

*Chair: Helen Ryu M.D.; Author(s): Elena F. Garcia-Aracena M.D., Carolina Jimenez M.D., Carl I. Cohen M.D.*

**SUMMARY:**

**Introduction:** A literature search found prevalence rates of depression in older adults with schizophrenia to range from 32% to 75%. However, no longitudinal studies of depression in this population have been conducted. This is important for understanding the stability of depression, identifying factors that predict depression, and determining the impact of depression on various outcome measures. This paper presents the results of a prospective analysis that addresses these concerns. **Methods:** The study recruited 252 subjects aged 55 and over living in New York City, diagnosed with schizophrenia spectrum disorders, who developed the disorder prior to age 45. Data on 101 follow-up interviews are presented. Mean age was 60 years; 55% were male; and 55% were white; and mean follow-up was 51 months (range: 12 to 95 months). Depression was assessed using the CESD scale then divided into 2 categories: no depression (CESD<8) and depression (CESD>8). **Results:** No differences were found in mean CESD scores between baseline (T1) and follow-up (T2) -- 11.2 versus 11.1, respectively -- or in the percentages of persons meeting criteria for depression, i.e. 60% at T1 versus 53% at T2. Forty three percent of the sample was depressed at both assessments, 30% was not depressed at T1 or at T2, 17% was depressed at T1 but not on T2, and 10% was depressed at T2 but not at T1. Based on a logistic regression analysis, only depression at T1 and the receipt of higher number of mental health services were identified as predictors of depression at T2. Partial correlations, controlling for each of the outcome variables at T1, gender and age, found that baseline depression was a significant predictor of 4 outcome variables at T2: suicidality, PANSS general psychopathology, self-esteem, and number

of psychotropic medications. Conclusions: There is a core group of older persons with schizophrenia suffering from persistent depression, about two-fifths of the sample; another core group, about one-third, remains non-depressed; and about one-quarter who may fluctuate between the two states. Notably, only two-thirds of persons found to be depressed in cross-sectional analysis are persistently depressed. Apart from depression at T1, there was a paucity of predictors of depression at T2, which suggests efforts to address depression must focus primarily on strategies to alleviate depressive symptoms rather than on other associated factors. Depression has an effect on several important outcome measures such as suicidality and general psychopathology and differs from some features of schizophrenia that tend to improve with age. The prevalence, persistence, and consequences of depression in this population make a compelling case for focusing more on the recognition and treatment of depression in older adults with schizophrenia. **KEYWORDS:** Schizophrenia, Aging, Depression. This study was funded by National Institute of General Medical Sciences grants SO6-GM-74923 and SO6-GM-54

**NR5-54**  
**VENOUS THROMBOEMBOLISM**  
**IN A PATIENT WITH CATATONIC**  
**SCHIZOPHRENIA TREATED WITH**  
**CLOZAPINE. A CASE STUDY AND REVIEW OF**  
**RECOMMENDATIONS ON RISK ASSESSMENT**

*Chair: Kapila Marambage M.D.; Author(s): Matis Shulman, Ye-Ming Sun, M.D.*

**SUMMARY:**

**Introduction:** Antipsychotic medication is associated with an increased risk for VTE. Clozapine in particular has been associated with fatal thromboembolism. We report a case of DVT precipitated by an atypical antipsychotic agent (Clozapine) in a patient with Catatonic Schizophrenia. **Case Presentation -** A 25 YO Caucasian male with Schizophrenia, who progressed to catatonia, on a PEG feeding tube, was admitted for ECT. He was on Clozaril 100mg PO HS and Ativan 2mg q4H via PEG, and DVT prophylaxis (Enoxaparin). His Clozaril was titrated up to 275mg Daily. After the 6th ECT treatment the patient started talking selectively, got out of bed and started pacing inside the room. His LMW Heparin was discontinued as per DVT risk analysis. After two days he developed a blanching erythematous rash in the ankles. His D-Dimer level was slightly elevated. **Discussion:** Venous thromboembolism (VTE), which clinically manifest as a deep vein thrombosis (DVT) or a pulmonary embolism (PE), is a multifactorial disease. Several hypotheses

have been suggested regarding pathogenesis, such as drug-induced sedation, obesity, increased levels of antiphospholipid antibodies, hyperhomocysteinemia and hyperprolactinemia. It has also been postulated that antipsychotic drugs may enhance platelet aggregation via either an indirect pathway involving hyperprolactinemia or secondary to an increased level of lupus anticoagulant and anticardiolipin antibodies. The reason for DVT in our patient, can be due to a combination of dehydration, immobility (catatonia), and Clozapine. We experienced that even after following a scoring system suggested for VTE risk analysis and prevention suggested by Radovan Malý et al, and other related studies, our patient, would have fallen in the mild category for DVT risk. Our case illustrates that DVT prophylaxis dictated by current conventional DVT risk analysis may not always be sufficient for preventing DVT in a catatonic psychiatric patient on Clozapine. **Conclusion:** In a patient with Catatonia, close monitoring for any evidence of VTE should be done to ensure early detection and prompt intervention. The threshold for considering prophylactic antithrombotic treatment should be low when risk situations for VTE arise, such as a Catatonic state.

**NR5-55**  
**COMPARISON OF HEART RATE VARIABILITY**  
**INDICES BETWEEN OBSTRUCTIVE SLEEP**  
**APNEA SYNDROME AND PRIMARY INSOMNIA**

*Chair: Jiwon Nam M.D.; Author(s): Doo-Heum Park, M.D.. Ph.D., Jaebak Yu, M.D.. Ph.D., Seung-Ho Ryu, M.D.. Ph.D., Ji-Hyeon Ha, M.D.. Ph.D.*

**SUMMARY:**

**Object:** Sleep disorders cause changes of autonomic nervous system (ANS) which effect cardiovascular system. Primary insomnia (PI) makes acceleration of sympathetic nervous system (SNS) by sleep deficiency and arousal, obstructive sleep apnea syndrome (OSAS) set off SNS by frequent arousal and hypoxemia during sleep. We aimed to compare the changes of heart rate variability (HRV) indices induced by PI or OSAS to analyze for ANS how much to be affected by PI or OSAS. **Methods:** Total 315 subjects carried out Nocturnal polysomnography (NPSG) were categorized into 4 groups - PI, Mild, Moderate and Severe OSAS. Severity of OSAS was determined by Apnea-hypopnea index (AHI). Then we selected 110 subjects considering age, sex and valance of each group's size [Group 1: PI (mean age=41.50±13.16 yrs, AHI <5, n=20), Group 2: Mild OSAS (mean age=43.67±12.11 yrs, AHI 5-15, n=30), Group 3: Moderate OSAS (mean age 44.93±12.38 yrs, AHI 16-30, n=30), Group 4: Severe OSAS (mean age=45.87±12.44 yrs, AHI >30, n=30)]. Comparative analysis of the four groups regarding HRV

indices from NPSG was achieved through ANCOVA (adjusted by age and body mass index) and Sidak test for post hoc analysis. Result: There were statistically significant differences in HRV indices between PI, mild or moderate OSAS group and severe OSAS group with no significant differences between PI, mild and moderate OSAS group. In HRV indices of PI and severe OSAS group showing the most prominent difference in the group comparisons, average RR interval were  $991.1 \pm 27.1$  and  $875.8 \pm 22.0$  ( $p=0.016$ ), standard deviation of NN interval (SDNN) was  $85.4 \pm 6.6$  and  $112.8 \pm 5.4$  ( $p<0.022$ ), SDNN index was  $57.5 \pm 5.2$  and  $87.6 \pm 4.2$  ( $p<0.001$ ), total power was  $11893.5 \pm 1359.9$  and  $18097.0 \pm 1107.2$  ( $p=0.008$ ), very low frequency (VLF) was  $7534.8 \pm 1120.1$  and  $11883.8 \pm 912.0$  ( $p=0.035$ ), low frequency (LF) was  $2724.2 \pm 327.8$  and  $4351.6 \pm 266.9$  ( $p=0.003$ ). Conclusion: VLF and LF which were correlated with SNS showed more increased differences between severe OSAS group and PI group than other group comparisons. We could suggest that severe OSAS group was more influential to increased SNS activity than PI group. Keyword: Obstructive sleep apnea syndrome, Primary insomnia, Heart rate variability, Autonomic nervous system

#### NR5-56

### BONE HEALTH AND NUTRITIONAL STATUS IN CHILDREN WITH INTELLECTUAL DISABILITY IN PAKISTAN

*Chair: Mohsin Cheema M.B.B.S Author(s): Khalid Parvez Lone, Ph.D., Muhammad Waqar Azeem, M.D.*

#### SUMMARY:

Background: Intellectual Disability (ID) is characterized by significant limitations in intellectual functioning and in adaptive behavior including conceptual, social and practical skills. In Pakistan, the prevalence of serious ID (IQ < 50) is 1.9% and mild ID (IQ 50-70) is 6.2%. Bone health is recognized to contribute to overall management of children with intellectual disability. People with ID have many factors that negatively affect bone health such as reduced mobility, decreased vitamin D levels, epilepsy and increased risk of fractures. Adequate nutrition is recognized as an important factor in improving overall physical and emotional wellbeing of children and adolescents and prevention of osteoporosis. Definite data on the relationship of bone health with nutritional status in children with ID is scarce globally and is acutely lacking in Pakistan and South Asia. This study is aiming to look at this knowledge gap. Objectives: 1. To Investigate the correlation of bone health with nutritional status in children with intellectual disability in the local population 2. To compare the bone health and nutritional status among

groups of children with mild and serious degrees of intellectual disability. Methodology: This is a cross-sectional analytical study and is approved by Institutional Review Board. A total of 60 subjects are being selected from special education schools of Lahore, the second largest city of Pakistan. For the purpose of comparative analysis, the subjects are being divided into 2 subgroups i.e. Group-I including children with mild ID (IQ 50-70) and Group-II including children with serious ID (IQ < 50). After obtaining a written informed consent from parents, each child undergoes thorough examination. IQ and adaptive behavior is being assessed by clinical psychologist using standardized scales. Bone health is being determined by assessing ultrasonographic bone profile parameters, serum calcium, serum phosphate, serum alkaline phosphatase and insulin like growth factor 1. Nutritional status is being determined by assessing height, weight, body mass index, triceps skin fold thickness, subscapular skin fold thickness, mid arm circumference, albumin and hemoglobin. The data obtained is being entered in SPSS version 18 and will be analyzed on completion of sample collection. Outcomes and Utilization: This study will look into the importance of adequate nutrition for good bone health in children with ID. Preventing the ill effects of inadequate nutrition on bone health in children with ID may help in reducing their fracture risk and improving their overall health. Improved bone health and mobility status would improve the overall quality of life of children with ID and their families.

#### NR5-57

### CHANGES IN BRAIN ACTIVITY AMONG SLEEP DEPRIVED PHYSICIANS

*Chair: Vincent Capaldi M.D.; Author(s): Steven Durning, M.D.*

#### SUMMARY:

One of the most contentious issues in the medical education community today is resident work hour restrictions. To our knowledge, no study to date has evaluated changes in internal mental processes among physicians who are sleep deprived. The data in this report was derived from a larger study to determine if fMRI can be used to help understand diagnostic clinical reasoning expertise as measured with vignette based multiple choice questions (MCQ) obtained from the American College of Physicians. As part of this study, participants were asked to complete the Epworth sleepiness scale and report if they had been on overnight call within the past 48 hours. As part of this exploratory study, differences emerged in brain activity among physicians who were sleep deprived compared to those who were well rested. Participants were 14 staff internal

medicine physicians at Walter Reed Army Medical Center or National Naval Medical Center. Subjects were scanned on a 3T Signa MRI scanner (General Electric, Milwaukee, WI) with a 32-channel head coil. An fMRI task presentation of the 32 questions was created using E-Prime software (Psychology Software Tools, Inc.) and displayed via a goggle system (Nordic NeuroLab Inc., Milwaukee, WI) while each participant was in the fMRI scanner. Activation analysis was performed using a general linear model (GLM) approach concatenating the four data sets for each subject. Hemodynamic response estimates were modeled for each of the three question phases (read, answer, reflect). The “read” and “answer” times varied from question to question and were modeled with a gamma-variate function with variable duration and variable amplitude. There was decreased effective activation of the medial prefrontal cortex (mPFC) in participants that had higher scores on the Epworth Sleepiness Scale (ESS) ( $p < .005$ ; figure 1). The blue color in the figure indicates a negative relationship between the Sleepiness scores and the fMRI effect contrast. The fMRI effect contrast is the effective activity size during the answering phase minus the effective activity size during the reflecting phase. The average answering phase effect in this region was negative and the average reflecting phase effect in this region was positive. Thus, the negative correlation of the answering phase was greater than the positive correlation of the reflecting phase. The negative correlation between the sleepiness score and the (Ans - Refl) effect size indicates increased sleepiness is correlated with a decrease in the difference between the answering and reflecting phases while answering questions. This is the first study to utilize functional neuroimaging to investigate neuroanatomic correlates of clinical reasoning in sleep deprived physicians. Further research in this field would be helpful to better elucidate this phenomenon. The implications from these data suggest that when physicians are sleep deprived it becomes more difficult to manipulate clinical data.

#### NR5-58

### FOOD INSECURITY, NUTRITIONAL RISK AND UTILIZATION OF PSYCHIATRIC EMERGENCY SERVICES

*Chair: Lauren McGuire B.S.; Author(s): Nina Sreshta, B.A., Hilary Seligman, M.D., M.A.S., Andrea Lopez, B.S., Christina Mangurian, M.D.*

#### SUMMARY:

The inability to reliably afford food and poor nutrition are associated with increased risk of mental illness. There has been little examination, however, of whether adults with severe mental illness (SMI) are more likely

to experience illness exacerbations if they are food insecure or lack adequate nutrition. Practitioners' clinical experiences suggest that food insecurity (FI) and high nutritional risk (NR) are common problems among SMI adults. We therefore sought to determine the prevalence of these conditions in a SMI population and whether they were associated with increased utilization of psychiatric emergency services (PES). We orally administered a cross-sectional survey to 111 clients at UCSF's Citywide and Community Focus Clinic, an outpatient mental health clinic serving San Francisco residents with SMI. We used the USDA's Household Food Security Survey Module (10 items) to assess food insecurity and the Nutritional Screening Initiative's DETERMINE Checklist (10 items) to assess nutritional risk. We abstracted the number of visits to PES in the past year from the EMR associated with the safety net hospital where 90% of this population receives psychiatric services. We examined the association between FI and high NR with utilization of PES using chi-square and one-way ANOVA tests. We approached 21% (146/700) of the client population, of whom 77% gave informed consent and were interviewed. Our sample was 37% White, 22% African American, 11% Asian, 9% Latino and 21% other/multiracial. The FI rate was 71%; DETERMINE scores showed 7% of participants to be at low NR, 14% at moderate NR, and 79% at high NR. The DETERMINE items most frequently answered affirmatively were: mostly eating alone (72%), not having enough money to buy food (67%), taking 3+ medications (66%), eating few fruits, vegetables or milk products (63%), eating fewer than 2 meals per day (43%), and having dentition problems (42%). Very low food secure participants had greater mean number of PES visits than food secure participants (1.93 vs 0.74,  $p=0.04$ ). After adjusting, very low food secure participants had an estimated 1.2 more PES visits in the previous year than food secure participants, although this no longer reached statistical significance ( $p=0.3$ ). Participants at high NR had no greater PES visits than participants at low NR (1.3 vs 0.25), either in unadjusted ( $p=0.4$ ) or adjusted analyses (0.9). The prevalence of food insecurity and nutritional risk is substantially higher in the SMI population compared to the general population. 71% of participants were food insecure versus 14% of general population, and 79% were at high NR versus <50% of general population. Food insecurity may be associated with high utilization of PES services. Further research is needed to determine the generalizability of these findings and whether interventions to decrease food insecurity prevent psychiatric exacerbations that result in increased use of PES services.

#### NR5-59

## ETHNIC DISPARITIES IN CHILD AND ADOLESCENT PATIENTS WHO PRESENT TO PSYCHIATRIC EMERGENCY SERVICES

*Chair: David Seigler M.D.; Author(s): Benjamin K Woo, M.D.*

### SUMMARY:

**Introduction:** Many children have mental health problems that can interfere with normal development and functioning. However, many children, as well as their parents, do not have access to the mental health system. For most of these children, Psychiatric Emergency Services (PES) can be the only gateway into the mental health system. Unfortunately, racial disparities exist in the psychiatric management of children in crisis, and have been observed in the use of PES. Whether the prevalence of racial disparities affect children who require acute care remains unclear. We hypothesized that ethnic background is a significant factor in whether patients will present to PES, and continue to seek further care. **Methods:** We examined 2423 involuntary evaluations during a one-year study period at the only psychiatric emergency service center for a population on approximately 760,000 people. An administrative database, from which epidemiological data was extracted for these analyses, was created by review of medical records. This database included both sociological demographics and information about each visit. From this database, we dichotomized the evaluations into those involving children (age < 18), and those involving adults (age ≥ 18) and compared the two populations' ethnic demographics. **Results:** Of the 2423 cases in the sample, 11.8% (n=285) were child and adolescent cases under the age of 18, and 88.2% of all admissions were over the age of 18. Within the child population, 50.5% (n=144) were Caucasian, 9.5% (n=27) were African American, 38.2% (n=109) were Hispanics, and 1.8% (n=5) were in the other various ethnicities. Within the adult population, 59.5% (n=1271) were Caucasian, 10.8% (n=231) were African American, 27.5% (n=588) were Hispanics, and 2.2% (n=48) were in the other various ethnicities. A Chi-Square analysis was used and found a statistically significant P-value of .0026 **Conclusions:** These results show that there are prominent ethnic disparities in the child and adolescent cases that are independent of those seen in the adult population. The reasons why such disparities exist could be multiple and include differing cultural ideas of mental illness, patients' (and their families) beliefs that PES are inaccessible, or simple lack of experience with mental illness and appropriate care.

**NR5-60**

## MUSCLE DYSMORPHIA IN BRAZILIAN

## WEIGHTLIFTERS: PREVALENCE AND CLINICAL CHARACTERISTICS

*Chair: Milena França M.D.; Author(s): Antonio Leandro Nascimento, M.D., MSc, Riane Marinbo, M.D.; Juliana Oliveira, M.D.; Livia Vasconcelos, M.D.; Katia Petribu, M.D., Ph.D.*

### SUMMARY:

**Introduction:** Muscle dysmorphia (M.D.) is variant of body dysmorphic disorder in which individuals develop a pathological preoccupation with their muscularity. Individuals with M.D. believe themselves to be of very small musculature, although they are usually highly muscular. This belief leads them to become obsessed with exercising, particularly weightlifting and is frequently associated with misusing anabolic-androgenic steroids. Individuals with M.D. also avoid situations and places where they might be seen without clothing often wear many layers of clothing, even in hot weather, to avoid their bodies being seen (and if that is unavoidable it causes them severe distress). Other behaviors, such as spending excessive amounts of money on ineffectual sports supplements and abnormal eating patterns are also associated with M.D.. Social relations and occupational functioning are adversely affected as a result of the hours dedicated to weightlifting and exercising. Symptoms of M.D. have been shown to be more prevalent in some groups of athletes, such as bodybuilders and weightlifters. **Objective:** to determine the prevalence and clinical characteristics of muscle dysmorphia in Brazilian weightlifters. **Method:** Weightlifters from seven gymnasiums in Recife (Pernambuco – Brazil) area have been evaluated in a cross-sectional study using the Structured Clinical Interview for the DSM-IV (SCID-I/DSM-IV) sections of anxiety and body dysmorphic disorders, the Yale-Brown Obsessive-compulsive Scale (YBOCS) and a Harrison G. Pope's questionnaires for Muscle Dysmorphia and Adonis Complex. **Results:** Thirty individuals have been included in the study. All of them were male and their mean age was 29.7± 6.15 years. 40% of the subjects were involved in strength-related professions (16.67% of the subjects were gymnasium instructors). 73.33% of the subjects spent more than two hours per day exercising. 33.33% of the subjects (10/30) met the proposed diagnostic criteria for M.D.. 43.33% of the subjects (13/30) presented a significant life impairment due to M.D. symptoms and 33.3% of the subjects presented M.D. symptoms but did fulfill the diagnostic criteria. According to the AC questionnaire, one third of the subjects presented a mild or moderate type of the complex and 10% of the subjects presented severe symptoms of the disorder. Nineteen subjects (63.33%) used anabolic-androgen steroids. High scores

in the AC questionnaire were associated with lower income and starting weightlifting at an earlier age. Conclusion: our findings suggest that M.D. is highly prevalent disorder in Brazilian weightlifters and that it interferes in social functioning due to pathological preoccupation with muscularity, expenses with diet foods and dietary supplements, impairment in occupational functioning and anabolic-androgen steroids abuse.

**NR5-61  
VIOLENCE, MENTAL ILLNESS, AND THE MEDIA: JUST HOW BAD IS IT?**

*Chair: George Annas M.D.*

**SUMMARY:**

Beliefs about those with mental illness being more prone to violence abound in society today. This is despite a great deal of literature suggesting that those with mental illness, with the exception of co-morbid or entirely substance abuse diagnoses, either pose a small fraction of greater risk or no greater risk of violence to the public (Elbogen et. al., 2009; Nielssen et. al., 2009). In a prior study, performed by the author, news stories about mental illness disproportionately focused on a violent theme. When the keyword “schizophrenia” was searched over 4 news sources in the last year (10/2010-7/2011), 50.6% of the articles made reference to or focused on violence. When the phrase “Mentally Ill” was searched, 37.8% of the stories focused on violence. By comparison, only 10% of the stories with the keyword “Alcoholism” made reference to or focused on violence. Comparison groups were searched with keywords for homeless and postal workers. None of the stories about postal workers was focused on violence and only one of the stories about homelessness made reference to a homeless person being violent (Annas, 2011). In this poster I will exhibit the results of a study of the media, updating the research, above, and improving on the standardization of methods. This will better determine the magnitude of how mental illness is disproportionally portrayed in the print media. I will also examine the extent to which accurate education is included in those stories that focus on violence. References: Annas, George D. The Link Between Violence and Mental Health: Fact or Fiction. Poster Presentation for the American Association of Psychiatry and the Law, Annual Meeting, presented: October 28. 2011 Elbogen EB, Johnson SC. The intricate link between violence and mental disorder: results from the National Epidemiologic Survey on Alcohol and Related Conditions. Arch Gen Psychiatry. 2009 Feb;66(2):152-61. Nielssen O, Bourget D, Laajasalo T, Liem M, Labelle A, Häkkänen-Nyholm H, Koenraadt F, Large MM. Homicide of strangers by people with a psychotic illness. Schizophr Bull. 2011

May;37(3):572-9. Epub 2009 Oct 12.

**NR5-62  
INVESTIGATIONS FOR RELATIONSHIP BETWEEN STRESS AND DEPRESSION IN HEALTH PROMOTION CENTER**

*Chair: Inbo Shim M.D.*

**Summary:**

In many studies, it is found that many chronic diseases are related with the stress and depression and how individuals perceived the stress has been focused recently. But its effects on self-perceived health status are not known so well in Korea. In this study, we identified the degree of perceived stress, the impact of stress on the individual's depressed mood, and the factors of perceived stress in general population. We enrolled a total 1,674 Koreans, visited to one general hospital health promotion center from Jan, 2009 through Dec, 2009. Data was collected by questionnaire including basic demographic variables, individual history of general diseases, metabolic variables, psycho-emotional factors, psychosocial variables. Also visitors filled in PSS(Perceived Stress Scale) and PHQ9(Patient Health Questionnaire-9) for the screen of depression. We found a positive relationship between the perceived stress and the degree of depression (B=.450, OR=.620, p=.000), 38 visitors(2.3%) could be diagnosed to the mild depressive disorder over PHQ9 cut-off 10. We found the relationship of underlying medical diseases and PSS, PHQ9 score, but other variables such as age, alcohol assumption, smoking, BMI, motivation to visit, psychosocial factors have not related with the perceived stress and depressed mood. We could recommend a screen tools of PSS, PHQ9 to the patients with variable underlying diseases although they could not appeal the severe stress or depressed mood.

**NR5-63  
The Safe Haven Program: A Model for Improving Outcomes for Undomiciled Patients with Serious Mental Illnesses**

*Chair: Victoria Brown-Nyseth M.D.; Author(s): S. Charles Schulz, M.D., John Vuchetich, M.D., Ph.D., Tim Burkett, Ph.D.*

**SUMMARY:**

**OBJECTIVE:** To assess the impact of the Safe Haven Program on patients who are homeless and severely mentally ill in the Twin Cities area of Minnesota. Unfortunately, more than half of the people who find themselves without stable housing in the Twin Cities have mental health diagnoses including schizophrenia

and bipolar disorder. Many of them have experienced significant traumatic life events and repeated traumatic brain injuries. After visits to numerous cities in the Midwest to study other programs, People Incorporated and the University of Minnesota teamed together to create the Safe Haven program. **METHOD:** A study was designed to compare measures of health for the patients in the two years prior to enrollment in the program with those during the post-enrollment period. The post-enrollment figures were adjusted to reflect two-year rates. Data was collected on 128 patients using a questionnaire. Matched t-tests were then performed on the data. Bonferonni correction was used for 9 independent tests to set the significant p-value for an overall alpha of 0.05, yielding a p-value of 0.0056 as the sign of a significant test. **RESULTS:** Enrollment in the Safe Haven Program was associated with a number of positive changes in self-care for the patients. Statistically significant changes in number of days spent in detoxification facilities, days spent in a shelter, emergency room visits, medical appointment visits and psychiatric visits were found. Days in detoxification changed from 6.42 to 2.62 ( $p=0.0017$ ) and days in shelters went from 154.1 to 74.1 ( $p=0.0033$ ). Emergency room visits dropped from 2.13 to 0.93 ( $p=0.0007$ ). Additionally, medical appointments increased from 4.44 to 12.96 ( $p=0.0001$ ) and psychiatric appointments increased from 3.88 to 13.90 ( $p=0.0003$ ). **CONCLUSIONS:** A comprehensive program including resources for active outreach, housing, psychiatric assessment and nursing follow-up offers significantly improved health outcomes for undomiciled patients with serious mental illnesses. This program has the added benefit of providing valuable education opportunities for psychiatric residents. Furthermore comprehensive programs such as the Safe Haven program have been shown to reduce costs for these patients.

#### NR5-64

### THE EFFECTIVENESS OF RESIDENTIAL CARE FOR COMBAT RELATED PTSD IN AN ACTIVE DUTY MILITARY POPULATION

*Chair: Adeniyi Alatise M.D.; Author(s): Paul Sargent, M.D.; Robert Mclay, M.D., Ph.D.; Amy Amidon, Ph.D.; Nancy Lin, Ph.D.; Ira Grossman, Ph.D.; and Jonathan Rapp, Ph.D..*

#### SUMMARY:

**BACKGROUND:** The treatment of combat-related PTSD still remains a challenge despite multiple published clinical practice guidelines and standardized evidence based treatments for this condition. **AIMS:** To demonstrate the effectiveness of a residential treatment program for PTSD for those who are still serving on

active duty. **METHOD:** A naturalistic, retrospective review of outcomes from Seventy Three (73) service members with combat-related PTSD and a variety of co morbidities, which include Traumatic Brain Injury, Chemical dependency, Major Depressive Disorder and chronic pain. All participants had either failed, or were considered unsuitable for outpatient treatment. Patients were treated at a residential treatment program run by Naval Medical Center San Diego. Treatment lasted 10 weeks, and included Cognitive Processing Therapy, psychopharmacology, and a variety of supportive treatments. To give feedback to providers, patients' progress was tracked using weekly administration the PTSD Checklist Military version (PCL-M), and the Patient Health Questionnaire (PHQ-9) for depression. For this review, the first and last of these measures for each patient was compared. Numerical scores were compared by paired t-tests, and descriptive statistics were gathered for percent (%) of individuals who met criteria for PTSD or depression according to these instruments. First and last observations were gathered from the patient's medical record. **RESULTS:** Average improvement in PTSD symptoms was 26.7 % ( $p < 0.0001$ ), and average improvement in depressive symptoms was 32.1% ( $P < 0.0001$ ). At the time of discharge; 25.1% of those admitted did not meet Criteria for PTSD and 50% of those with M.D.D diagnosis no longer met criteria for M.D.D. **CONCLUSION:** Residential care based on Cognitive Processing Therapy was associated with significant improvements in combat-related PTSD and depression. Further study will be needed to determine the relative clinical effectiveness of the treatment, cost effectiveness of treatment, and the most beneficial active components of treatment.

#### NR5-65

### COMPARISON OF FOUR COMMONLY-USED SLEEP MEDICATIONS

*Chair: Adeniyi Alatise M.D.; Author(s): Robert Mclay, M.D., Ph.D..*

#### SUMMARY:

**BACKGROUND:** Insomnia is a common problem in many psychiatric disorders, notably Post Traumatic Stress Disorder (PTSD), Major Depressive Disorder (M.D.D), Generalized Anxiety Disorder (GAD) and Post concussional Disorder (TBI). There are a large number of psychopharmacological interventions that address insomnia, but little evidence to determine which medication in the best option for which individual with sleep problems. Although psychometric instruments are commonly available to track sleep outcomes, few providers make a systematic study of their patient

populations to determine which is working best. We established a randomized effectiveness trial by which psychiatry residents could track the results of the sleep medications they prescribed. **AIMS:** Have psychiatry residents compare the effectiveness of four, commonly-used medications to treat insomnia in their clinical practice. **METHOD:** IRB approval was obtained to conduct a randomized, open label, head to head comparison of four the medications that are commonly used to treat insomnia: zolpidem, trazodone, quetiapine and diphenhydramine. Psychiatry residents act as clinical investigators, enrolling participants, and tracking results in their practice. Psychometric instruments are used to track results, and results shared among residents and staff to see which medications are working best for insomnia in common psychiatric conditions. **RESULTS:** The study has been approved by the hospital review board. The investigator is in the process of data collection. The study can easily be replicated in other settings because it mimics clinical practice.

**NR5-66**

**THE USE OF MENTALIZATION IN  
OUTPATIENT PSYCHIATRIC CLINIC.  
RESIDENTS' CAPACITY TO THINK  
PSYCHOLOGICALLY IMPROVE THEIR  
PATIENT-DOCTOR INTERACTION**

*Chair: Magdalena Romanowicz M.D.; Author(s): T. Oesterle, M.D., M. Romanowicz, M.D., EK. Milliner, M.D., B. Sutor, M.D.*

**SUMMARY:**

**Introduction:** A good patient's satisfaction with their health care is important as it has been shown in various studies to be linked with better quality of life. The most basic definition of mentalization is an ability to hold somebody's mind in mind. If we think about the doctor- patient interaction in everyday psychiatric practice, mentalization can be viewed as an antidote to traditional 'medical model' psychiatry in which symptoms are taken at face value without considering the contribution of doctor and patient's states of mind, and their interactions. **Objective:** The purpose of this study was to assess Mentalization ability of psychiatric patients treated in the outpatient residents' clinic. We also wanted to check whether a brief mentalization skills training of general psychiatry residents influenced satisfaction ratings(as measured by the Patient Satisfaction Questionnaire, PSQ-18). We hypothesized that the residents who were taught about mentalization would show improvements in their patient satisfaction scores. **Methods:** This was a prospective case- control study. We enrolled patients who were considered new intakes in the outpatients

resident's clinic. We tested the patient's Mentalization ability utilizing the interpersonal reactivity index (IRI). Target variables were the subscales of the PSQ-18 for patients treated before the physician's Mentalization based training and after. We used univariate analysis to identify those variables significantly associated with the subscales and multiple linear regression to determine those independently significant. **Results:** The study population consisted of 157 (90 pre 67 post physician training) patients who were seen in outpatient resident's clinic. The mean age of subjects was 41.2 (+/- 15.4) years. 60% of patients were married, 29% single and 11% were either divorced or widowed. 57% of patients were employed. The patients were mostly satisfied with clinician communication and interpersonal manner (PSQ-18 average scores of 4.21 +/- 0.66 and 4.15 +/- 0.69 respectively). There was no significant difference between the composite PSQ-18 rating before or after the mentalization training. However, there was a significant difference in the communications sub scale scores for male patients treated by physicians with Mentalization based training compared to the same physicians without Mentalization based training (4.28 pre-training to 3.86 post training CI(4.07 , 4.48) P-value 0.028). There was no significant difference between mean IRI scores for general standard outpatients versus our psychiatric patient's population. **Conclusions:** Our study reveals that psychiatric outpatients seen for the first time in a resident clinic have mentalization skills that are comparable with a general population. Furthermore, it shows that a brief Mentalization based training can improve the perceived communication between male patients and their resident psychiatrists as measured by the PSQ-18.

**NR5-67**

**THE BENEFITS OF A CAMBODIAN HEALTH  
PROMOTION PROGRAM**

*Chair: Sarah Berkson B.A.; Author(s): Shin Daimyo, M.P.H*

**SUMMARY:**

Cambodian refugees suffer from an increased burden of preventable diseases. For example, according to Massachusetts mortality data, Cambodians are dying from diabetes at a rate 6 times higher than the general population, and from stroke at a rate 2.5 times higher. In response to this health crisis, the Harvard Program in Refugee Trauma developed the Cambodian Health Promotion Program over a decade ago and continues to enroll participants. Participants have been primary or secondary Cambodian survivors of torture recruited from the patient population at Lynn Community Health Center and the Cambodian Mutual Assistance Association, and from the local community in Lynn

and Lowell, Massachusetts. In the current curriculum, participants attend five 90-minute classes covering (1) health promotion, (2) exercise, (3) nutrition, (4) stress management and sleep hygiene, and (5) the patient-provider relationship. An English-speaking behavioral healthcare provider and a Khmer-speaking Cambodian health educator co-teach the culturally adapted curriculum through a combination of didactics, activities, video presentations and discussion in a small classroom setting. In order to evaluate the program, the Cambodian health educator verbally administers a questionnaire individually to each participant before and after each health promotion class. Here, we present the questionnaire data of 162 participants from 2007 to 2011. Our analysis using paired samples t-tests shows significant ( $p < 0.05$ ) improvements in depression symptoms, hours of sleep per night, frequency of nightmares, number of minutes spent exercising per week, health, energy, body pain, social functioning, confidence that health can improve, confidence in understanding causes of illnesses, and confidence in communicating with the doctor. Our results suggest that the Cambodian Health Promotion Program offers significant benefits for its participants and that health education can play a powerful role in promoting health and quality of life in survivors of torture.

**NR5-68**  
**LONG-TERM IMPROVEMENT IN**  
**SELF-INJURIOUS BEHAVIOR AND**  
**CONTINUAL STABILIZATION OF MOOD**  
**SYMPTOMS OVER THREE YEARS OF**  
**MAINTENANCE ECT IN AN AUTISTIC CHILD**

*Chair: Katherine Lubarsky B.A.; Author(s): George P. Tatmo, BS Susan Zafarlotfi, Ph.D. Giovanni Caracci, M.D. Ye-Ming Sun, M.D. Ph.D.*

**SUMMARY:**

**Introduction:** Self-injurious behavior (SIB) occurs regularly in children with autism and other developmental disabilities. Severe cases of self-injury pose a significant clinical challenge, as they are often refractory to pharmacological and behavioral interventions. The literature has shown that acute ECT treatment is effective in decreasing rates of self-injury, but there is scarce data on the long-term outcome of these patients or follow-up after maintenance ECT. **Case Report:** We report the long-term improvement in self-injurious behavior in a 12 year-old autistic child receiving ECT treatment. A profound and consistent reduction in rates of self-injurious behaviors has occurred over a 3 year time period of weekly (6 month) and twice monthly (2.5 years) maintenance ECT, with continual stabilization of mood symptoms. The

self-injury rate was not only maintained at the low level attributed to an initial acute ECT treatment course (previously reported in the literature), but further reduced by an additional 66% during maintenance treatment course. Over this time period, no brain structural changes are evident on CT. **Conclusion:** This case provides further support for using ECT as safe and effective long-term management of severe and refractory self-injury behavior in autism.

**NR5-69**  
**EXPLORING THE IMPACT OF MATERNAL**  
**STRESS EXPOSURE ON FETAL ADRENAL**  
**VOLUMES**

*Chair: Samantha Powell None Author(s): C. Neill Epperson, M.D., Grace C. Ewing, Eileen Wang, M.D., Mary Sammel, Sc.D., Deborah R. Kim, M.D.*

**SUMMARY:**

**Objective:** To investigate the impact of maternal stress and early life trauma on fetal HPA axis health. **Methods:** Pilot data from the first phase of an ongoing longitudinal cohort study are presented here. 51 pregnant women, 19-22 weeks gestation, were recruited from the Hospital of the University of Pennsylvania. All subjects were greater than or equal to 18 years of age, medically healthy with no active psychiatric diagnoses or history of pre-term birth. Enrolled subjects completed a brief health and demographic questionnaire and the 10-item Perceived Stress Scale (PSS) (1). In 28 of these women the Adverse Childhood Experience Questionnaire (ACE) (2) was administered. Subjects received a 3D ultrasound of the fetal adrenal gland. Two volumes were obtained per subject and an average of the two volumes was determined. A corrected fetal adrenal gland volume calculated using estimated fetal weight (3,4) was used as the outcome of interest. Histograms and normal probability plots were used to assess distributional assumptions. Multivariable linear regression was used to estimate associations and adjust for gestational age at the time of adrenal volume measurement. **Results:** 51 women completed the study. Mean age of the subjects was 26.5 years (SD 5.6) and mean gestational age was 20.8 weeks (SD 0.94). Mean PSS score was 16.17 (SD 8.4). In the 28 subjects for whom we had ACE scores, 25% of the sample reported ACEs greater than or equal to 2, 21% greater than or equal to 1 and 54% no ACEs. Mean fetal adrenal volume was 0.25 cc (SD 0.11). As expected, PSS and ACE were significantly correlated ( $\rho = 0.58$ ,  $p = 0.001$ ). Corrected adrenal volume was negatively associated with the number of ACEs. In a multivariable linear regression model adjusting for gestational age, each additional ACE corresponded to a decrease in adrenal volume of 0.09

cc/kg,  $p=0.032$ . In a similar model which also adjusted for gestational age, PSS scores were not significantly associated with adrenal volume,  $p=0.95$ . Conclusions: Maternal early stress exposure may be more important to fetal HPA axis health than perinatal stress levels. These data show that although early life stress predicts high PSS during pregnancy, ELS (ELS) is a stronger predictor of decreased fetal adrenal volume.

#### NR5-70

### A CASE OF CLOZAPINE INDUCED ACUTE RENAL FAILURE

*Chair: Na-Young An M.D.; Author(s): Jai Sung NOH, M.D., Department of Psychiatry & Behavioral Sciences, Ajou University, School of Medicine*

#### SUMMARY:

**Introduction:** There have been a few case reports that clozapine, an atypical antipsychotic, caused acute renal failure of interstitial type. Here we report a case of acute renal failure developed just after introduction of clozapine to a patient diagnosed with Bipolar I disorder. We describe the clinical and laboratory findings and discuss the measures for early detection of this life threatening condition. Within our knowledge, this is the first report of clozapine induce acute renal failure in South Korea. **Case presentation:** A 38-year-old Korean man with treatment-resistant recurrent bipolar I disorder, with psychotic symptoms developed acute renal failure following initiation of treatment with clozapine. He developed fever, abrupt weight gain (8kg), generalized edema, and urinary difficulty within 2 weeks at a dose of 200mg per day. On arrival he was hemodynamic stable, and there was no abnormality on physical examination. Blood biochemistry confirmed severe renal failure with urea 34.7mg/dl, and creatinine 5.1mg/dl. No acute infection and systemic disease were discovered in him. After clozapine had been withdrawn, the patient's renal functions returned to normal. There was close temporal relationship of the initiation of clozapine treatment to the onset of renal failure, and rapid resolution after cessation. **Conclusion:** Clozapine-induced acute renal failure is extremely rare but may prove fatal. Psychiatrists keep in mind this possible complication when clozapine started and alert close monitoring for renal as well as agranulocytosis.

#### NR5-71

### MORE SEVERE LONGITUDINAL BIPOLAR ILLNESS COURSE ASSOCIATED WITH EARLY LIFE STRESS IN BDNF MET ALLELE CARRIERS BUT NOT NON-MET ALLELE CARRIERS

*Chair: Shefali Srivastava M.D.; Author(s): Joachim Hallmayer, M.D.; Po Wang, M.D.; Shelley Hill, MS; Sheri Jobson, Ph.D.; Terence Ketter, M.D.*

#### SUMMARY:

**Background:** Emerging findings support interaction effects of brain-derived neurotrophic factor (BDNF) val66met genotype with environmental factors, such that individuals in non-clinical samples who carry the met allele may be more susceptible to the affective consequences of early life stress (ELS). However, there are limited data regarding the impact of this gene-environment interaction on severity of illness in individuals diagnosed with bipolar disorder (BD). We conducted a study to examine whether BDNF met carrier status moderates the negative impact of ELS upon longitudinal bipolar illness severity. **Methods:** Stanford University Bipolar Disorders Clinic patients were initially assessed with the Systematic Treatment Enhancement for Bipolar Disorders (STEP-BD) Affective Disorders Evaluation (ADE), and monitored longitudinally for at least one year with the STEP-BD Clinical Monitoring Form (CMF), while receiving open measurement-based care based on model practice procedures. Patients provided a blood or saliva sample for BDNF val66met genotyping and completed the Childhood Trauma Questionnaire (CTQ). BDNF met allele carrier status, CTQ total score (ranging 25-125, with higher scores indicating greater childhood trauma), and presence or absence of childhood sexual abuse (CSA, ascertained from the CTQ-sexual abuse subscale), were evaluated in relation to mean prior-year Clinical Global Impressions-Severity of Illness (CGI-S) score. **Results:** 80 patients (43 BD I, 33 BD II, 4 BD not otherwise specified, mean  $\pm$  SD age  $46 \pm 14$  years, 63.7% female) completed the CTQ and BDNF val66met genotyping. For these 80 individuals, who were seen in the clinic on average every  $58 \pm 38$  days, mean  $\pm$  SD prior-year CGI-S score was  $3.1 \pm 0.9$ , CTQ total score was  $45.1 \pm 16.1$ , 31.3% reported a history of CSA, 37.5% were BDNF met carriers (7.5% met/met, 30.0% val/met), and 62.5% were non-met carriers (val/val). Among BDNF met carriers but not non-met carriers, individuals with compared to without CSA had significantly higher mean prior-year CGI-S scores ( $3.5 \pm 0.7$  vs.  $2.9 \pm 0.7$ ,  $t = -2.4$ ,  $df = 28$ ,  $p = 0.025$ ), and CTQ total score tended to correlate with mean prior-year CGI-S score ( $r = 0.35$ ,  $df = 28$ ,  $p = 0.058$ ). Notably, patients with compared to without CSA had earlier onset age ( $16 \pm 8$  vs.  $22 \pm 10$  years,  $t = 2.6$ ,  $df = 77$ ,  $p = 0.012$ ), yet when stratified by genotype the effect was significant for BDNF met carriers ( $15 \pm 6$  vs.  $23 \pm 8$  years,  $t = 3.0$ ,  $df = 27$ ,  $p = 0.006$ ) but not non-met carriers ( $17 \pm 9$  vs.  $21 \pm 10$  years,  $p = 0.215$ ). **Discussion:** History of ELS in general, and especially CSA, were associated with greater

longitudinal illness severity in BD patients who carried the BDNF met allele, consistent with earlier reports of a gene-environment interaction between BDNF val66met and ELS with respect to affective outcomes in non-clinical samples. Further studies are warranted to explore the impact of BDNF val66met genotype and ELS on individuals with BD.

**MONDAY MAY 07, 2012**

**New Research Poster Session 6**

**SCHIZOPHRENIA AND OTHER PSYCHOTIC DISORDERS**

**NR6-01**

**LURASIDONE FOR THE ACUTE TREATMENT OF ADULTS WITH SCHIZOPHRENIA: WHAT IS THE NNT, NNH AND LHH?**

*Chair: Leslie Citrome M.D.*

**SUMMARY:**

**Objective:** To describe the efficacy, safety and tolerability of lurasidone for the acute treatment of schizophrenia using the metrics number needed to treat (NNT) and number needed to harm (NNH). **Methods:** Study data were pooled from the 6 phase II and III, 6-week, randomized placebo-controlled trials that were conducted to test the efficacy and safety of lurasidone for the acute treatment of schizophrenia. Included were the following interventions: fixed doses of lurasidone 20, 40, 80, 120 and 160 mg/d; haloperidol 10 mg/d; olanzapine 15 mg/d; quetiapine extended-release 600 mg/d; placebo. The following outcomes were assessed: responder rates as defined by a reduction of  $\geq 20, 30, 40$  or  $50\%$  from baseline on the Positive and Negative Syndrome Scale (PANSS); study completion; discontinuation due to an adverse event (AE); weight gain  $\geq 7\%$  from baseline; incidence of spontaneously reported AEs; incidence of total cholesterol  $\geq 240$  mg/dl, low-density lipoprotein cholesterol  $\geq 160$  mg/dl, fasting triglycerides  $\geq 200$  mg/dl and glucose  $\geq 126$  mg/dl at endpoint. NNT for the efficacy outcomes and NNH for the safety/tolerability outcomes were calculated. Likelihood of being helped or harmed (LHH) was also calculated to illustrate trade-offs between outcomes of improvement  $\geq 30\%$  on the PANSS vs. incidence of akathisia, nausea, sedation, somnolence and parkinsonism. **Results:** NNT vs. placebo for PANSS reductions  $\geq 30\%$  were 8, 7, 7 and 4 for lurasidone doses of 40, 80, 120 and 160 mg/d, respectively, and 4 and 3 for olanzapine 15 mg/d and quetiapine extended-release 600 mg/d, respectively. Lurasidone was not associated with any statistically

significant disadvantages over placebo for weight gain or metabolic abnormalities; NNH vs. placebo for weight gain  $\geq 7\%$  from baseline was 4 for olanzapine and 9 for quetiapine extended-release in contrast to a NNH for this outcome ranging from 43 to 150 for lurasidone 40-160 mg/d. The 5 most consistently encountered adverse events attributable to lurasidone were akathisia, nausea, sedation, somnolence and parkinsonism, with NNH vs. placebo for lurasidone 40-120 mg/d ranging from 6 (akathisia with 120 mg/d) to 30 (parkinsonism with 80 mg/d). Lurasidone 160 mg/d appeared better tolerated than doses of 40, 80 or 120 mg/d for akathisia, nausea, sedation or somnolence, with no NNH values for these adverse events for 160 mg/d vs. placebo being statistically significant. LHH was favorable for lurasidone when contrasting PANSS reductions vs. adverse events. **Conclusions:** NNT and NNH can help quantify outcomes and place lurasidone into clinical perspective. Advantages for lurasidone include a low propensity for weight gain and metabolic abnormalities. More commonly encountered adverse events include akathisia, nausea, sedation, somnolence and parkinsonism, but NNH values are generally in the double digits, reflecting an overall tolerable profile.

**NR6-02**

**CLINICAL FUNCTIONAL DIMENSIONS AND COGNITIVE FUNCTIONS IN FEMALE SCHIZOPHRENIC PATIENTS**

*Chair: Ioana Valentina Miclutia Ph.D.; Author(s): Craciun Ioana, M.D., Ph.D. Iftene Felicia, M.D., Ph.D. Popescu Codruta, Ph.D.*

**SUMMARY:**

**Background:** There is a growing body of literature supporting the observation that schizophrenia could be a neurocognitive disorder. Valid cognitive deficits in schizophrenia are now well characterized: general poor performance with disproportionate deficits in aspects of memory and executive function. Cognitive dysfunction, along with the dimension of schizophrenic symptoms, can be predictive for the course of the disease, especially with regard to social functioning. Various factors may influence the cognitive functions: age, gender, duration of illness. **Aims:** This study aims to evaluate the relationship between demographics, clinical symptoms and cognitive functions in schizophrenic female patients. **Methods:** 44 female (inpatients and outpatients) patients with schizophrenia were evaluated with PANSS, Global Assessment Functioning (GAF) and BACS (Brief Assessment of Cognition in Schizophrenia). **Results:** Various cognitive functions evaluated by BACS tests followed an expected pattern concordant with age and level of educations. Negative PANSS score strongly

correlated with results to some of the BACS tasks: list learning (TVM), Symbol Coding and Tower of London; GAF correlated with results of Tower of London. Conclusions: Our study emphasized that cognitive function has been associated with age, level of education, duration of illness; it has been strong associated also with negative PANSS score and functional outcome. No difference of cognitive dysfunction between outpatient and inpatient could be noticed. Keywords: cognition, schizophrenic symptoms, course, social function

### NR6-03

#### ADHERENCE TO MEDICATION IN PATIENTS WITH SCHIZOPHRENIA OR SCHIZOAFFECTIVE DISORDER INCLUDED IN THE PRECOG STUDY: A THREE YEAR SURVEY

*Chair: Mario Pena M.D.; Author(s): Luis San, M.D., Psy.D. Miquel Bernardo, M.D., Psy.D.*

#### SUMMARY:

Aims of the study: The PRECOG study was designed to define the clinical profile for relapse in patients with schizophrenia. We analyzed the data of adherence in the three years previous to the patient inclusion,. Methods: Epidemiological, multicenter and non-interventional study including a cross-sectional design for a 6-month recruitment period, an observational design for data collected retrospectively within the last 3 years, and a prospective design for data collected during the 12-month follow-up period. The study was conducted in routine clinical practice conditions. Patients older than 18 years with schizophrenia and schizoaffective disorder according to DSM-IV criteria admitted to short-stay/acute-care psychiatric units throughout Spain were eligible. Inclusion criteria were duration of disease of at least 2 years, access to the patient's medical history for the previous 3 years, and available data for a 12-month follow-up period after discharge. Data collected included demographics, educational level, family support, history of substance use, current main diagnosis, duration of the disease, number of hospitalizations in the preceding 3 years, the Clinical Global Impression Severity scale (CGI-S), main reason for the index admission, antipsychotic treatment, adherence, and relapse at follow-up. Summary of results: Data were collected from 1646 patients 67.6% men, mean age 38 years. Schizophrenia was the most frequent diagnosis (77%), followed by schizoaffective disorder (20%), and schizophreniform disorder (3%). In 60% of the patients, disease's duration was > 10 years. The total number of previous treatments from which data was obtained, was 2937. Adherence was poor in 31% of cases and moderate in 41%. There were significant

differences in adherence according to antipsychotic medication ( $p < 0.0001$ ), with maximum rates of 42% for depot atypical drugs, followed by typical injectable (34.7%), atypical oral (25.8%) and typical oral (22.4%). 22.2% of atypical injectables were associated to low adherence. At discharge, atypical drugs were prescribed to 90% of patients. Conclusion: In this study carried out in a routine clinical setting, we confirm that patients with schizophrenia, schizoaffective disorder and schizophreniform disorder are treated using various antipsychotic drugs, and maintain poor to moderate adherence patterns in the outpatient condition. Long acting injectable atypical antipsychotics were associated with maximum adherence rates.

### NR6-04

#### EFFICACY AND EFFECTIVENESS OF DEPOT VS. ORAL ANTIPSYCHOTICS IN SCHIZOPHRENIA: SYNTHESIZING RESULTS ACROSS DIFFERENT RESEARCH DESIGNS

*Chair: Noam Kirson Ph.D.; Author(s): Bruce Wong, M.D. Sander Yermakov, MS Wayne Huang, MPP Thomas Samuelson, BA, Steve Offord, Ph.D. Paul E. Greenberg, MS*

#### SUMMARY:

Background: Depot formulations of antipsychotic agents are often used in clinical practice to address compliance issues in the management of schizophrenia. However, randomized controlled trials (RCTs), observational studies, and various meta-analyses have yielded inconsistent findings regarding their comparative effectiveness across the different study designs. This raises important practical questions of therapy in managing schizophrenia, but also of how study design should be viewed in comparative effectiveness research and the possible tension between efficacy and effectiveness of medications. In order to reconcile these inconsistencies in results, this study implements a novel approach to systematically account for the effect of study design on the relative efficacy of antipsychotic formulations. Methods: A PubMed literature review targeted English-language articles published since 2000, with efficacy information for depot and oral antipsychotic treatment arms in schizophrenia, and which reported relapse, hospitalization or all-cause discontinuation as endpoints. Data reported in the studies were used to calculate risk ratios (RR) [depot/oral;  $RR < 1$  favors depot]. Where available, average baseline characteristics were used to adjust endpoints for age and gender within each treatment arm, using marginal effects reported in the literature. Adjusted RR were pooled by study design (RCT, prospective observational, and retrospective observational), corresponding to qualitative differences in the level

of researcher control over patient treatment. Within each study design grouping, meta-analysis with random effects was used to estimate the pooled RR and 95% confidence interval (CI) of all endpoints combined. In turn, average conversion factors between study designs were calculated as the ratios of pooled RR. Results: Preliminary literature search criteria resulted in 389 studies. Further refinement and systematic review of full-text versions yielded 13 relevant studies (5 RCTs, 4 prospective, 4 retrospective), including information on 19 depot-oral comparisons. Meta-analysis of adjusted endpoints resulted in RR [CI, p-value] of 0.88 [0.64-1.20, p=0.416] for RCTs. In contrast, there was a significant advantage for depot formulations in both prospective (RR=0.62 [0.48-0.81, p<0.001]) and retrospective (RR=0.56 [0.44-0.71, p<0.001]) studies. These imply conversion factors of 1.41 and 1.57 between RCTs and prospective and retrospective designs, respectively. Conclusions: In tightly controlled RCTs, the benefits of depot antipsychotics were not significantly superior to oral formulations. In contrast, as study design shifts towards prospective and retrospective studies in real-world clinical settings, depot formulations display significant advantage. Furthermore, the estimated conversion factors quantify the average effect of study design on comparative effectiveness and facilitate meaningful comparison across studies.

**NR6-05**  
**PATIENT SATISFACTION AND CAREGIVER BURDEN RELATED TO OLANZAPINE LONG-ACTING INJECTION**

*Chair: David McDonnell M.B.; Author(s): Holland C Detke, Ph.D.; Chunxu Liu, Ph.D.; Rodney J Moore, Ph.D.*

**SUMMARY:**

**Background:** Depot antipsychotics are an important option for patients with schizophrenia who struggle with adherence to their oral medication. However, injectable medications are sometimes thought to be associated with their own psychological barriers to adherence, such as fear of injections or perception of the injections as coercive or invasive. For olanzapine long-acting injection (LAI), there can be further potential psychological barriers to use, such as the post-injection observation period. Thus, the purpose of the present analyses was to assess patients' attitudes toward and satisfaction with olanzapine LAI as well as determine the effects of its use on caregiver burden. **Methods:** Data were analyzed from 2 long-term, open-label olanzapine LAI studies. Study 1 (N=931) was a single-arm study assessing the long-term safety of olanzapine LAI for up to 6.5 years in patients with schizophrenia or schizoaffective disorder. Study 2 was

a 2-year randomized study comparing the treatment effectiveness of olanzapine LAI (N=264) with that of oral olanzapine (N=260) in outpatients with schizophrenia. Patients were included in the analyses if they received at least 1 dose of study medication. Measures included the Patient Satisfaction with Medication Questionnaire-Modified (PSMQ) in both studies and the Drug Attitude Inventory (DAI-10) in Study 2. Study 2 also included the Burden Assessment Scale (BAS), a self-report measure completed by the patient's caregiver. Measures were assessed at 6- to 12-month intervals. Results: For the PSMQ in Study 1, 73% of patients were satisfied with olanzapine LAI at first assessment, 87% at 6 years (observed case), and 73% at endpoint (last-observation-carried-forward [LOCF] method). Similar results were found in Study 2, with 75% of patients satisfied with olanzapine LAI at first assessment, 88% at 2 years (observed case), and 73% at LOCF endpoint. This was similar to the pattern seen in the oral-treated patients in Study 2 (78% satisfied at first assessment, 85% at 2 years, and 71% at LOCF endpoint). On the DAI-10, there were no statistically significant differences between the LAI- and oral-treated patients, with more than 80% of the LAI-treated patients endorsing positive statements about their medication at each time point, including 90% stating that "the good things about the medication outweigh the bad" at 2 years. On the BAS, caregivers of LAI- and oral-treated patients reported statistically significant improvement in their overall burden at 2 years (LAI: LS mean change [SE] in total score: -6.9 [1.3], P<0.001; oral: -6.2 [1.4], P<0.001). Conclusions: Overall patient satisfaction with olanzapine LAI and attitudes toward the medication were very positive and were not significantly different from oral olanzapine. Caregivers reported that their burden improved over the course of the study. Taken together, these results suggest that olanzapine LAI is viewed positively by patients and their caregivers.

**NR6-06**  
**ADJUNCTIVE TREATMENT OF BIMODAL TMS IN PHARMACOLOGICALLY NON-RESPONSIVE PATIENTS WITH SCHIZOPHRENIA**

*Chair: Yong-Ku Kim M.D.; Author(s): Yong-Ku Kim, So-Young Oh Department of Psychiatry, College of Medicine, Korea University, Korea*

**SUMMARY:**

**Objectives:** The efficacy of bimodal repetitive transcranial magnetic stimulation (rTMS) was evaluated in pharmacologically non-responsive

patients with schizophrenia. Methods: Ten patients with DSM-IV schizophrenia, who were not responsive to pharmacological treatment, were treated with 15 sessions of rTMS as an adjunctive therapy for three weeks. Each session consisted of 40 trains which start every 30 seconds; 20 trains of 10Hz rTMS to the left dorsolateral prefrontal cortex (DLPFC) with 3-sec-duration and 20 trains of 1Hz rTMS to the left temporoparietal cortex (TPC) with 30-sec-duration. Patients were assessed with the Positive and Negative Syndrome Scale (PANSS), Korean Version of Calgary Depression Scale for Schizophrenia (K-CDSS) at five time points: baseline, Day 8, 15, 22 and 1 week after the last treatment (Day 29). Patients who agreed to take neurocognitive tests were evaluated on neurocognitive function at baseline and 1 week after the last treatment. Results: At Day 29, all the subscale scores in PANSS were significantly decreased compared with the baseline ( $Z=-2.214$ ,  $p=0.027$ , positive;  $Z=-2.132$ ,  $p=0.033$ , negative;  $Z=-2.023$ ,  $p=0.043$ , general pathology;  $Z=-2.371$ ,  $p=0.018$ , total). Effect over time was significant in the positive and negative subscale scores and total score of PANSS ( $\eta^2=13.35$ ,  $p=0.010$ ;  $\eta^2=10.27$ ,  $p=0.036$ ;  $\eta^2=16.50$ ,  $p=0.002$ , respectively) but not in the general pathology subscale. For neurocognitive tests, the 4th and 5th trial and total score in K-AVLT showed a significant increase ( $Z=-2.041$ ,  $p=0.041$ ;  $Z=-2.251$ ,  $p=0.024$ ;  $Z=-2.201$ ,  $p=0.028$ ; respectively), suggesting the improvement in short-term auditory verbal memory. Conclusions: Bimodal rTMS stimulating the left DLPFC and the left TPC induced clinical improvement in pharmacologically non-responsive patients with schizophrenia, and might have improved short-term verbal memory.

**NR6-07****ACTIVE MEDICAL AND PSYCHIATRIC COMORBIDITIES IN ADULT SCHIZOPHRENIC INPATIENTS: IMPACT ON LENGTH OF STAY**

*Chair: Javad Moamai M.D.*

**SUMMARY:**

**OBJECTIVE:** To determine the prevalence rates of Active Medical Comorbidity (AMC) and Active Psychiatric Comorbidity (APC) in a schizophrenic inpatient population and examine their impact on Length of Stay (LOS) at the hospital. Active illnesses are defined as those currently requiring treatment or continuing medical surveillance. **METHOD:** Data were taken from discharge summaries (ICD-10 format) of all 716 adult (18-64 years old) admissions, for schizophrenia related disorders to a Quebec regional psychiatric

hospital between 2006 and 2010. Non parametric descriptive statistics were used for analysis. **RESULTS:** The observed prevalence rate of any comorbidity was 81%, while APC (62%) was more frequent than AMC (57%). Hypothyroidism, hypertension, diabetes mellitus and morbid obesity (5% to 16%) were the most observed AMC. Anxiety disorders, delusional disorders, personality disorders and substance related disorders (2% to 51%) were the most frequent APC. Logistic regression analysis indicated that AMC was correlated with LOS (median 53.5 vs. 21 days,  $p<0.001$ ). No correlation was observed between APC and LOS in this population. **CONCLUSIONS:** AMC but not APC prolongs hospital stay among schizophrenic patients. Improved recognition and treatment of AMC in this clinical population may be necessary to lessen illness burden and social cost.

**NR6-08****ASSESSMENT OF CHANGE IN BODY WEIGHT AFTER ANTIPSYCHOTIC TREATMENTS IS CONFOUNDED BY REGRESSION TO THE MEAN**

*Chair: Jane Xu Ph.D.; Author(s): Cynthia Siu, Ph.D., Josephine Cucchiaro, Ph.D., Andrei Pikalov, M.D., Antony Loebel, M.D.*

**SUMMARY:**

**Background** Since weight gain is linked to antipsychotic drug treatment and obesity is highly prevalent in patients with severe mental illness, the effect of initial BMI on drug-induced weight change is of particular interest and importance. The aim of this study was to examine whether previous observed correlation between initial BMI ranges and subsequent weight change reflects in part a statistical artifact, regression to the mean (RTM), not true effect modification as suggested by Allison et al. (2009). **Methods** Body weight and BMI were measured at baseline and at the 6-week endpoint in a double-blind, placebo- and active-controlled trial of lurasidone (LUR) and olanzapine (OLZ). Regression analysis was applied to estimate the magnitude of bias due to RTM on measurement of change in body weight over time. To correct for the RTM bias, a control group was used in the ANCOVA model to estimate weight gain between the treatment groups by baseline BMI ranges using a statistical interaction test. The RTM bias is nullified when the difference in body weight between the randomized treatment and control group(s) is calculated and included in the analysis model. **Results** Among the placebo (untreated) subjects, the magnitude of RTM bias in the obese subgroup (baseline BMI  $\geq 30$ ) was -5 kg at the week-6 endpoint, due to

a non-perfect correlation between baseline BMI and follow-up measurements of body weight ( $r=0.87 < 1$ ) and non-random selection (median baseline weight for the obese subgroup was 34.8 kg or 9 kg above the placebo group mean of 25.7 kg). A similar magnitude of RTM bias (-4 kg) was observed in the subgroup of obese subjects in both the olanzapine and lurasidone treatment groups. Compared to placebo, weight change in the baseline obese, overweight, and normal groups were +4.4 kg, +5.3 kg, and +2.7 kg, respectively, for the olanzapine-treated subjects (treatment-by-baseline BMI interaction tests,  $p=0.09$ ); and +0.40 kg, +0.02 kg, and +0.68 kg, respectively, for the lurasidone-treated subjects (treatment-by-baseline BMI interaction tests,  $p=0.72$ ). Conclusions Contrary to previous studies, we found no evidence to support that the magnitude of drug-induced weight gain is less in subjects with higher initial BMI compared to subjects with average or low baseline BMI. Our findings suggest that the previously observed inverse relationship between baseline BMI and weight change following antipsychotic treatment reflects, in part, RTM bias. In this study, the estimation of weight gain in the baseline obese group ( $BMI > 30$ ) group was under-estimated by 4 to 5 kg due to RTM bias. Antipsychotic drugs appear to cause similar weight changes in both high and low baseline BMI groups when a treatment comparison with appropriate control groups is adopted. Research supported by Sunovion Pharmaceuticals Inc.

**NR6-09**  
**REAL-WORLD USE PATTERNS OF**  
**OLANZAPINE LONG-ACTING INJECTION**

*Chair: Michael Case M.S.; Author(s): Kory Schub Ph.D. Jamie Karagianis M.D.*

**SUMMARY:**

Background Despite the benefits, many patients with schizophrenia have difficulty adhering to treatment with oral antipsychotics. Practice guidelines for treating patients with schizophrenia recommend long-acting injection (depot) antipsychotics for patients who are nonadherent with their medication, including those with recurrent relapses related to nonadherence. Olanzapine long-acting injection (olanzapine-LAI), approved by the United States (US) Food and Drug Administration in December 2009, was shown to be effective for treating schizophrenia in both acutely ill and stable patients. Recommended doses are 150 mg/2 weeks, 210 mg/2 weeks, 300 mg/2 or 4 weeks, and 405 mg/4 weeks. However, the real-world doses and use patterns are not known. This study evaluated the dosing and interval patterns of patients being treated with

olanzapine-LAI to compare the actual dosing patterns with the recommended dosing strategy. Methods These data, as of September 30, 2011, were collected by United BioSource Corporation as part of a mandatory patient registry that captures all post-approval injections in the US. This registry includes both active and inactive (60+ days since last injection) patients. These data included the number of injections per patient, dose of each injection, time between injections, and patterns of injections. Results A total of 1694 patients with at least one injection were included in the database. The mean number of injections received was 6.6 (range of 1-40). The most frequent numbers of injections were 1 (26.3%) and 2 (12.9%). For the 11,228 injections in the database, the most common doses were 300 mg and 405 mg, accounting for 92.9% of the injections. Although the most common time intervals between injections was about 14 days for 150 mg and 300 mg, and about 28 days for 405 mg, the intervals ranged from less than 10 days to more than 60 days. Among active patients (48.2% of registry), the number of days since the last injection was around 2 weeks or less for 61.2% of patients, around 3 weeks for 16.5% of patients, and around 4 weeks for 7.1% of patients. For the pattern of the first 5 doses, most patients (70.9%) received 4 subsequent injections of the same dose as their initial injection. Conclusions This registry as of September 30, 2011 contains a subset of data from newly treated, ongoing and discontinued patients and will continue to change as newly treated patients begin to reflect the dosing patterns of patients who are treated for a longer time period. Although the registry does not capture the information, the number of patients receiving a single injection might be related to issues with access, tolerability, etc. The broad range in time between injections suggests that clinicians are using the medication flexibly to meet the needs of their patients. Most patients continue to receive the same initial dose instead of receiving a dose change as is recommended in the product label for most initial doses.

**NR6-10**  
**NOVEL SYSTEM FOR MONITORING**  
**QUALITY AND CONSISTENCY OF**  
**INTERVIEW TECHNIQUE AND RATINGS IN**  
**GLOBAL SCHIZOPHRENIA CLINICAL TRIALS**

*Chair: David Daniel M.D.; Author(s): Alan Kott, M.D.*

**SUMMARY:**

Introduction: In international clinical trials settings accurate and precise diagnosis and measurement of symptom severity is a cornerstone of success. Cultural and linguistic diversity among patients and investigators and relatively complex and lengthy measurement tools

present challenges in international schizophrenia trials. We describe the initial results of a system for monitoring the quality of evaluations and providing rapid feedback to local raters in geographically and culturally diverse global clinical trial settings. Method: Multiple schizophrenia clinical trials involving North America, Europe, South America and Asia are underway utilizing the techniques described below. All raters were trained prior to study initiation utilizing highly interactive procedures including slide presentations, rating of videotaped patient interviews, and in some cases interview and rating of live actors trained to portray schizophrenia symptoms. After study initiation a video/ audio recording system was installed at the sites for assessment of the accuracy and quality of site diagnostic and rating procedures. Sites uploaded videotaped diagnostic and ratings assessments for review by calibrated external reviewers of the same language and culture. The external reviewers provided feedback on an ongoing basis to the site and sponsor on diagnostic and scoring accuracy and interview quality. Interview quality was evaluated by the Research Interview Assessment Scale (RISA) (1). Results: Early data and preliminary analyses are available from the ongoing studies. Additional data and analyses will be reported. Of 201 patients considered eligible at screening by sites 92% were considered eligible by external reviewers based on review of videotaped interviews. 155 videotaped PANSS administrations at sites were graded for interview quality by external reviewers using the RISA. 74.7% were regarded as excellent (RISA Score 28-30), 20.7% as acceptable (RISA score 24-27) and 4.6% as poor or unacceptable. Exact matches were obtained between the site and external rater on 60% or more of ratings for all 30 PANSS items. Mismatches between the site and external raters of 2 anchor points or greater in scoring any PANSS item were relatively uncommon and only exceeded 10% of ratings on items P2 (Conceptual Disorganization) and N7 (Stereotyped Thinking). Discussion: External review of videotaped diagnostic and ratings interviews with timely feedback to sites and sponsors is feasible in global clinical trial settings. Interview quality at the sites and agreement between site and external PANSS ratings was relatively high. These findings are based on early data and preliminary analyses from multiple ongoing studies. New patterns may emerge and the results and conclusions may change as the size and cultural diversity of the sample increases.

**NR6-11**  
**EFFECT OF BODY MASS INDEX ON**  
**METABOLIC EVENTS IN PATIENTS WITH**  
**SCHIZOPHRENIA DURING LONG-TERM**  
**TREATMENT WITH PALIPERIDONE**

**PALMITATE**

*Chair: Jennifer Sliwa Ph.D.; Author(s): Ibrahim Turkoz, MS; Dong-Jing Fu, M.D., Ph.D.; Cynthia A Bossie, Ph.D.; Larry Alphas, M.D., Ph.D.*

**SUMMARY:**

A post-hoc analysis explored the relationship between body mass index (BMI) and metabolic events in patients with schizophrenia receiving once-monthly injectable paliperidone palmitate (PP). Methods: Data were from a multiphase maintenance PP study in patients with schizophrenia (DSM-IV) (33-week open-label [OL] transition [TR] and maintenance phases; variable duration randomized double-blind [DB] placebo-controlled relapse prevention phase; and 52-week OL extension [OLE]) (NCT00111189). Patients received PP continuously from study entry through discontinuation or study completion, and were grouped by baseline BMI (kg/m<sup>2</sup>): underweight (BMI<19; n=29), normal (BMI 19-24; n=229), overweight (BMI 25-29; n=232) and obese (BMI=30; n=154). Metabolic treatment-emergent adverse events (TEAEs) and related lab results were examined. Baseline group differences were examined by Chi-square test for discrete variables and analysis of variance model for continuous variables. RESULTS: 644 patients met inclusion criteria for the analysis: mean (SD) age 37 (10.6) years, mean (SD) BMI 27 (5.88) kg/m<sup>2</sup>, majority were men (n=379, 59%) and white (n=387, 60%). Mean (SD) exposure to PP was 317.5 (276.36) days; mean (SD) dose was 109.6 (26.78) mg (70.3 [17.17] mg eq.) per month; median modal dose was 78 mg for each group. Exposure and doses were similar among BMI groups. One patient (overweight) discontinued for a metabolic TEAE (weight increase). At least 1 metabolic TEAE was reported in 14.9%, 14.7%, and 24.0% of patients in normal, overweight, and obese groups, respectively (TR baseline to OLE endpoint). The most common metabolic TEAEs: weight increase 11.4%, 7.3% and 11.7%, respectively; blood glucose increase 2.2%, 3.9% and 4.6%, respectively; and blood cholesterol increase 2.6%, 1.3% and 4.6%, respectively. No metabolic TEAE was reported in the underweight group. Mean (SD) change in BMI (kg/m<sup>2</sup>) from TR baseline to DB endpoint in the underweight, normal, overweight and obese groups, respectively, were: .6 (0.64), .8 (1.72), .7 (1.88) and .7 (2.87); change to OLE endpoint were: 1.4 (1.76), 1.2 (2.07), .6 (1.73) and .3 (3.95). Mean (SD) change in weight (kg) from TR baseline to DB endpoint in the underweight, normal, overweight and obese groups, respectively were: 1.9 (2.15), 2.4 (4.99), 1.7 (5.17), 1.7 (8.13); and to OLE endpoint were: 3.8 (4.83), 3.5 (5.99), 1.6 (4.84), .8 (11.12). Corresponding

mean change in plasma glucose and cholesterol appeared to be similar across all groups. **LIMITATIONS:** Lack of control group, low patient number in the underweight group and in the OLE. **Conclusion:** Except in underweight patients, metabolic TEAEs were reported in all BMI groups; however, the proportion of patients reporting metabolic TEAEs was numerically highest in the obese group. No trend for increased metabolic-related lab values by BMI group was detected. The result from this analysis was consistent with the known profile of PP. Supported by Janssen Scientific Affairs, LLC

#### NR6-12

### **BUILDING A TEAM INVOLVED IN PREVENTION AND TREATMENT OF PRIMARY POLYDIPSIA IN A PSYCHIATRIC OUTPATIENT/INPATIENT POPULATION: A PILOT STUDY**

*Chair: Peter Szymczak M.D.; Author(s): Varinderjit Parmar, M.D., Richard Millson, M.D., Roumen Milev, M.D., Ph.D., Emily Hawken, Ewa Talikowska-Szymczak, M.D., Dianne Groll, Ph.D., Felicia Iftene, M.D., Ph.D.*

#### **SUMMARY:**

Queen's University, Department of Psychiatry, Kingston, Ontario, Canada **Key Words:** Schizophrenia, Polydipsia, Team. **Educational Objectives** At the conclusion of this session, the participant will be able to: 1. Recognize Primary Polydipsia; 2. Be involved as an active part in a professional network; 3. Make a therapeutic intervention, appropriate for his/her educational level. **Abstract Background:** The disturbances of water homeostasis among psychiatric patients have been widely recognized, particularly the condition whereby patients consume excessive quantities of liquid, which is termed "polydipsia." Long-term effects of excessive fluid consumption may include bladder dilatation, potentially leading to hydronephrosis and renal failure, hypocalcaemia, congestive heart failure, gastrointestinal dilatation and hypotonicity, hypothermia, and osteopenia with an increased incidence of fractures. Seen in both episodic and chronic polydipsia, water intoxication can be a reoccurring condition, which carries with it a substantial risk of morbidity and mortality. In a previous study we found that there is a lack of information on this topic, not only regarding the patients, but also the caregivers' professionals involved in their care. **Purpose:** This study we try to increase the awareness of the professionals on this topic and actively involve them in the prevention /therapeutic process. **Methods:** Approximately 100 mental Health Professionals and Volunteers will be approached to participate in 5 types

of small groups workshops (5-10 participants/group) on the topic of Primary Polydipsia in psychiatric population (Community Outreach Teams -COT; Provincial Psychiatric Hospital -Providence Care, Kingston Ontario. The groups will include: case managers, nurse, social workers, psychologists recreational, case managers, occupational therapists, spiritual care; family doctors and nurse practitioners; medical residency program; home operators. Initial and final evaluation of their knowledge, will be done by using a questionnaire with 10 questions (7 multiple choice and 3 open questions) related to this topic. The open questions will offer us the opportunity to have ideas related to how to build a possible network, where each professional has his place and is able to perform his specific role. A brochure with the materials collected (guidelines) will be publishing in the future. The change in knowledge were measured pre-post intervention using t-tests **Results.** An increase awareness of the professionals on this topic was demonstrated, as well as an actively involvement in building a network, finding the best intervention strategies and realize a guideline of intervention at each level. **Conclusion:** Results from this study help us to understand whether more needs to be done in the direction of actively involve the medical staff and volunteers in a well-coordinated assistance of the psychiatric patients who associated Primary Polydipsia.

#### NR6-13

### **TRIES: AN OPEN, RANDOMIZED, PROSPECTIVE, MULTICENTER STUDY, SEARCHING THE BEST SWITCH POLICY OF SERTINDOLE IN PATIENTS WITH SCHIZOPHRENIA**

*Chair: Koksal Alptekin M.D.; Author(s): Prof Berna Akdede, M.D., Ass Prof Haldun Soygur, M.D., TRIES Study Group*

#### **SUMMARY:**

**Background:** There are different types of switch strategies when there is necessary to change the antipsychotic medicine if no response or side effects happen in the treatment of schizophrenia. Rapid discontinuation of an antipsychotic medicine during schizophrenia treatment may cause worsening of symptoms whereas prolongation of combined antipsychotics use may cause increase in severity of side effects. However there is not enough evidence about the efficacy and safety of different switching strategies. Sertindole is an effective atypical antipsychotic medicine that is associated with significant improvements in schizophrenia symptoms including depressive, positive and negative symptoms as well as cognitive dysfunctions. There are mainly 2 types of switching

from other antipsychotics to Sertindole; a) Rapid discontinuation of the first antipsychotic, slowly increasing the second antipsychotic, b) Cross-tapering: decreasing the dosage of the first antipsychotic, slowly increasing the second one. There is not any switch study investigating advantages and disadvantages between these switch strategies. The aim was to explore the best switch strategy for Sertindole regarding efficacy and tolerability issues. Methods: This study was a eight-week, open-label, randomized, multicenter, baseline-controlled, single-treatment, flexible-dose study of Sertindole (12-20 mg/day) in the treatment of schizophrenia. Patients with DSM-IV diagnosis of schizophrenia and who need to switch to Sertindole because of ineffectiveness of the previous drug treatment or side effects. Subjects were randomly switched to one of two treatment strategies: Strategy A: Slowly increasing the dose of Sertindole with immediate discontinuation of the current antipsychotic after randomization. Strategy B: Slowly increasing the dose of Sertindole with decreasing the dose of the current antipsychotic (with ½ of the dosage after 1 week and discontinuation after 2 weeks) after randomization. Results: Sixty seven patients were screened and 61 patients were included in the study. Thirty one patients were randomized to switch strategy A while 30 patients were randomized to switch strategy B. Fifteen patients were dropped out during the study. The drop-out ratio was % 24.59. Although patients in two different switch strategy groups showed significant improvement in depressive, negative and schizophrenia symptoms as well as quality of life scores and cognitive dysfunctions. There was no significant group and time interaction between two groups regarding PANSS total, positive and negative scores, depression, and quality of life. Time effect was significant for RAVLT trial 1 scores, DST forward and total scores. Group and time interaction was significant only for DST total scores. The patients on strategy B showed greater improvement compared to the patients on strategy A. There were no significant differences between two switch strategy groups regarding EPS, metabolic parameters and

**NR6-14**  
**PSYCHOTHERAPEUTIC APPROACH OF**  
**PRIMARY POLYDIPSIA IN PSYCHIATRIC**  
**OUTPATIENT POPULATION: A PILOT STUDY**

*Chair: Varinderjit Parmar M.D.; Author(s): Peter Szymczak, M.D., Richard Millson, M.D., Roumen Milev, M.D., Ph.D., Emily Hawken, Ewa Talikowska-Szymczak, M.D., Dianne Groll, Ph.D., Felicia Iftene, M.D., Ph.D.*

**SUMMARY:**

Queen's University, Department of Psychiatry, Kingston, Ontario, Canada  
 Key Words: Schizophrenia, Polydipsia, Group Psychotherapy Intervention.  
 Educational Objectives At the conclusion of this session, the participant will be able to: 1. Recognize a patient with Primary Polydipsia; 2. Determine perceptions of outpatients using SIWI (self-induced water intoxication) in relation to reasons for drinking excessive fluids, symptoms patients experience and behavioural patterns associated with SIWI; 3. Make an educational group intervention for clients with Primary Polydipsia, in an outpatient setting.  
 Abstract Background: Primary Polydipsia is commonly associated with chronic psychiatric illness, and has been found to be prevalent in over 20% of long-term inpatients with schizophrenia. We studied the occurrence of excessive drinking behaviors in non-hospitalized patients. The incidence of Polydipsia among our study population was 15.1% (115 subjects were included in the initial clinical assessment). We determine perceptions of outpatients using SIWI (self-induced water intoxication) in relation to reasons for drinking excessive fluids, symptoms patients experience and behavioural patterns associated with SIWI. We showed that these patients are not fully aware of the severity of and possible complications from their problem. Purpose: Primary Polydipsia, seen (at least partially) as a form of addiction, might benefit from psychotherapeutic intervention used to treat substance abuse. Methods: A number of outpatients (14) from the Community Outreach Teams (COT) in Kingston, Ontario were approached for participation in this study. Patients (or their designated proxy) provided informed consent. Data collection at the initial evaluation of these patients included chart review, daily weight measurements, structured interviews, and urine collection. We randomly assigned one member from each of the seven pairs (14 clients) to the psychotherapy treatment group. They received two 60-minute sessions of psycho-educational group therapy for 2 months, followed by one/week for a month. The weight measurements (2/day, 3 days consecutively) and the structured interview were applied monthly for 4 months (including the last month without psychotherapy). The control group received "placebo psychotherapy" - non-directive group therapy, approaching daily possible problems but not "touching" their water seeking behavior. The two groups were compared using t-tests and correlation coefficients. Results: A decrease of the water seeking behavior in the study group was demonstrated, as well as a change in their attitude related to self-induced water intoxication. The results of an educational program in an inpatient setting done in 1993 showed that the effect of Psychotherapy quickly dissipated in the follow-up period (one month). We have

much better results and maintenance, perhaps because our clients are more stable. Conclusion: Results from

#### NR6-15

### COMPARISON OF OUTCOMES IN PATIENTS WITH EARLY PHASE VERSUS LATER PHASE SCHIZOPHRENIA

*Chair: Holland Detke Ph.D.; Author(s): Christoph U. Correll, M.D.; Chunxu Liu, Ph.D.; John Landry, M. Math.; Peter D. Feldman, Ph.D.1; David P. McDonnell, M.D.*

#### SUMMARY:

**OBJECTIVE:** Use of depot antipsychotics earlier in the course of treatment has been proposed to improve outcomes in schizophrenia. The present analyses were conducted to compare treatment outcomes for patients initiating olanzapine long-acting injection (LAI) within 5 yrs of onset of illness (“Early Phase” group) versus those initiating olanzapine LAI greater than 5 yrs after illness onset (“Later Phase” group). **METHOD:** Data were obtained from the 8 studies in the clinical trial database involving olanzapine LAI. Patients were included in analyses if they received at least 1 injection of olanzapine LAI at a therapeutic dose (>45 mg/4 weeks to 300 mg/2 weeks). Outcome measures included rates of and time to study discontinuation, relapse, remission, and sustained remission, as well as mean changes from baseline to endpoint in Positive and Negative Syndrome Scale (PANSS) or Brief Psychiatric Rating Scale (BPRS) total and subscale scores. Relapse was defined as: (1) hospitalization or study discontinuation due to worsening of schizophrenia or due to suicidality or aggression; or (2) a 25% increase from baseline on the PANSS or BPRS (or increase of  $\geq 10$  points on PANSS if baseline  $\leq 40$ , or  $\geq 6$  pts on BPRS if baseline  $\leq 24$ ) with a  $\geq 1$  point increase on the Clinical Global Impressions–Severity scale (CGI-S) such that the CGI-S score is  $\geq 4$ . Remission was defined as a score of  $\leq 3$  on each of 8 key PANSS items; sustained remission was defined as meeting remission criteria for  $\geq 6$  months, per Andreasen et al. (2005). Time to events was assessed using Kaplan–Meier methodology. **RESULTS:** Of the 1879 patients in the analysis, 24.2% were in the Early Phase group and 75.8% were in the Later Phase group. The Early Phase group showed a longer median time to discontinuation (28.6 months versus 20.7 months,  $P=.003$ ), longer time to relapse ( $P=.018$ , median times unavailable due to  $< 50\%$  relapse rates), and, among patients not in remission at study initiation (45.8%), a shorter median time to sustained remission (11.8 months versus 29.4 months,  $P=.012$ ). Rates of remission and sustained remission were also higher for the Early Phase group relative to the Later Phase group (83.3%

versus 74.1%,  $P<.001$ ; and 62.2% versus 48.2%,  $P<.001$ , respectively). The Early Phase group also showed greater symptom reduction in their mean PANSS total, negative, positive, and general psychopathology scores, and in their BPRS total, positive and anxiety/depression scores ( $P<.01$ , all measures). **CONCLUSIONS:** Consideration must be given to the post-hoc nature of this analysis and the fact that these clinical trials were not specifically designed to address the issue of treatment timing and clinical outcomes. Nevertheless, these findings support the assertion that clinical outcomes of receiving a depot antipsychotic such as olanzapine LAI are significantly improved in patients who begin the depot earlier in the course of their illness compared with patients who begin the depot later.

#### NR6-16

### EFFECT OF ADDING LISDEXAMFETAMINE DIMESYLATE TO ANTIPSYCHOTICS ON PREDOMINANT NEGATIVE SYMPTOMS OF SCHIZOPHRENIA: ANALYSIS OF PANSS FACTORS

*Chair: Bryan Dirks M.D.; Author(s): Robert Lasser, M.D.; Henry Nasrallah, M.D.; Courtney Kirsch, BS; Ben Adeyi, MS; Brian Scheckner, Phar M.D.; Jelena Kunovac, M.D.; Jean-Pierre Lindenmayer, M.D.*

#### SUMMARY:

**Objective:** This multicenter study examined the effects and safety of adjunctive lisdexamfetamine dimesylate (LDX), a d-amphetamine prodrug, in clinically stable adults with predominant negative symptoms of schizophrenia (NSS). We present results of a post hoc analysis of PANSS factors. **Methods:** After a 3-wk screening period, outpatients with schizophrenia ( $\geq 2$ y) with predominant NSS (SANS-18 [items 1-6, 8-12, 14-16, 18-21] score  $\geq 55$ , score  $\geq 3$  on  $\geq 2$  SANS Global items, and PANSS positive score  $< 20$ ) maintained on antipsychotics ( $\geq 12$ wk) underwent 10-wk open-label (OL) LDX augmentation (20-70mg/d). Eligible participants (any SANS-18 improvement at wk 10) entered a 4-wk, double-blind, placebo-controlled randomized withdrawal (RW; wk 10-14). Efficacy measures included SANS-18 (primary) and PANSS subscales. Post hoc analysis examined response to LDX on PANSS factors: negative, positive, disorganized thought, hostility/excitement, and anxiety/depression. Safety evaluations included treatment-emergent adverse events (TEAEs) and Calgary Depression Scale for Schizophrenia (CDSS). **Results:** 92 participants received OL LDX; 69 entered RW (LDX,  $n=34$ ; placebo,  $n=35$ ); 13 discontinued during RW (LDX,  $n=7$ ; placebo,  $n=6$ ). At baseline (wk 0), mean (SD) SANS-18 score was

60.2 (4.36). Mean change (95% confidence interval [CI]; wk 0-10 OL; last observation carried forward [LOCF]) was -12.9 (-15.0, -10.8) (primary endpoint;  $P < .0001$ ). Changes (95% CI) for the PANSS factors in wk 0-10 (LOCF) for negative, positive, disorganized thought, uncontrolled hostility/excitement, and anxiety/depression were -4.8 (-5.7, -4.0), -1.6 (-2.2, -1.0), -2.0 (-2.6, -1.5), -0.4 (-0.8, -0.1), and -1.0 (-1.5, -0.5), respectively. During RW, no meaningful differences were noted between LDX and placebo for change from randomization baseline to endpoint in SANS-18 scores, PANSS positive scores, or PANSS factors except a slight increase in mean (SD) uncontrolled hostility/excitement score for LDX (0.7 [1.76]) vs placebo (-0.5 [1.40]). In OL phase, TEAEs were reported in 60.9% (56/92) of participants; serious TEAEs in 3.3% (3/92). TEAEs with incidence  $\geq 5\%$  were headache (14.1%), decreased appetite (10.9%), insomnia (10.9%), dizziness (8.7%), dry mouth (6.5%), and diarrhea (5.4%). During RW phase, TEAEs were reported in 32.4% (11/34) and 20.0% (7/35) in LDX and placebo groups, respectively. There was no meaningful change in CDSS (wk 0-14) for LDX or placebo with mean (SD) change from baseline to wk 14 of -0.1 (2.34) for LDX and -0.7 (2.30) for placebo. Conclusion: With adjunctive LDX, there was improvement in NSS by SANS-18 without worsening of positive symptoms, confirmed by improvement in negative PANSS factor scores with no worsening in positive PANSS factor scores. Improvement in disorganized thought, uncontrolled hostility/excitement, and anxiety/depression PANSS factors mirrored overall improvement in PANSS general psychopathology.

#### NR6-17

### THE EFFECTIVENESS OF PALIPERIDONE EXTENDED-RELEASE (ER) IN IMPROVING SUBJECTIVE SYMPTOMS IN PATIENTS WITH SCHIZOPHRENIA

*Chair: Chul-Eung Kim M.D.; Author(s): Kyoung-Sae Na, M.D.*

#### SUMMARY:

**Objective:** Several recent studies have found that patients with remitted schizophrenia or in a non-acute phase of schizophrenia are able to measure and report their subjective symptoms. Subjective domains have been used as outcome measures in recent clinical trials. The present study investigated the effect of switching from an oral antipsychotic to flexibly dosed paliperidone extended-release (ER) on subjective experiences in patients with schizophrenia. **Method:** We conducted a 24-week, multicenter, non-comparative, open-label trial (ClinicalTrials.gov identifier:

NCT00761605). The primary outcome change in subjective symptoms from baseline was measured using the Symptom Checklist-90-Revised (SCL-90-R). The Sleep Visual Analogue Scale (S-VAS) were used for secondary subjective assessments. The Clinical Global Impressions-Severity (CGI-S) and the Krawiecka-Goldberg Scale (KG) assessed objective overall symptom severity. Social functioning was evaluated using the Personal and Social Performance (PSP) scale. The safety of paliperidone ER treatment was measured by the incidence, relationship, and severity of adverse events (AEs) and the results of clinical laboratory data, vital sign measurements, physical examination, electrocardiogram, and the Drug-Induced Extrapyrimal Rating Scale (DIEPSS). **Results:** A total of 387 patients with schizophrenia participated, and 321 patients were included in the intent-to-treat sample. Total severity and most of the SCL-90-R subscales were continuously and significantly reduced over the 24-week period. Symptom severity was significantly lower throughout the study in early responders, those who achieved a greater than 20% reduction in the SCL-90-R within 1 week, than in later responders. The CGI-S, KG, and PSP scores significantly improved. The S-VAS showed that daytime somnolence significantly improved, whereas nocturnal sleep quality was not altered. **Conclusion:** Our results suggest that switching to paliperidone ER improves subjective symptoms, overall symptom severity, and social functioning. Moreover, the results suggest that early detection and reduction of subjective symptoms improve treatment outcome. Further studies using a placebo control and comprehensive objective psychopathology scales are needed to confirm the efficacy of paliperidone ER for subjective symptoms.

#### NR6-18

### EFFICACY AND SAFETY OF PALIPERIDONE EXTENDED RELEASE(ER) IN SCHIZOPHRENIA PATIENTS REQUIRING A SWITCH IN ANTIPSYCHOTIC MEDICATION

*Chair: Young Moon M.D.; Author(s): Chul Eung Kim, M.D., Ph.D. Hee Won Lee, M.D.*

#### SUMMARY:

**Objectives:** This study aimed to evaluate the clinical efficacy, safety, and tolerability of paliperidone extended release(ER) in patients with schizophrenia by switching previous antipsychotics to paliperidone ER. **Method:** An open-label, 24 weeks, prospective, non-comparative, multi-center study evaluated patients with schizophrenia requiring a switch in antipsychotic medication because current medication was not well tolerated and/or clinical symptoms were not well

controlled. Patients were switched to flexible-dose trial of paliperidone ER (3-12 mg/day) within 4 weeks. Efficacy assessments included Krawiecka Scale, clinical global impression-schizophrenia-severity(CGI-SCH-S), clinical global impression-schizophrenia-improvement(CGI-SCH-I), sleep visual analog scale(VAS), and personal and social performance(PSP) scale. Safety assessments included adverse events(AEs), evaluation of extrapyramidal symptoms(EPS) using drug induced extra pyramidal symptoms scale(DIEPSS), vital signs, electrocardiography(ECG), weight, waist circumference, and laboratory tests. Result: Switching to paliperidone ER led to significant improvement of Krawiecka Scale, CGI-SCH-S, CGI-SCH-I, PSP, and DIEPSS. However, serum prolactin levels and metabolic parameters including body weight and waist circumference were significantly increased. Insomnia was the most common adverse event. Conclusion: This study suggested that patients with schizophrenia who showed insufficient response or intolerance to other previous antipsychotics can be switched to paliperidone ER, with efficacy, safety, and tolerability.

**NR6-19**  
**SUICIDE HISTORY AS A MODERATOR OF EFFECT OF PALIPERIDONE ER ON DEPRESSIVE SYMPTOMS IN ADULTS WITH SCHIZOAFFECTIVE DISORDER: RESULTS OF A PATH ANALYSIS**

*Chair: Ibrahim Turkoz M.S.; Author(s): Dong-Jing Fu, M.D., Ph.D., Cynthia A. Bossie, Ph.D., Larry Alphs, M.D., Ph.D.*

**SUMMARY:**

Introduction: It is valuable to understand whether improvement observed in depressive symptoms with antipsychotic treatment in subjects with schizoaffective disorder occur as a direct effect or indirectly through improvement in other symptoms. Our analysis examined this association and the impact of suicidal history as a moderator in adult subjects with schizoaffective disorder. Methods: Post hoc database (N=614) analysis of two 6-week, randomized, placebo-controlled studies of paliperidone ER vs placebo in adult subjects with schizoaffective disorder. Subjects with baseline depressive symptoms (HAM-D-17 $\geq$ 16) were included. Structural equation models (path analysis) were used to separate total effects of paliperidone ER treatment into direct and indirect effects on depressive symptoms. Change from baseline in HAM-D-17 score at the week 6 endpoint was the dependent variable; change in PANSS positive and negative factors and SAS

(extrapyramidal symptom) scores at the week 6 endpoint were independent variables (possible mediators of depressive symptom changes). Partial correlations between positive and negative symptoms were accounted for. In each structural model equation, a factor for treatment was included for comparisons between paliperidone ER and placebo. Potential moderators of treatment effect (i.e., age, race, gender, suicide history, hospitalization, substance abuse, comedication strata [antidepressants and/or mood stabilizers], and schizoaffective subtype) were analyzed by multiple regression models. Significant baseline moderators identified were additional factors in the path analysis. Results: 333/614 (54.2%) of schizoaffective subjects met the inclusion criteria. Initial path analysis determined that 45.8% and 28.4% of the paliperidone ER vs placebo effect on depressive symptoms was indirectly attributed to improvements in positive and negative symptoms, respectively; up to 26.4% was attributed to direct treatment effect. Among potential moderators, suicide attempt history was significantly associated ( $P<0.01$ ) with changes in depressive symptoms. For subjects with a suicide attempt history, paliperidone ER vs placebo improvement in HAM-D-17 was indirectly mediated through effects on positive (30.2%) and negative (19.6%) symptoms; 50.6% of the total effect represented a direct treatment effect. For subjects without suicide attempt history, improvement in HAM-D-17 was indirectly mediated through improvement in positive (60.1%) and negative (38.9%) symptoms; 1.8% of the total effect represented a direct treatment effect. Effect was not attributed to extrapyramidal symptom changes in any model. Conclusions: Results suggest that paliperidone ER treatment may have a direct effect on depressive symptoms in adult subjects with schizoaffective disorder, with indirect effects mediated through positive and negative symptom changes. These effects appeared strongly modulated by a suicide attempt history. Funding, Janssen Scientific Affairs, LLC

**NR6-20**  
**FIRST CONTROLLED STUDY OF A LONG-ACTING INJECTABLE ANTIPSYCHOTIC FOR THE MAINTENANCE TREATMENT OF SCHIZOAFFECTIVE DISORDER: BASELINE DATA**

*Chair: Dong-Jing Fu M.D.; Author(s): Ibrahim Turkoz, MS, Richard Bruce Simonson, BS, David Walling, Ph.D., Nina Schooler, Ph.D., JP Lindenmayer, M.D., Larry Alphs, M.D., Ph.D.*

**SUMMARY:**

Background: Schizoaffective disorder is characterized

by the presence of symptoms of both schizophrenia and major mood disorder, with a lifetime prevalence of 0.3%–0.8%. Few large controlled clinical trials have systematically studied the clinical characteristics and the course of these patients. Key design elements and demographic and clinical characteristics of patients enrolled in the first ongoing maintenance study of a long-acting injectable antipsychotic for the treatment of schizoaffective disorder are presented. Method: This ongoing randomized, double-blind, placebo-controlled international study (NCT01193153) includes subjects who met SCID-confirmed DSM-IV diagnosis of schizoaffective disorder: an acute exacerbation of psychotic symptoms; a score  $\geq 4$  on  $\geq 3$  PANSS items of delusions, conceptual disorganization, hallucinatory behavior, excitement, suspiciousness/persecution, hostility, tension, uncooperativeness, and poor impulse control; and prominent mood symptoms ( $\geq 16$  on YMRS and/or HAM-D-21). Subjects may receive adjunctive stable doses of antidepressants (AD)/mood stabilizers (MS). After stabilization with paliperidone palmitate (PP; 78–234 mg [50–150 mg equivalents of paliperidone]) during a 13-week, open-label, flexible-dose lead-in period, stable subjects (PANSS total score  $\leq 70$ , YMRS  $\leq 12$ , and HAM-D-21  $\leq 12$ ) continue into the 12-week open-label fixed-dose stabilization period. Those who meet stabilization criteria are randomized (1:1) to PP (at stabilized dose) or placebo in the 15-month double-blind relapse prevention period. The primary end point is the first occurrence of relapse. Baseline demographic and clinical characteristics results are summarized using descriptive statistics. Results: As of 11/25/2011, 491 patients had enrolled in the open-label period. Planned total randomization of clinically stabilized patients is 288. Mean age (range): 40.0 years (19–64). 52.3% were male and 59.1% were white. Mean BMI (range): 28.3 (18–40). Mean age (range) at first psychiatric and schizoaffective disorder diagnosis: 25.9 (3–55) and 31.3 (7–59) years, respectively. 27.6% of patients had a history of suicide attempt. Mean prior lifetime psychiatric hospitalizations (range): 6.2 (0–150). 55.4% of patients were taking concomitant AD or MS. Current mood episode: 24.7% manic, 48.6% depressive, 25.9% mixed, and 0.8% not reported. Mean (SD) baseline symptom scores: PANSS total, 85.7 (12.9); CGI-S-SCA, 4.4 (0.6); HAM-D-21 total, 20.9 (7.7); YMRS total, 18.0 (9.4). Conclusions: Baseline data of the first 491 subjects of this first large maintenance treatment for patients with schizoaffective disorder provides information on the clinical characteristics of this population. They demonstrate a full range of psychotic and mood symptoms, repeated prior hospitalizations, a high rate of suicide attempts and of combination treatments, and a late emergence of

the schizoaffective diagnosis. Funding, Janssen Scientific Affairs, LLC

#### NR6-21

### TIMING OF RISPERIDONE LONG-ACTING INJECTION INITIATION IN NEWLY DIAGNOSED SCHIZOPHRENIA PATIENTS IN THE VETERANS HEALTH ADMINISTRATION

*Chair: Pesa Jacqueline Ph.D.; Author(s): Xinhua S. Ren, Ph.D., Lewis E. Kazis, ScD, Shirley Qian, MS, Dilesh Doshi, Phar M.D.*

#### SUMMARY:

**Background** Little is known about the characteristics of newly diagnosed schizophrenia patients treated with long-acting antipsychotic therapy and the potential benefits. **Objectives** To examine the timing of initiating risperidone long-acting injection (RLAI) in newly diagnosed patients with schizophrenia and to compare outcomes in terms of treatment adherence and healthcare utilization in patients who started RLAI within 1 year vs 366 days to 5 years after initial diagnosis. **Methods** Data were from the Veterans Health Administration (VA) between fiscal years 2004–2008. New cases of schizophrenia were defined as patients with no diagnoses of schizophrenia in the prior 2 or more years (no outpatient or inpatient use) but 1 or more diagnosis for another condition (indicating VA enrollment). Two study groups were created: early intervention (EI) initiated RLAI within year 1, and later intervention (LI) initiated RLAI 366 days to 5 years after initial schizophrenia diagnosis. Data were summarized using t tests for continuous variables and chi-square tests for categorical variables, with no adjustments made for multiplicity. **Results** Of the total sample of VA patients who were within 5 years of initial schizophrenia diagnosis (n=28,709), 5.7% (n=1635) were treated with RLAI, 63.4% (n=1037) making up the EI group and 36.6% (n=598) the LI group. 58.6% of patients initiated RLAI during hospitalization and 60.7% received oral risperidone before RLAI. The EI group had a higher proportion of whites (28.3% vs 21.4%,  $P=0.0132$ ), had more comorbidities (mean  $\pm$  SD 3.3  $\pm$  2.6 vs 2.9  $\pm$  2.4,  $P=0.0049$ ), were less likely to have received any antipsychotic before RLAI (77.2% vs 90.5%,  $P<0.0001$ ), and were less adherent with oral antipsychotics before RLAI (89.4% vs 69.4% MPR  $\leq 0.5$ ,  $P<0.0001$ ). In the 12 months after RLAI initiation, EI patients had lower psychiatric-related inpatient costs (mean  $\pm$  SD \$27,692  $\pm$  \$44,181 vs \$29,886  $\pm$  \$49,143,  $P=0.5622$ ) and lower outpatient costs (mean  $\pm$  SD \$6930  $\pm$  \$8835 vs \$7653  $\pm$  \$9927,  $P=0.1280$ ) compared with LI patients. **Discussion and Conclusion** Only 6% of newly

diagnosed patients were initiated on RLAI within the first 5 years following their schizophrenia diagnosis. There was a trend toward lower costs for some measures of healthcare utilization among EI vs LI groups. EI with RLAI may have a beneficial impact in terms of inpatient costs; however, further research is needed to examine longer-term patient outcomes. Funded by Janssen Scientific Affairs, LLC

#### NR6-22

### REMISSION WITH CONTINUED PALIPERIDONE PALMITATE TREATMENT IN STABLE SUBJECTS WITH SCHIZOPHRENIA

*Chair: Joseph Huliban M.D.; Author(s): Cynthia A. Bossie Ph.D., Dong-Jing Fu, M.D., Ph.D., Jennifer Kern Sliwa, Phar M.D., BCPP, Yi-Wen Ma, Ph.D., Larry Alphas, M.D., Ph.D.*

#### SUMMARY:

**Introduction:** Stability, remission, and recovery are important concepts in chronic disease management, but no widely accepted definitions exist for these concepts in schizophrenia. Nonetheless, achieving remission, or a persistent low level of symptoms, is an important treatment goal. Adherence with treatment is a critical component to achieving remission. Research has shown that withdrawing antipsychotic treatment from stable patients increases the risk for symptom recurrence and, sometimes, relapse and hospitalization. Long-acting injectable antipsychotics obviate the need for taking daily medication and can help with adherence to treatment regimens, which may contribute to achieving remission. Research criteria for remission, suggested by a working group (Andreasen et al 2005), were applied to a database of once-monthly injectable antipsychotic paliperidone palmitate (PP) in subjects with schizophrenia. **Methods:** A post hoc analysis of a long-term multiphase study (NCT00111189) of PP in subjects with schizophrenia was conducted to characterize remission with continued treatment. The study consisted of open-label (OL) single-arm transition and maintenance phases (33 weeks) where subjects received PP. Those who met stabilization criteria were eligible to enter a double-blind (DB) placebo-controlled relapse prevention phase ( $\leq 104$  weeks). Remission criteria were defined as absent to mild core symptoms (score 1-3) for a duration of  $\geq 6$  months on the following PANSS items: P1 delusions, P2 conceptual disorganization, P3 hallucinatory behavior, G9 unusual thought content, G5 mannerisms and posturing, N1 blunted affect, N4 passive/apathetic social withdrawal, N6 lack of spontaneity and conversation flow. Remission status was determined, as well as PSP

scores for remitted and nonremitted subjects during the DB phase. Descriptive statistics summarized the data. **Results:** 410 subjects were stabilized on PP and entered the DB relapse prevention phase. Of these, 149 (36.3%) met remission criteria for  $\geq 6$  months during the OL phase before entering the DB phase; 261 (63.7%) did not. Of the 261 subjects not remitted at entry into the DB phase (n=130 PP, n=131 placebo), 47 (36.2%) and 19 (14.5%), respectively, met remission criteria for  $\geq 6$  months during the DB phase. Mean (SD) PSP scores in each group: 69.9 (10.8) and 72.8 (7.2), respectively, at DB baseline; and 72.7 (11.0) and 74.4 (7.9), respectively, at DB end point. Of the 149 who were remitted at entry into the DB phase (n=76 PP, n=73 placebo), 36 (47.4%) and 22 (30.1%), respectively, continually remitted for  $\geq 6$  months during the DB phase. Mean (SD) PSP scores in each group: 78.0 (8.3) and 81.7 (8.4), respectively, at DB baseline; and 77.5 (7.9) and 78.1 (9.8), respectively, at DB end point. **Conclusions:** These preliminary post hoc data are the first to characterize remission with continued PP treatment vs treatment discontinuation in subjects with schizophrenia. Supported by Janssen Scientific Aff

#### NR6-23

### ACHIEVEMENT OF REMISSION IS SIMILAR WITH ILOPERIDONE AND HALOPERIDOL: A META-ANALYSIS OF 3 YEAR-LONG, DOUBLE-BLIND STUDIES

*Chair: Marla Hochfeld M.D.; Author(s): Saeeduddin Ahmed, M.D., Adam Winseck, Ph.D., Xiangyi Meng, Ph.D.*

#### SUMMARY:

**Objective:** To assess remission following iloperidone treatment using criteria modified from Andreasen et al.<sup>1</sup> **Data** were pooled from 3 randomized, double-blind studies lasting up to 52 weeks in which iloperidone was equivalent to haloperidol in time to relapse (primary efficacy variable).<sup>2</sup> **Methods:** Patients with schizophrenia or schizoaffective disorder received a flexible dose of 4–16 mg/d of iloperidone (n = 1231) or 5–20 mg/d of haloperidol (n = 403). The intent-to-treat population, consisting of all randomized patients who received at least 1 dose of study medication and had at least 1 postbaseline efficacy assessment, was analyzed. Remission was defined as a rating of  $\leq 3$  (mild or less) at 1 or more study visits (occurring every 1-5 weeks) for the following Positive and Negative Syndrome Scale (PANSS) items (item number): delusions (P1), unusual thought content (G9), hallucinatory behavior (P3), conceptual disorganization (P2), mannerisms/posturing (G5), blunted affect (N1), social withdrawal (N4), and lack of spontaneity (N6). Patients achieving consecutive

remission met these criteria at 2 or more consecutive assessments. Hazard ratios (HRs) and 95% confidence intervals (CIs) for iloperidone over haloperidol were determined using Cox proportional hazards regression. Results: For patients with schizophrenia or schizoaffective disorder, 670/1146 (58.5%) receiving iloperidone and 222/379 (58.6%) receiving haloperidol achieved remission at 1 or more study visits (HR [CI] of 0.93 [0.80, 1.09]). A total of 568/1087 (52.3%) of these iloperidone-treated patients and 193/351 (55.0%) of haloperidol-treated patients experienced consecutive remission (0.91 [0.78, 1.08]). When schizophrenia patients were analyzed separately, 627/1080 (58.1%) receiving iloperidone and 210/365 (57.5%) receiving haloperidol achieved remission at one or more study visits (0.94 [0.80, 1.09]). Remission at consecutive study visits occurred in 530/1027 (51.6%) schizophrenia patients receiving iloperidone and 181/338 (53.6%) receiving haloperidol (HR [CI] of 0.92 [0.78, 1.09]). Conclusions: In studies lasting up to 1 year, a similar percentage of patients on iloperidone and haloperidol achieved remission at individual and consecutive study visits. Funding: Novartis Pharmaceuticals Corporation. References: 1. Andreasen NC, Carpenter JC, Kane JM, et al. Remission in schizophrenia: proposed criteria and rationale for consensus. *Am J Psychiatry*. 2005;162:441–449. 2. Kane JM, Lauriello J, Laska E, et al. Long-term efficacy and safety of iloperidone: results from 3 clinical trials for the treatment of schizophrenia. *J Clin Psychopharmacol*. 2008;28(2 Suppl 1):S29–S35.

**NR6-24**  
**CHARACTERISTICS OF MEDICAID PATIENTS INITIATING PALIPERIDONE PALMITATE COMPARED WITH ORAL ATYPICAL ANTIPSYCHOTICS**

*Chair: Elaine Morrato D.P.H.; Author(s): Elizabeth Campagna, MS, Joseph Parks, M.D., Paul Stuve, Ph.D., Deborah Thomas, Ph.D., Hai Fang, Ph.D., Eva Dilbert, MHA, Erik Muser, Ph.D., John W. Newcomer, M.D.*

**SUMMARY:**

Objective: Paliperidone palmitate (PP) is a long-acting atypical antipsychotic approved for the treatment of schizophrenia. Information on real-world use of PP in the community is limited. The aim of this retrospective cohort study was to compare characteristics of patients starting PP versus oral atypical antipsychotics (OAs) within the Missouri Medicaid system. Methods: Healthcare claims (08/2008–04/2011) from the Missouri Medicaid program were analyzed. Patients newly initiated (i.e., no use in prior 12 months) on PP or a specific OA (aripiprazole, iloperidone,

olanzapine, paliperidone, quetiapine, risperidone, or ziprasidone) and  $\geq 12$  months of continuous Medicaid eligibility before and after drug initiation (index) were included. Medicare dual-eligibles (19.1% and 8.4%, respectively) were excluded. 9982 patients met study eligibility criteria (355, PP; 9627, OAA). Baseline patient characteristics studied were demographics (age, sex, race/ethnicity), mental health diagnoses (using the Agency for Healthcare Research and Quality clinical classification scheme), healthcare resource utilization in the 12 months preindex (hospitalization, emergency department [ED], and outpatient [OP] visits). Measures were compared between groups using t tests or chi-squared tests. No adjustment was made for multiplicity. Results: PP patients were more likely than OAA patients to be male (51.0% vs 42.2%,  $P < 0.01$ ), older (mean age = 37.3 vs 27.9 years,  $P < 0.01$ ), and African American (40.6% vs 18.9%,  $P < 0.01$ ). PP patients had more mental health diagnoses than OAA patients (mean = 4.2 vs 3.1,  $P < 0.01$ ) and were more likely to have schizophrenia or other psychotic disorder (89.6% vs 18.3%,  $P < 0.01$ ), an alcohol-related (28.0% vs 13.5%,  $P < 0.01$ ) or substance-related disorder (49.2% vs 25.7%,  $P < 0.01$ ), or an intentional self-inflicted injury (24.3% vs 12.8%,  $P < 0.01$ ). The prevalence of anxiety (54.5% vs 57.7%,  $P = 0.23$ ) and mood (78.3% vs 83.1%,  $P = 0.02$ ) disorders were clinically more similar between groups. PP patients were more likely to have received care in a community mental health center (83.1% vs 35.5%,  $P < 0.01$ ) and were more likely to reside in an urban county (74.9% vs 65.3%,  $P < 0.01$ ) than OAA patients. Relative to OAA patients, PP patients were more likely to have been hospitalized with a primary diagnosis for a mental health disorder (41.4% vs 21.4%,  $P < 0.01$ ) and less likely to have had an OP visit (69.0% vs 81.0%,  $P < 0.01$ ) but ED utilization (67.9% vs 66.5% with an ED visit,  $P = 0.58$ ) in the 12 months preindex appeared to be similar. Conclusion: Patients initiating PP differed significantly from patients initiating OAs on important demographic and clinical measures known to be associated with drug adherence and resource utilization. These findings should guide future analysis comparing the effectiveness of PP vs OAs.

**NR6-25**  
**CHARACTERISTICS ASSOCIATED WITH ANTIPSYCHOTIC DRUG ADHERENCE AMONG SCHIZOPHRENIC PATIENTS IN A US MANAGED CARE ENVIRONMENT**

*Chair: Bruce Wong M.D.; Author(s): Steve Offord, Ph.D., Dario Mirski, M.D., Jay Lin, Ph.D.*

**SUMMARY:**

Background: Antipsychotic drug therapy for treating schizophrenia is effective in managing symptoms and preventing relapses. However, non-adherence to antipsychotic drug therapy in patients with schizophrenia is prevalent. Methods to improve adherence are of critical importance to reduce the burden of the disease. Objective: To identify potentially distinguishing factors that are predictive of patients who adhere to antipsychotic therapy. Methods: Patients in the US with schizophrenia between 1/1/2005 and 9/30/2010 were identified from the MarketScan Commercial healthcare claims database. Patients included in the study were  $\geq 13$  years of age and had at least 12 months of continuous coverage before (baseline) and after (follow-up) the earliest antipsychotic usage (index event). Medication adherence was estimated with a medication possession ratio (MPR), which represents the time each patient possessed a drug compared to the total expected duration of therapy. Patients with an MPR  $\geq 0.7$  during the follow-up period were allocated to the high-adherence cohort. Those with an MPR  $< 0.7$  were assigned to the low-adherence cohort. Patient demographics, comorbidities, and concomitant medication usage were measured during the baseline period. Statistical analysis was carried out using SAS. Results: 1,462 patients with schizophrenia met the inclusion criteria; 396 (27%) were classified as highly adherent with a mean  $\pm$  standard deviation (SD) MPR of  $0.92 \pm 0.10$  and 1,366 (73%) were classified as having low adherence with a mean  $\pm$  SD MPR of  $0.24 \pm 0.19$ . With the exception of the highly adherent patients being older (41.1 vs. 38.4 years;  $p=0.004$ ), demographic characteristics were similar between the two cohorts. A greater proportion of highly adherent patients were diagnosed with peripheral vascular disease (2.0% vs. 0.8%;  $p=0.04$ ) and had concomitant use of anticonvulsants (42.4% vs. 34.1%;  $p=0.003$ ) and antihyperlipidemics (20% vs. 13.8%;  $p=0.004$ ), although the overall Charlson comorbidity index was not different between the high-adherence and low-adherence cohorts. Conclusions: Only 27% of patients with commercial health plans in this analysis were highly adherent to antipsychotic medication, reflecting the magnitude of the adherence problem in patients with schizophrenia. Highly adherent patients were older, experienced more peripheral vascular disease, and received more antihyperlipidemic and anticonvulsant medications. These results could indicate that adherence to antipsychotic agents is assisted by a “reminding event”, such as an illness or use of concomitant medication. Further study is required to clarify the role of the co-morbid diseases vs. concomitant medications in the risk of antipsychotics non-adherence.

**NR6-26****THE SEVERITY AND DEMOGRAPHICS OF SCHIZOPHRENIA PATIENTS SWITCHING TO DEPOT ANTIPSYCHOTIC AGENTS**

*Chair: Dario Mirski M.D.; Author(s): Jay Lin, Ph.D.; Steve Offord, Ph.D.; Bruce Wong, M.D.*

**SUMMARY:**

Background: Depot antipsychotic agents were developed to improve compliance to therapy in schizophrenia patients. Current practice in newly diagnosed schizophrenia is to start with an oral agent then switch to a depot agent if compliance is inadequate. However, this therapeutic sequence potentially selects the most severe patients for depot therapy. We examined the severity and demographics of patients prior to the initiation of depot agents in comparison to incident schizophrenia prior to oral therapy. Method: Schizophrenia patients were identified from the MarketScan Commercial database, a US national health plan database, between 1/1/2005 and 9/30/2010. Index events were patients initiating treatment with depot antipsychotics compared to patients initiating treatment with an oral antipsychotic. The 12 months prior to the index event dates were compared. Patients were required to be  $\geq 13$  years at the index event and have  $\geq 12$  months of continuous health plan coverage prior to the index event. Schizophrenia severity was estimated from the need for hospitalization for schizophrenia, the length of stay in hospital (LOS) for schizophrenia and requirement for outpatient care. Charlson comorbidity index (CCI) was calculated to determine general disease severity. Medication possession ratio (MPR) was used as a measure of drug compliance. Statistical analysis was undertaken in SAS. Results: 3,004 patients met inclusion criteria. 394 patients initiated depot agents and 2,610 oral agents with a mean age of  $41.7 \pm 15.5$  and  $37.1 \pm 15.9$  years, respectively. CCI scores ( $0.58$  vs.  $0.47$ ;  $p=0.06$ ) were similar between groups. Prior to the initiation of depot agents, the median MPR for prior oral antipsychotic agents was  $0.28 \pm 0.37$ . The number of hospital admissions in the 12 months leading up to the initiation of depot therapy was higher than that in newly diagnosed schizophrenia initiating oral therapy,  $1.6 \pm 1.66$  vs.  $0.82 \pm 1.10$ ,  $p<0.0001$  and the hospitalization LOS was  $16.93 \pm 20.68$  vs.  $6.18 \pm 11.02$  days. The number of outpatient healthcare claims were significantly higher in the group subsequently receiving depot drugs,  $51.37 \pm 53.56$  vs.  $41.54 \pm 46.62$ ,  $p=0.0001$ . Total medication claims were also higher in this group,  $27.87 \pm 30.10$  vs.  $19.77 \pm 28.14$ ,  $p<0.0001$ . Emergency room visits were numerically higher prior to the receipt of depot agents vs. oral agents, but not

statistically significant  $2.98 \pm 7.75$  vs.  $2.33 \pm 8.40$ .  
 Conclusions: In current psychiatric practice, patients initiating depot therapy had more severe and difficult to control schizophrenia than newly diagnosed patients, creating a channeling bias in any real-world assessment of effectiveness of depot medication.

**NR6-27**  
**BARRIERS TO THE UTILIZATION OF LONG-ACTING INJECTABLE ANTIPSYCHOTICS IN SCHIZOPHRENIA**

*Chair: Dale D'Mello M.D.; Author(s): Marie Beasley, D.O. Hayley Getzen, M.P.H Candidate*

**SUMMARY:**

Long-acting injectable antipsychotic medications reduce rates of relapse and re-hospitalization in schizophrenia by 30%, when compared to oral equivalent compounds. Nevertheless, current treatment guidelines favor initial treatment with oral medications. Hence, long-acting injectable agents are employed only after successive relapses caused by treatment non-adherence. Nationwide only a minority of patients receive long-acting intramuscular antipsychotics. Objective: The purpose of the present study was to examine the barriers psychiatrists face in implementing long-acting injectable antipsychotics. Methods: We sent an internet survey to all Michigan State University affiliated psychiatrists, attempting to explore their practice characteristics, access, opinions and barriers to using long-acting intramuscular injectable antipsychotics in patients with schizophrenia. We checked insurance drug formulary access to a standard long-acting injectable compound (haloperidol decanoate), using the Epocrates iPhone app. The survey responses were analyzed statistically using SPSS software. Results: Thirty-six of 157 (23%) psychiatrists responded. Of the respondents, 10 (28%) worked in community mental health centers, 7 (19%) in hospitals, 6 (17%) in academic clinics, and 2 (6%) in veteran medical centers. Whereas 33 (83%) psychiatrists acknowledged having patients in their practices who would benefit from long-acting injectable antipsychotics, only 22 (61%) had the capacity to deliver these medications in their practice settings. The leading barriers to utilizing long-acting injectable antipsychotics were (a) lack of nursing support at the practice location, (b) personal preference for oral compounds, and (c) limited insurance coverage. As expected, psychiatrists who had the capability to administer long-acting antipsychotic compounds were 10 times more likely to utilize them as compared to others who lacked the capability: 9.67% (SD=10) versus 1.43% (SD=3);  $df=1$ ,  $F=8.59$ ,  $p<0.005$ . Only 13 of 37 (35%) of Michigan

insurance drug formularies provide access to generic long-acting depot haloperidol decanoate. Discussion: In the long-term treatment of schizophrenia the difference in relapse between intramuscular long-acting injectable antipsychotics and their oral equivalents approximates the absolute difference in the efficacy between oral antipsychotics and placebo. Psychiatrists practicing in the state of Michigan face daunting barriers in utilizing these agents. Insurance carriers need to revise their formularies to provide easier access. Psychiatrists need to inform all eligible patients of the superiority of long-acting injectable antipsychotics versus their oral equivalents on long-term treatment outcome. Treatment algorithms need to be updated to include long-acting injectable antipsychotics in the initial treatment in first-episode schizophrenia.

**NR6-28**  
**TIME COURSE OF DROPOUT RATES IN SCHIZOPHRENIA TRIALS CONDUCTED FROM 1966 TO 2010: A SYSTEMATIC REVIEW AND META-ANALYSIS**

*Chair: Ofer Agid M.D.; Author(s): Ofer Agid, M.D., Cynthia Siu, Ph.D., Robert B. Zipursky, M.D., Gary Remington, M.D., Ph.D., FRCPC*

**SUMMARY:**

Background: High dropout rates have been reported in clinical trials of psychotropic agents. Despite this widely observed trend, evidence-based evaluations of its time course and potential moderators are still limited. The objective of this study was to conduct a systematic review and meta-analysis of dropout rates in double-blind, randomized controlled trials (RCTs) in schizophrenia conducted between 1966 and 2010. Methods: We searched the MEDLINE database for RCTs published from 1966 to 2010, supplemented by other electronic databases and hand searches. Meta-analysis was based on data extracted from published reports of 49 eligible RCTs, which included patient characteristics, trial design and clinical variables. Risk ratio (RR), risk difference (RD), and NNTp (number needed to treat to prevent 1 outcome) were used as effect measures comparing placebo (PBO) and active antipsychotic drugs (DRUG) as a group (12 atypicals, 17 conventional agents) in short-term (2 – 12 weeks) trials. Effect measures across studies were analyzed using the random-effects model. The quality of RCTs analyzed was evaluated using a validated omnibus rating of overall quality. Results: Our findings indicate significant heterogeneity in dropout rates within and between PBO and active antipsychotic DRUG arms across trials ( $p<0.01$ ). The dropout rate in the PBO arm

was significantly higher than that in the DRUG arm (RR = 1.36, 95% CI 1.27 to 1.47), with NNT<sub>p</sub> of 7.5 (RD=13.3%) (95% CI for NNT<sub>p</sub> 6.0 to 10.0). Within the PBO arm, the overall dropout rate was 44.6% (95% CI 37.6% to 51.5%). The attrition rate in the PBO arm increased significantly over time, from 16% before 1980 to 59% between 1990 to 1995 (p<0.001), followed by a significant decrease (48% between 2006 and 2010) (p<0.001). The overall attrition rate for the DRUG arm was 6% before 1980, increasing to 36% between 1990 and 1995 (p<0.001), and then leveling off to 37% between 2006 and 2010. Study year was a significant moderator for placebo-drug difference in dropout rates, with the estimated risk difference between the PBO and DRUG arms increased between 1970 and 1990 (p=0.02), followed by a significant decrease (p=0.03). We also found study quality to be a significant moderator of RD in dropout rates, with RCTs of higher overall quality associated with increased RD favoring the active antipsychotic treatment arms. Conclusions: High dropouts have posed a major challenge to the design, analysis and interpretation of RCTS in psychiatric disorders such as schizophrenia. Our findings suggest there has been a decrease in drug-placebo difference in dropout rates since 1995, possibly due to decreased dropout rates in the placebo arm. We found both study year and study quality as significant moderators of dropout rate differences between placebo and antipsychotic treatments in schizophrenia. Further studies to verify these results are warranted to mitigate the considerable challenge these pose to drug development.

#### **NR6-29 ARE PATIENTS WITH SCHIZOPHRENIA HAPPY?**

*Chair: Ofer Agid M.D.; Author(s): Gary Remington, M.D., Ph.D., FRCPC, Ofer Agid, M.D., Cynthia Siu, Ph.D., Krysta Mc Donald, BSc, Christopher Tsoutsoulas, BSc, Caroline Wass, Ph.D., George Fousias, M.D., MSc*

#### **SUMMARY:**

Background Happiness is a core dimension of a person's life, related to both functioning and success. The purpose of this study was to assess level of happiness in schizophrenia vis-à-vis both clinical and functional measures of outcome. Method Thirty-one first-episode remitted patients and 29 age- and sex-matched controls participated in the study. Happiness was assessed by Subjective Happiness Scale (SHS), a self-report questionnaire used to measure levels of happiness. Satisfaction with life was measured using the Satisfaction with Life Scale (SWLS). Patients' clinical status

and severity of psychiatric symptoms were assessed by the Positive and Negative Syndrome Scale for Schizophrenia (PANSS), Clinical Global Impression scale (CGI), and Calgary Depression Scale (CDS). Social withdrawal was assessed by the social withdrawal domain of the Social Functioning Scale (SFS). Insight was measured using the Schedule for Assessment of Insight (SAI), while cognitive functioning was evaluated using the Brief Assessment of Cognition in Schizophrenia (BACS). Functional performance was assessed by Social and Occupational Functioning Assessment Scale (SOFAS) based on observation by the clinician or study personal. Results The study sample consisted of 31 patients with first-episode schizophrenia and 29 matched (age, gender, years of schooling) controls. Mean age was 24 (SD 3) for male and 27.6 (SD 7.1) for female. The average years of schooling was 12.8. Duration of illness for the patients was < 18 months (range 8 – 18 months). Mean PANSS total score was 41.4, and mean BACS composite score standardized to healthy controls (z-score) was -2.05 (SD 1.27). Patients experienced marked functional impairment (49.8, 95% CI 47.8, 52.2) versus healthy controls (84.0, 95% CI 81.5, 86.5; P<0.001), while reporting comparable levels of happiness (5.16, 95% CI 4.85, 5.47 vs. 4.80, 95% CI 4.5, 5.1 in controls, P=0.113) and satisfaction with life (24.3, 95% CI 22.0, 25.1 vs. 22.8, 95% CI 20.4, 25.1, P=0.350). In the patient group, we found higher happiness ratings were significantly associated with less depression (P<0.05), less negative symptoms (P<0.05), less social withdrawal (P<0.05), greater life satisfaction (P<0.05), and higher social and occupational functioning (SOFA, P<0.05). There was a significant correlation between cognitive performance and SOFA functioning total score (P<0.05), but the association was not independent of the effect of insight (SAI T total score) on the SOFA functioning outcome. Both cognitive functioning and insight had no significant direct effects on ratings of happiness in the patient group. Conclusions The results of this study raise questions regarding the underlying mechanisms of insight and efforts related to rehabilitation that assume an individual holds to the same drives and goals as before the illness' onset and/or that the person is unhappy with his/her present functional status.

#### **NR6-30 CLINICAL DECISION-MAKING IN OUTPATIENT MENTAL HEALTH CARE**

*Chair: Malene Krogsgaard Bording Other Author(s): Prof. dr.med. Munk-Jørgensen, Poul Research nurse, MHS-stud. Sørensen, Helle Østermark*

**SUMMARY:**

Introduction: Research on clinical decision-making in health care has primarily focused on well-defined situations in physical conditions. Consequently, there is a major lack of knowledge on outpatient treatment in mental health, especially a deficiency on research in clinical decision-making in people with schizophrenia with its high demands on treatment adherence and therapeutic relationships. Most psychiatric treatment is based on consultations between the clinician and the mentally ill patient. During the treatment session the necessary decisions are made concerning course of treatment; which type of treatment, how the treatment should be carried out, change in treatment, hospitalization or outpatient treatment, when to discharge the patient, intensity of treatment. Considering how many decisions are to be made during the treatment sessions it is a paradox what little research exists concerning this decision-making process. Objective: This study is about clinical decision-making in outpatient mental health care with specific focus on patients diagnosed with schizophrenia. Aims of the study: To identify the style of decision-making between patient and therapist (paternalistic, shared and informed). Investigate the patient's understanding of the decision-making and identification of factors leading to this understanding. Furthermore the study will include an analysis of style of decision-making as a possible predictor of adherence to treatment. An anticipation of more knowledge about the clinical decision-making process can lead to patients' higher degree of adherence in the treatment. Thus, this enables us to meet the many and serious complications which characterizes the long-term psychotic mentally ill patients. Methods: This study is an open, explorative study using a combination of both qualitative and quantitative methods. The study population consists of severe mentally ill outpatients diagnosed with schizophrenia. Data consist of questionnaires, field observation and patient interviews. Expected results and conclusion: An expected result of the study is specifications of primary areas for further improvement in clinical decision-making. Recommendations will be extracted and formulated from the study data to implement elements of best practice in clinical decision-making in the routine outpatient care for people with schizophrenia in particular, and severe mental illness in general. The explicit focus will contribute to strengthening of the patient perspective.

**NR6-31****HOW RELATED ARE OBSESSIVE COMPULSIVE DISORDER AND SCHIZOPHRENIA? A FAMILIAL****AGGREGATION STUDY FROM DANISH HEALTH REGISTRY SYSTEM**

*Chair: Hale Yapici Eser M.D.; Author(s): Thomas Hansen, Thomas Werge, Klaus Damgaard Jacobsen*

**SUMMARY:**

Obsessive-compulsive disorder (OCD) and schizophrenia show a great level of comorbidity. 20-50 % of schizophrenia patients are reported to have a comorbid obsessive-compulsive spectrum (OCS) diagnosis. To hint whether this comorbidity is a result of antipsychotic treatment provocation or a result of an unknown shared vulnerability, we analyzed the familial aggregation of OCD and OCS diagnosis. Method: All patients admitted to Child and Adolescent Psychiatry Departments (CAP) in Denmark between 1969-2003 and their first degree relatives were identified from the Danish Health Registry System. After excluding patients that had an organic mental disorder, mental and behavioral disorders due to psychoactive substance use and childhood developmental disorder, 9807 patients were classified into five diagnostic categories: depressive disorders, anxiety disorders, bipolar disorder, schizophrenia and psychotic spectrum disorders. A five set Venn diagram has been used to depict the five categories. All Patients were matched with three sex, birth year, month and place matched population controls with no admission to CAP and their first degree relatives. Patients and matched controls were compared for having an OCD or OCS diagnosis in their first-degree relatives. Results: Compared to their matched controls, patients with schizophrenia or depressive disorder diagnosis had a higher OCD and OCS diagnosis in their first-degree relatives (OR: 2.0, 95% CI: 1.2-3.3,  $p < 0.01$  and OR: 1.98, 95% CI: 1.4-2.8,  $p < 0.001$ , for OCD, respectively, OR: 1.4, 95% CI: 1.0-1.9,  $p = 0.03$  and OR: 2.0, 95% CI: 1.6-2.5,  $p < 0.001$ , for OCS, respectively). Patients with a psychotic spectrum diagnosis had a higher OCS diagnosis compared to controls (OR: 1.4, 95% CI: 1.0-1.7,  $p = 0.01$ ). Excluding patients with more than one of the five category diagnosis, only patients diagnosed with depression or schizophrenia had a higher frequency of OCD or OCS diagnosis in their first degree relatives (OR: 2.0, 95% CI: 1.35-2.9,  $p < 0.001$  and OR: 2.2, 95% CI: 1.3-3.8,  $p = 0.006$ , for OCD, respectively, OR: 2.2, 95% CI: 1.7-2.7,  $p < 0.001$  and OR: 1.5, 95% CI: 1.0-2.11,  $p = 0.02$ , for OCS, respectively). Patients with anxiety, bipolar or psychotic spectrum disorder other than schizophrenia did not have a significant difference. Conclusion: First degree relatives of patients with schizophrenia or depressive disorder had the highest of having an OCD or OCS diagnosis. The increased risk

in first degree relatives of schizophrenia patients to have obsessive symptoms, supports the hypothesis of shared risk factors between these disorders and antipsychotics may be unmasking the obsessive symptoms in schizophrenia patients rather than coursing them.

#### NR6-32

### COGNITIVE PERFORMANCE IN PATIENTS WITH SCHIZOPHRENIA TREATED WITH LURASIDONE: RESULTS FROM A 6-WEEK CORE STUDY AND 6 MONTH DOUBLE-BLIND EXTENSION

*Chair: Cynthia Siu Ph.D.; Author(s): Cynthia Siu, Ph.D., Philip Harvey, Ph.D., Jay Hsu, Ph.D., Debra Phillips, Josephine Cucchiaro, Ph.D., Paul Maruff, Ph.D., Antony Loebel, M.D.*

#### SUMMARY:

**Background:** Cognitive impairment is a core feature of schizophrenia. This multiregional study of lurasidone in schizophrenia, consisted of a 6-week, double blind, placebo- and active-controlled study, followed by a 12-month, double-blind extension. Results of a computerized cognitive battery (CogState) evaluating change in cognitive performance, from acute study baseline to week-6 and week-32 (6-month extension) endpoints, are reported here. Methods Clinically unstable patients with schizophrenia were randomized to once-daily treatment with lurasidone 80 mg (n=125, LUR80), lurasidone 160 mg (n=121, LUR160), quetiapine XR 600 mg (n=120, QXR600) and placebo (n=122, PBO). Subjects who completed the initial 6-week trial were eligible to enroll in a double-blind extension study, involving continued treatment with flexible once-daily doses of lurasidone (40-160 mg; n=151, LUR) or quetiapine XR (200-800 mg; n=85, QXR). Subjects initially treated with PBO were started on LUR (40-160 mg/d; n=56). Cognitive performance was examined with the CogState system at acute phase baseline, after 6 weeks, and at 3 months and 6 months in the extension phase. Results In the acute 6-week period, task completion rates averaged 94%, but data integrity failures, based on pre-planned criteria, were noted in 23% of the cases. At 6 weeks, no statistically significant differences in the CogState composite score were found between lurasidone dose groups, the active control and the placebo group in the full ITT sample (N=488). When patients whose data failed the prespecified integrity checks were excluded in a secondary analysis (N=267), LUR160 was superior on the cognitive composite score to both PBO (p<0.05, d=.25) and QXR (p<0.05, d=.28), while QXR, LUR80, and PBO did not differ from each other.

UPSA-B scores were also superior to PBO at 6 weeks for all active treatments. In the 6-month, flexible-dose, extension study, we found a significant cognitive benefit for LUR compared to QXR treated patients, assessed from core baseline to the week-32 (6-month) endpoint. Analysis of cognitive composite score and UPSA-B total score showed significant associations both at baseline (cross-sectionally) and over time (longitudinally) using a mixed-effects model. Conclusions This is the first pharmacological study to date where the investigational treatment was superior to placebo on cognitive assessments and a functional co-primary measure (at 6-week endpoint), as well as demonstrating superiority to an active comparator on neurocognitive improvement over an initial 6-week acute phase and subsequently a 6-month extension study period. These findings require replication, but cannot be attributed to practice effects due to the use of appropriate control groups for treatment comparisons. Levels of data integrity failures were relatively high compared to that of previous trials that used other cognitive assessments, such as the MCCB. Research supported by Sunovion Pharma

#### NR6-33

### THE EFFECT OF MODIFIED ELECTROCONVULSIVE THERAPY ON EEG GAMMA ACTIVITIES IN PATIENTS WITH SCHIZOPHRENIA

*Chair: Masatomo Suetsugi M.D.; Author(s): Yasushi Mizuki2, M.D., Ph.D., Toshio Watanuki1, M.D., Ph.D., Kazuteru Egashira1, M.D., and Yoshifumi Watanabe1, M.D., Ph.D.*

#### SUMMARY:

**Background:** The activity of fast-spiking GABAergic interneurons that contain the calcium-binding protein parvalbumin (PV) is essential to generate gamma oscillations. Recent evidence suggests that deficit in PV interneurons and frontal gamma oscillations are the major pathophysiologic feature of schizophrenia. Task-induced frontal lobe gamma band oscillations play an important role in higher-order cognitive processes such as working memory. Although there are a few reports of the resting gamma oscillations in schizophrenic patients, MEG study showed the reduction of resting gamma power in the patients with schizophrenia, and we reported the negative correlation between the resting EEG gamma power value and the severity of the symptoms in the schizophrenic patients. Modified electroconvulsive therapy (mECT) is one of the most effective treatments for medication-resistant schizophrenia. A couple of groups reported that ECT increased cortical GABA concentrations in patients

with depression. Here we hypothesized that ECT could increase the EEG gamma activities followed by an increase in cortical GABA concentrations, and ameliorate the symptoms of the schizophrenia. Methods: Schizophrenia was diagnosed according to the DSM-IV criteria. 6 patients have failed to respond to the pharmacotherapy and planning to receive treatment with ECT was enrolled in the study after providing written informed consent. ECT was performed with Thymatron after a standardized ECT dose titration protocol along with standard anesthetics and muscle relaxants. All patients were treated with bilateral ECT. Clinical symptoms were evaluated on Positive and Negative Symptoms Scale (PANSS). Resting EEG was recorded at 6 electrodes (Fp1, Fp2, F3, F4, F7 and F8), and FFT power (30-50 Hz) was calculated in artifact free epochs of 60 sec. This protocol was approved by the Institutional Review Board of Yamaguchi University Hospital. Results: ECT improved the symptoms in all patients. Contrary to our expectation, gamma power values did not increase by mECT treatment, however, ECT induced the gamma power asymmetry at F7 and F8 (F7 < F8). This pattern is similar to our previous results of the pharmacotherapy responder schizophrenia. Conclusions: The present results suggest the possibility that ECT could ameliorate the symptoms of schizophrenia through the lateralization of frontal gamma activity.

**NR6-34**

**ADJUNCTIVE LISDEXAMFETAMINE DIMESYLATE WITH ANTIPSYCHOTICS: EFFECTS ON NEGATIVE SYMPTOMS OF SCHIZOPHRENIA AND SELF-REPORTED EXECUTIVE FUNCTION**

*Chair: Henry Nasrallah M.D.; Author(s): Bryan Dirks, M.D.; Jean-Pierre Lindenmayer, M.D.; Courtney Kirsch, BS; Jianwong Wang, Ph.D.; Steven James, M.D.; Brian Scheckner, Phar M.D.; David P. Walling, Ph.D.; Robert Lasser, M.D.*

**SUMMARY:**

**Objective:** To examine effects on self-reported executive function (EF) of adjunctive lisdexamfetamine dimesylate (LDX), a d-amphetamine prodrug, for treatment of predominant negative symptoms of schizophrenia (NSS) in clinically stable adults on atypical antipsychotics. **Methods:** After 3-wk screening, outpatients with stable schizophrenia ( $\geq 2$ y) with predominant NSS (Scale for the Assessment of Negative Symptoms [SANS-18; items 1-6, 8-12, 14-16, 18-21] score  $\geq 55$ , score  $\geq 3$  on  $\geq 2$  SANS Global items, Positive and Negative Syndrome Scale [PANSS] positive score  $< 20$ ) maintained on

antipsychotics ( $\geq 12$ wk) underwent 10-wk open-label (OL) LDX augmentation (20-70mg/d). Eligible participants (any SANS-18 improvement at wk 10) entered a 4-wk, double-blind, placebo-controlled randomized withdrawal (RW; wk 10-14). Efficacy measures included the SANS-18 (primary). EF was assessed with the Behavior Rating Inventory of Executive Function-Adult version (BRIEF-A). Safety evaluations included treatment-emergent adverse events (TEAEs). Results: 92 adults received OL LDX; 69 entered RW (LDX, n=34; placebo, n=35); 13 discontinued during RW (LDX, n=7; placebo, n=6). At baseline (wk 0), mean (SD) SANS-18 score was 60.2 (4.36). Mean change (95% confidence interval [CI]), in SANS-18 (OL; wk 0-10) was -12.9 ([-15.0, -10.8]; primary endpoint,  $P < .0001$ ). Mean (SD) baseline BRIEF-A Global Executive Composite (GEC) T-score was 60.2 (14.33) and improved at wk 10 by mean change (95% CI) of -3.8 (-6.6, -1.1) ( $P = .0064$ ). Mean change (95% CI) during OL LDX was -3.0 (-5.7, -0.4) for BRIEF-A Behavioral Regulation Index (BRI) and -3.9 (-6.6, -1.2) for Metacognition Index (MI) T-scores ( $P = .0267$  and  $P = .0047$ , respectively). BRIEF-A domains of initiate, shift, self-monitor, plan/organize, working memory, and monitor tasks showed improvement ( $P \leq .0286$ ) while inhibit, emotional control, and organization of materials did not ( $P \geq .1611$ ). During RW, no meaningful differences were noted (LDX vs placebo) in change from randomization baseline to endpoint in SANS-18 scores or BRIEF-A indices or domains. Post hoc analysis showed no meaningful correlation between change in SANS-25 (full SANS scale) total score and BRIEF-A GEC, MI, and BRI ( $r = -0.172, -0.194, \text{ and } -0.117$ , respectively;  $P \geq .0772$ ). In the OL phase, TEAEs were reported in 60.9% (56/92) of participants; serious TEAEs in 3.3% (3/92). In the RW phase, TEAEs were reported in 32.4% (11/34) and 20.0% (7/35) of participants taking LDX and placebo, respectively. Conclusion: OL LDX augmentation to stable antipsychotic therapy showed small but significant self-reported improvement in global EF scores as well as in particular domain scores including initiate, shift, and self-monitor. The improvement in certain executive cognitive functions appeared to parallel NSS improvement. This is consistent with the notion that frontal dopamine activity may affect both neurocognition and negative symptoms.

**NR6-35**

**SWITCHING TO ARIPIPIRAZOLE DECREASES NON-HDL-C LEVELS IN PATIENTS WITH SCHIZOPHRENIA OR BIPOLAR I DISORDER WHO HAVE PRE-EXISTING METABOLIC SYNDROME**

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#### **SUMMARY:**

**Objective:** The prevalence of Metabolic Syndrome (MetS) is higher in patients with psychiatric disorders, and some medications used to treat psychiatric disorders carry some risk of worsening metabolic parameters.<sup>1,2</sup> Non-HDL cholesterol (non-HDL-C) is a robust predictor of future cardiovascular disease (CVD) events<sup>3</sup>, particularly nonfatal myocardial infarction, and angina. This post-hoc analysis pooled data from two similar multicenter international trials to compare the effects of switching to aripiprazole vs. remaining on another atypical antipsychotic on fasting levels of non-HDL-C in adult patients with schizophrenia or bipolar I disorder who had pre-existing MetS. **Methods:** Data from two open-label, randomized, multicenter studies were pooled. Adult patients with a Diagnostic and Statistical Manual of Mental Health Disorders – Fourth Edition – Text Revision (DSM-IV-TR) diagnosis of schizophrenia, schizoaffective disorder, or bipolar I disorder and MetS who had been treated for ≥3 months with oral olanzapine, risperidone, or quetiapine, were randomized to switching to aripiprazole (Arm A) or continuing on their current atypical antipsychotic (Arm B). Dosing adjustments were allowed within the range of 10–30 mg/day for aripiprazole, and within country-approved ranges for the other atypical antipsychotics. Mean percent change from baseline in fasting non-HDL-C at endpoint (Week 16) was measured. Non-HDL-C was defined as the difference between total cholesterol and HDL-C. **Results:** This analysis included 34 randomized patients per group. At baseline, mean weights were 92.5 kg and 91.3 kg, and mean BMIs were 31.0 kg/m<sup>2</sup> and 32.1 kg/m<sup>2</sup> in Arm A and Arm B, respectively. The adjusted mean percent change (standard deviation) from baseline to endpoint (Week 16) in fasting non-HDL-C was –3.5% (3.0) in Arm A and +7.6% (3.3) in Arm B for a treatment difference of –10.3% (P=0.007). Similar results were seen for MetS parameters. At endpoint, rates of MetS (last observation carried forward) were 60.6% and 81.8% (P=0.059) in Arm A and Arm B, respectively, and in the observed case analysis they were 57.7% and 77.8% (P=0.121), respectively. **Conclusions:** Switching to aripiprazole treatment is associated with improvements in the non-HDL-C profiles of schizophrenia, schizoaffective disorder, and bipolar I disorder patients compared with worsening among

patients who remained on olanzapine, risperidone or quetiapine. Consideration of CVD risk is critical when prescribing antipsychotics, as is close monitoring for metabolic changes during treatment. **References** 1. Fagiolini A, et al: Bipolar disorder and the metabolic syndrome. Causal factors, psychiatric outcomes and economic burden. *CNS Drugs* 2008;22:655–669. 2. Correll CU, et al: Antipsychotic drugs and obesity. *Trends Mol Med* 2011;17:97–107. 3. Cui Y, et al: Non-High-Density Lipoprotein Cholesterol Level as a Predictor of CVD Mortality. *Arch Intern Med*. 2001;161:1413–1419.

#### **NR6-36**

#### **EFFECTIVENESS OF LURASIDONE VS. QUETIAPINE XR FOR RELAPSE PREVENTION IN SCHIZOPHRENIA: A 12-MONTH, DOUBLE-BLIND STUDY**

*Chair: Antony Loebel M.D.; Author(s): Josephine Cucchiaro, Ph.D.; Jane Xu, Ph.D.; Kaushik Sarma, M.D.; Andrei Pikalov, M.D., Ph.D.; John M. Kane, M.D.*

#### **SUMMARY:**

**Objectives:** To evaluate the efficacy and safety of lurasidone vs. quetiapine XR (QXR) in preventing relapse in subjects with chronic schizophrenia. **Methods:** After completing an initial double-blind, placebo-controlled, 6 week trial with fixed doses of lurasidone (80 mg; 160 mg) or QXR (600 mg), subjects received 12 months of double-blind, flexible once-daily doses of lurasidone (40–160 mg) vs. QXR (200–800 mg). The primary a priori efficacy comparison was between subjects treated with lurasidone (n=139) and QXR (n=79) who were clinical responders after acute treatment. The primary endpoint, time-to-relapse, was analyzed using a Cox proportional hazards model, with a pre-specified non-inferiority margin for the risk of relapse hazard ratio of 1.93. **Results:** Lurasidone was non-inferior to QXR in risk for relapse over the 12 month treatment period (hazard ratio 0.728, 95% CI [0.410, 1.295]). The risk of relapse in lurasidone treated subjects was reduced by 27.2% (hazard ratio 0.728) compared with QXR. The Kaplan-Meier estimate of the probability of relapse at 12 months was lower for lurasidone vs. QXR (0.237 vs. 0.336). Treatment with lurasidone (modal daily dose 120 mg) was associated with a significantly greater change in PANSS total scores compared with QXR (modal dose 600 mg) on an MMRM analysis. Rates of adverse events occurring in at least 5% of subjects in the lurasidone group were akathisia (12.6%), headache (10.6%), insomnia (7.9%), anxiety (6.0%), parkinsonism (6.0%), and weight increased (6.0%). Analysis of changes from

acute study baseline to 12 months of treatment (OC) with lurasidone and QXR, respectively, showed a mean change in weight of +0.7 vs. +1.2 kg; a median change in glucose of +1.0 vs. +1.0 mg/dL; a median change in cholesterol of 0.0 vs. +4.0 mg/dL; and a median change in triglycerides of -18.0 vs. -7.0 mg/dL. There were no clinically meaningful changes in other laboratory or ECG parameters on either drug. Conclusions: This long-term, double-blind study demonstrated non-inferiority of lurasidone to QXR in prevention of relapse over a 12 month period, with a 27.2% reduction in relapse risk compared with QXR. Treatment with lurasidone was associated with few adverse effects on metabolic parameters, and a minimal effect on weight. Funded by Sunovion Pharmaceuticals, Inc.

**NR6-37**  
**LONG-TERM SAFETY AND EFFECTIVENESS OF LURASIDONE IN SCHIZOPHRENIA: RESULTS OF A 22 MONTH, OPEN-LABEL EXTENSION STUDY**

*Chair: Robert Silva Ph.D.; Author(s): Christoph Correll, M.D.; Doreen Simonelli, Ph.D.; Joseph Severs, M.S.; Josephine Cucchiaro, Ph.D.; Antony Loebel, M.D.*

**SUMMARY:**

Objective: To evaluate the safety, tolerability, and effectiveness of lurasidone in the long-term treatment of subjects with a DSM-IV diagnosis of schizophrenia. Methods: Subjects who completed a multiregional, 6 week, double-blind (DB), placebo-controlled trial continued in a 22 month open-label (OL) study during which they received once-daily, flexible-doses of lurasidone, 40-120 mg. Results: In an observed case [OC] analysis of the safety sample (n=250), treatment with lurasidone was associated with a mean change, from DB baseline, in weight of +0.45 kg at Month 12 (n=99), and +0.7 kg at Month 24 (n=67). Median change from DB baseline to Month 12 and Month 24, respectively, was -1.0 and -9.0 mg/dL for total cholesterol; 0.0 and -1.0 mg/dL for LDL; +1.0 and -11.0 mg/dL for triglycerides; +4.0 and +2.0 mg/dL for glucose; 0.0 and +0.1 % for HbA1c; and -1.3 and -1.1 ng/mL for prolactin. The mean PANSS total score was 69.5 at OL baseline. The mean (95% CI) change from OL baseline in the PANSS total score at 12 months was -8.0 (-11.3, -4.7), and at 24 months was -12.3 (-16.2, -8.4). The mean daily dose of lurasidone during OL treatment was 91.8 mg, and the proportion of subjects with modal daily doses were 13% for 40 mg, 42% for 80 mg, and 45% for 120 mg. The proportion of subjects who discontinued was 48.6% at Month 6, 63.3% at Month 12, and 73.3% at Month 24. Thirty-seven subjects (14.7%)

discontinued due to an AE during the course of OL treatment. Three AEs occurred in =10%: schizophrenia (12.4%), akathisia (10.8%) and somnolence (10.8%); and 19.2% reported at least one movement disorder-related AE. Conclusion: In this 22 month open-label extension study, treatment with lurasidone was associated with minimal effects on weight, glucose, and lipids. No clinically meaningful changes in prolactin or movement disorder symptoms were observed. Subjects demonstrated sustained improvement in the PANSS total score for up to 24 months of treatment with flexible doses of lurasidone in the range of 40-120 mg, administered once-daily. Funded by Sunovion Pharmaceuticals Inc.

**NR6-38**  
**ADDING LISDEXAMFETAMINE DIMESYLATE TO ANTIPSYCHOTICS: DOES FUNCTIONAL CAPACITY IMPROVE IN TANDEM WITH NEGATIVE SYMPTOMS OF SCHIZOPHRENIA?**

*Chair: Jean-Pierre Lindenmayer M.D.; Author(s): Robert Lasser, M.D.; Bryan Dirks, M.D.; Philip Harvey, Ph.D.; Courtney Kirsch, BS; Jianwong Wang, Ph.D.; Michael Pucci, Ph.D.; Brian Scheckner, Phar M.D.; Henry Nasrallah, M.D.*

**SUMMARY:**

Objective: To examine efficacy, safety, and effects on functional life skills of lisdexamfetamine dimesylate (LDX), a prodrug of d-amphetamine, for treatment of predominant negative symptoms of schizophrenia (NSS) in clinically stable adults on atypical antipsychotics. Methods: Outpatients with stable schizophrenia ( $\geq 2$ y) with predominant NSS (SANS-18 [items 1-6, 8-12, 14-16, 18-21] score  $\geq 55$ , score  $\geq 3$  on  $\geq 2$  SANS global items and PANSS positive score  $< 20$ ) maintained on antipsychotics ( $\geq 12$ wks) underwent 10-wk open-label (OL) LDX augmentation (20-70mg/d). Eligible participants (any SANS-18 improvement at wk 10) entered a 4-wk, double-blind, placebo-controlled randomized withdrawal (RW; wk 10-14). Efficacy measures included SANS-18 (primary) and PANSS subscales. The present analysis examined change in functional capacity using the University of California Performance-Based Skills Assessment, Brief Version (UPSA-B), total, communications, and finances subscale. Safety evaluations included treatment-emergent adverse events (TEAEs) and Calgary Depression Scale for Schizophrenia (CDSS). Results: 92 adults received OL LDX; 23 discontinued OL and 69 entered RW (LDX, n=34; placebo, n=35); 13 discontinued during RW (LDX, n=7; placebo, n=6). From mean (SD) baseline scores of 67.3 (18.04), 32.7 (10.04), and 34.6 (10.94) for UPSA-B total, communications, and finances

scores, OL (wk 0-10; last observation carried forward [LOCF]) mean changes (95% confidence intervals [CIs]) were 6.2 (3.5, 8.9), 3.7 (1.8, 5.5), and 2.5 (0.9, 4.1), respectively ( $P \leq .0028$  for all). During RW, no meaningful differences were noted between LDX and placebo for change from randomization baseline to endpoint in UPSA-B scores; UPSA-B scores did not return to OL baseline for LDX or placebo groups. At OL baseline (wk 0), mean (SD) SANS-18 score was 60.2 (4.36). Mean change (95% CI) in SANS-18 score (wk 0-10 [OL]; LOCF) was -12.9 (-15.0, -10.8) (primary endpoint,  $P < .0001$ ). PANSS positive score mean change (95% CI) during OL phase (wk 0-10; LOCF) was -1.0 (-1.4, -0.5;  $P < .0001$ ). In the OL phase, TEAEs were reported in 60.9% (56/92) of participants; serious TEAEs occurred in 3.3% (3/92). In the OL phase, TEAEs with incidence  $\geq 5\%$  were headache (14.1%), decreased appetite (10.9%), insomnia (10.9%), dizziness (8.7%), dry mouth (6.5%), and diarrhea (5.4%). During RW phase, TEAEs were reported in 32.4% (11/34) and 20.0% (7/35) in LDX and placebo groups, respectively; serious TEAEs occurred in 3 participants. There was no meaningful change in CDSS (wk 0-14) for LDX or placebo. Conclusion: There was an overall substantial improvement in performance-based assessment of functional life skills after open-label adjunctive LDX treatment accompanied by improvement in NSS without worsening of positive symptoms. Randomized withdrawal of LDX over 4 weeks did not result in return to baseline functioning for these measures of functional capacity.

**NR6-39**  
**SAFETY AND TOLERABILITY OF SWITCHING TO ASENAPINE FROM OTHER ANTIPSYCHOTIC AGENTS IN STABLE PATIENTS WITH PERSISTENT NEGATIVE SYMPTOMS**

*Chair: Armin Szegedi M.D.; Author(s): Pilar Cazorla Ph.D., Mary Mackle Ph.D., Jun Zhao Ph.D., Xianwei Ha Ph.D.*

**SUMMARY:**

**Objective:** In chronic conditions such as schizophrenia it is common clinical practice to switch between different antipsychotic medications to optimize treatment outcomes. The aim of this study was to evaluate the safety and tolerability of switching stable patients from a variety of antipsychotics to asenapine (ASE) or olanzapine (OLA) monotherapy using regimens similar to clinical practice. **Method:** This post hoc analysis incorporates pooled results from 2 randomized, double-blind, multicenter clinical trials (NCT00145496

and NCT00212836) and assesses safety profiles of ASE and OLA monotherapy as switch therapies from other antipsychotics for the treatment of persistent negative symptoms of schizophrenia. Patients were clinically stable, as shown by positive symptom control on their previous antipsychotic(s) medication(s) for at least 5 months prior to screening plus a further 30-day prospective observation period. Subjects were randomized to ASE 5mg bid (n=485) or OLA 10mg qd (n=464) for 1 wk, then 5–10mg bid or 5–20mg qd and previous antipsychotic(s) were tapered off at variable speed at investigator's discretion (maximum tapering period-28 days followed by monotherapy-a total of 26 wks of treatment). **Results:** Median time to taper off previous antipsychotic(s) was 7 days. More than 40% of patients in both treatment groups switched on the first day of study drug. 76.9% of switched patients in the ASE group and 75.2% in the OLA group reported at least 1 treatment emergent adverse event (AE) during the in-treatment period. Most frequently reported AEs were somnolence (ASE:14.0%,OLA:14.6%), headache (ASE:14.9%,OLA:11.0%), insomnia (ASE:14.9%,OLA:9.9%), and weight gain (ASE:7.6%,OLA:20.9%). Most AEs occurred in the first 28 days of treatment (ASE:53.1%,OLA:49.3%) and the majority were mild or moderate. 11.6% of patients in the ASE group and 6.0% in the OLA group experienced at least 1 SAE over the full treatment period mostly relating to the underlying disease. 15.8% in the ASE group and 10.6% in the OLA group discontinued due to AE/SAE and 4.1% of ASE and 2.7% of OLA patients due to lack of efficacy. AE rates reported over the first 28 days for rapid (=3 days) vs. slow tapered switching (=14 days) were 48.8% and 52.4% for ASE and 50.3% and 44.5% for OLA. Similar AE rates were reported over the full treatment period when switching from first- or second-generation antipsychotics to ASE (75.5%,76.9%) or OLA (79.7%,75.2%) and greater when switched from a depot medication (ASE: 85.0%,OLA 86.8%). **Conclusions:** Switching to ASE from other antipsychotic was generally well tolerated across a variety of switching techniques in patients with schizophrenia with persistent negative symptoms and showed comparable results to OLA. **Educational Objective:** After studying this material, the participant should be able to identify the relative merits of switching patients with persistent negative symptoms of schizophrenia to either ASE or OLA. Study funded by Merck.

**NR6-40**  
**DOSE-RESPONSE MODEL OF LURASIDONE TREATMENT IN SCHIZOPHRENIA**

*Chair: Sunny Chapel Ph.D.; Author(s): Yu-Yuan Chiu,*

*Ph.D.; Jay Hsu, Ph.D.; Jane Xu, Ph.D.; Josephine Cucchiaro, Ph.D.; Antony Loebel, M.D.*

### SUMMARY:

Objective: Characterization of dose-response relationships for new psychotropic agents may be difficult to determine based on results of individual clinical trials, due to various confounds such as variability in attrition and placebo-response rates. As a consequence, post-marketing changes in recommended therapeutic dosing ranges for antipsychotic drugs are not uncommon. The goal of this exposure-response analysis was to more precisely clarify dose-response effects for lurasidone. Method: Data were pooled from five 6-week, randomized, double-blind, placebo-controlled, once-daily, fixed-dose studies of lurasidone in the dosing range of 40-160 mg for the treatment of an acute exacerbation of schizophrenia. The PANSS and exposure data were fitted using the nonlinear mixed effects modeling methodology implemented in the NONMEM software (Version VI). Results: In the final exposure-response model, LS mean change-from-baseline in PANSS exhibited a linear trend relative to dose of lurasidone. The 160 mg dose provided the greatest clinical benefit in terms of PANSS reduction relative to lower doses. In addition, the 120 mg dose produced improvement in PANSS that was intermediate between 80 mg and 160 mg. LS mean change in PANSS exhibited a linear trend relative to dose on treatment days 14, 28, 35, and 42. A time effect rate analysis indicated that 50% of the reduction in PANSS total score observed during acute treatment for each dose group occurred at 9 days. Between-study variability in clinical response was evident in the placebo group, but not in the lurasidone group, and was contributed to by demographic covariates (e.g., age, weight, race). A log-linear hazard model indicated that patients were more likely to drop out when baseline PANSS scores were higher, and during the initial hospitalization period. However, dropout rate was not correlated with dose of lurasidone. Conclusion: The effect of lurasidone was described using a linear dose-response model for drug effect, with increased treatment response observed at higher doses of lurasidone. Attrition was not correlated with lurasidone dose. This research was funded by Sunovion Pharmaceuticals Inc.

### NR6-41

#### EFFICACY OF ARIPIPRAZOLE INTRAMUSCULAR DEPOT (ARI-IM-DEPOT) FOR THE LONG-TERM MAINTENANCE TREATMENT OF SCHIZOPHRENIA

*Chair: John Kane M.D.; Author(s): Raymond Sanchez,*

*M.D.; Pam Perry, M.S.; Na Jin, M.S.; Brian Johnson, M.S.; Robert A. Forbes, Ph.D.; Robert D. McQuade, Ph.D.; William H. Carson, M.D.; Wolfgang Fleischbaker, M.D.*

### SUMMARY:

Objective: To evaluate the efficacy and tolerability of once-a-month aripiprazole intramuscular depot (ARI-IM-depot), a dopamine partial agonist, for maintenance treatment in adults with schizophrenia. Methods: Subjects requiring chronic treatment with an antipsychotic were eligible and subjects not already on aripiprazole monotherapy were cross-titrated during weekly visits from other antipsychotic(s) to oral aripiprazole monotherapy during the 4-6 weeks oral conversion phase (Phase 1). All subjects entered a 4-12-week oral stabilization phase (Phase 2) and received oral aripiprazole (10-30 mg/day). Subjects meeting stability criteria for 4 weeks then entered an intramuscular depot stabilization phase (Phase 3), wherein they received ARI-IM-depot injections every 4 weeks (400 mg, single decrease to 300 mg permitted) with co-administration of oral aripiprazole tablets in the first 2 weeks. Subjects meeting stability criteria for 12 consecutive weeks were randomized (2:1) to ARI-IM-depot or placebo during a 52-week, double-blind maintenance phase (Phase 4). The primary endpoint was time to impending relapse. Safety and tolerability were also assessed. Results: Seven hundred and ten subjects entered the oral stabilization phase, 576 progressed to ARI-IM-depot stabilization and 403 patients were randomized to double-blind, placebo-controlled treatment. The study was stopped early because efficacy was demonstrated by the pre-planned interim analysis (conducted after 64 relapses). Time-to-impending relapse was significantly delayed in ARI-IM-depot compared with placebo in both interim and final analyses ( $p < 0.0001$ , log-rank test). The rate of impending relapse was significantly lower with ARI-IM-depot than placebo at endpoint (final analysis 10.0%,  $n = 27/269$  vs. 39.6%,  $n = 53/134$ ; hazard ratio [HR], 5.0; 95% confidence interval [CI], 3.15-8.02,  $p < 0.0001$ ). Improvements in Positive and Negative Syndrome scale (PANSS) Total score were maintained with ARI-IM-depot treatment but showed significant worsening with placebo (mean change at Week 52: PANSS, ARI-IM-depot = 1.4, placebo = 11.6,  $p < 0.0001$ ). Additionally, Clinical Global Impression of severity (CGI-S) scores showed significant differences favoring ARI-IM-depot ( $p < 0.0001$ ). The most common treatment-emergent adverse events (AEs occurring = 5% of aripiprazole-treated subjects and greater than placebo) were insomnia (10.0% vs. 9.0%), tremor (5.9% vs. 1.5%), and headache (5.9% vs. 5.2%), respectively. Most AEs were mild or moderate in severity. The

incidence of injection site pain in the ARI-IM-depot stabilization phase was 5.9%, while in the ARI-IM depot maintenance phase was, respectively, 3.0% vs. 3.7% for ARI-IM-depot compared with placebo. Conclusions: ARI-IM-depot significantly delayed time to impending relapse compared with placebo and was a well-tolerated maintenance treatment option in schizophrenia.

#### NR6-42

### PATIENT-REPORTED OUTCOMES WITH ARIPIRAZOLE INTRAMUSCULAR DEPOT (ARI-IM-DEPOT) FOR LONG-TERM MAINTENANCE TREATMENT IN SCHIZOPHRENIA

*Chair: Raymond Sanchez M.D.; Author(s): Brian Johnson, M.S.; Na Jin, M.S.; Robert A. Forbes, Ph.D.; William Carson, M.D.; Robert McQuade, Ph.D.; John M. Kane, M.D.; Wolfgang Fleischhacker, M.D.*

#### SUMMARY:

**Objective:** To characterize the adherence profile of ARI-IM-depot by examining patient-reported outcomes from a long-term treatment trial of pts with schizophrenia. **Methods:** Pts requiring chronic treatment with an antipsychotic were eligible. Pts not already on ARI monotherapy were cross-titrated during weekly visits from other antipsychotic(s) to oral ARI monotherapy during a 4–6-week oral conversion phase (Phase 1). Subjects entered a 4–12-week oral stabilization phase (Phase 2) and received oral ARI (10–30 mg/day). Subjects meeting stability criteria for 4 weeks then entered an intramuscular depot stabilization phase (Phase 3) in which they received 400 mg ARI-IM-depot injections every 4 weeks (single decrease to 300 mg permitted) with co-administration of oral ARI oral tablets in the first 2 weeks. Subjects meeting stability criteria for 12 consecutive weeks were randomized (2:1) to ARI-IM-depot or placebo during a 52-week, double-blind maintenance phase (Phase 4). Mean changes in patient-reported outcomes were assessed from baseline to last visit in Phases 2–4 using the Drug Attitude Inventory (DAI)<sup>1</sup>, Medication Adherence Questionnaire (MAQ)<sup>2</sup>, and the Patient Satisfaction with Medication Questionnaire (PSMQ) modified<sup>3</sup>. **Results:** 710 pts entered oral stabilization (633 of which had been titrated to oral ARI during Phase 1); 576 progressed to intramuscular depot stabilization and 403 pts were randomized to double-blind treatment. The study was stopped early because efficacy was demonstrated by the pre-planned interim analysis (conducted after 64 relapses). Between Phases 2–4 mean DAI scores remained similar across phases (Phase 2, 21.5; Phase 3, 21.4; Phase 4, 21.1

ARI-IM-depot vs. 22.2 placebo) indicating a positive (adherent) attitude towards medication. Mean MAQ scores were between 0–1 indicating high adherence behavior. PSMQ scale scores were assessed for Phases 3–4 and showed that the percentage of pts with high levels of treatment satisfaction between baseline and last visit, respectively, was Phase 3: 97.0% vs. 92.8%; Phase 4 ARI-IM-depot: 97.0% vs. 92.7%; Phase 4 placebo: 96.2% vs. 85.0%. The percentage of pts with a preference for the current medication between baseline and last visit, respectively, was also high (Phase 3: 93.4% vs. 89.1; Phase 4 ARI-IM-depot: 94.8% vs. 86.2%; Phase 4 placebo: 97.7% vs. 85.7%). Finally, there was a sustained percentage of pts reporting less to no side-effects between baseline and last visit, respectively, Phase 3: 88.0% vs. 86.9%; Phase 4 ARI-IM-depot: 90.3% vs. 88.9%; Phase 4 placebo: 92.6% vs. 89.0%. **Discussion:** ARI-IM-depot offers a new treatment option for the long-term management of schizophrenia with the potential to improve adherence to medication resulting from improved patient-reported outcomes and medication satisfaction. **References** 1. Hogan T, et al. *Psychol Med* 1983;13:177–183. 2. Morisky D, et al. *Med Care* 1986;24:67–74. 3. Kalali A. *Curr Med Res Opin* 1999;15:135–137.

#### NR6-43

### EFFECT OF 12 MONTHS OF LURASIDONE ON WEIGHT IN SUBJECTS WITH SCHIZOPHRENIA

*Chair: Jonathan Meyer M.D.; Author(s): Yongcai Mao, Ph.D.; Andrei Pikalov, M.D., Ph.D.; Josephine Cucchiaro, Ph.D.; Antony Loebel, M.D.*

#### SUMMARY:

**Objective:** Individuals with schizophrenia have an increased prevalence of obesity (Newcomer et al, *CNS Drugs*. 2005;19 (suppl 1):1-93). Furthermore, notable differences have been reported among atypical antipsychotics in effects on weight (ADA et al, *J Clin Psych* 2004;65:267-72). The current study was conducted to evaluate the effect of 12 months of treatment with lurasidone on weight and body mass index (BMI) in subjects with schizophrenia. **Method:** A post-hoc, observed case (OC) analysis was performed on pooled data from 6 clinical studies that evaluated the safety of 12 months of treatment with lurasidone (40-120 mg/day). **Results:** The analysis sample consisted of 371 subjects who completed 12 months of treatment with lurasidone (mean age, 42 years; male, 67%; white, 31%; black, 25%, Asian, 40%; other, 4%). The mean (SD) weight at baseline was 74.0 (19.1) kg and the mean BMI was 25.9 (5.3) kg/m<sup>2</sup>, with 3.2% of subjects

meeting standard BMI criteria for being underweight, 48.8% normal weight, 26.4% overweight, and 21.6% obese. On an OC analysis, the mean change in weight was -0.7 kg at 3 months (n=370), -0.6 kg at 6 months (n=360), and -0.7 kg at 12 months (n=347). The mean change in BMI was -0.3 kg/m<sup>2</sup> at 3 months, -0.2 kg/m<sup>2</sup> at 6 months, and -0.2 kg/m<sup>2</sup> at 12 months. An increase of =7% in weight occurred in 2.7% of subjects at 3 months, 8.6% at 6 months, and 17.6% at 12 months. No dose-response effect was evident in the dosing range of 40 mg to 120 mg (23.4% to 14.1% with =7% increase in weight). However, clinically significant weight gain at 12 months was more common in subjects who were normal or underweight at baseline (22.8%) compared to subjects who were overweight (11.0%) or obese (12.5%). Overall, 6.3% of subjects shifted, by month 12, from the underweight/normal BMI category to the overweight category, and none to obese. Conversely, 7.5% of subjects shifted, by month 12, from overweight to normal weight. Conclusion: The results of this pooled analysis of 371 subjects who completed 12 months of treatment suggest that lurasidone is associated with a low potential for clinically significant weight gain. No dose-related effect on weight was evident. Funded by Sunovion Pharmaceuticals, Inc.

**NR6-44**  
**EFFECTS OF A LONG-ACTING INJECTABLE FORMULATION OF ARIPIPRAZOLE ON SECONDARY EFFICACY OUTCOMES IN MAINTENANCE TREATMENT OF SCHIZOPHRENIA**

*Chair: William Carson M.D.; Author(s): Pam Perry, M.S.; Raymond Sanchez, M.D.; Na Jin, M.S.; Robert A. Forbes, Ph.D.; Robert McQuade, Ph.D.; Wolfgang Fleischhacker, M.D.; John Kane, M.D.*

**SUMMARY:**

**Objective:** To evaluate the secondary efficacy outcomes from a clinical trial of a once-monthly intramuscular depot formulation of aripiprazole (ARI-IM-depot) as maintenance treatment in adults diagnosed with schizophrenia. **Methods:** Subjects requiring chronic treatment with an antipsychotic were eligible and subjects not already on aripiprazole monotherapy were cross-titrated during weekly visits from other antipsychotic(s) to oral aripiprazole monotherapy during a 4–6-week oral conversion phase (Phase 1). All subjects entered a 4–12-week oral stabilization phase (Phase 2) and received oral aripiprazole (10–30 mg/day). Subjects meeting stability criteria for 4 weeks then entered an intramuscular depot stabilization phase (Phase 3), wherein they received ARI-IM-depot

injections every 4 weeks (400 mg, single decrease to 300 mg permitted) with co-administration of oral aripiprazole tablets in the first 2 weeks. Subjects meeting stability criteria for 12 consecutive weeks were randomized (2:1) to ARI-IM-depot or placebo during a 52-week, double-blind maintenance phase (Phase 4). Secondary efficacy assessments included mean changes in the Personal and Social Performance scale scores, mean changes in Positive and Negative Syndrome Scale (PANSS) positive and negative scores and mean change in the Investigator's Assessment Questionnaire (IAQ) scores, a scale designed to evaluate response to antipsychotics. Results: Seven-hundred-ten patients entered oral stabilization, 576 progressed to ARI-IM-depot stabilization and 403 patients were randomized to double-blind treatment. The study was stopped early because efficacy was demonstrated by the pre-planned interim analysis (conducted after 64 relapses). Mean changes in Personal and Social Performance (PSP) scale scores (LOCF) showed improvement during the oral (3.0) and ARI-IM-depot stabilization (2.6) phases. Mean change in PSP scores during double-blind treatment showed greater functional stability with ARI-IM-depot (-1.7) than placebo (-6.2) (p=0.0002 vs. placebo). Mean PANSS Positive and Negative subscale scores (LOCF) improved during the oral (-2.1 and -1.2, respectively) and ARI-IM-depot stabilization phases (-1.0 and -1.2). Mean change during double-blind treatment in PANSS Positive (Week 52 LOCF, 0.4 vs. 4.3; p<0.0001) and Negative (Week 52 LOCF, 0.2 vs. 1.6; p<0.0001) subscale scores all showed symptom stability with ARI-IM-depot treatment but showed significant worsening with placebo. Mean IAQ total score also remained stable (Phase 2, 31.3; Phase 3, 30.6). During double-blind treatment, the mean change was +1.3 for ARI-IM-depot vs. +3.8 for placebo (p<0.0001). Conclusions: Improvements in symptoms, functioning and overall response to treatment were achieved during stabilization and maintained in patients during Phase 4. ARI-IM-depot, thus, offers a new option for maintenance therapy of schizophrenia with a different risk–benefit profile than currently available treatments.

**NR6-45**  
**ECONOMIC IMPACT OF RELAPSE-RELATED HOSPITALIZATION IN ADULTS WITH SCHIZOPHRENIA USING DATA FROM 12-MONTH DOUBLE-BLIND LURASIDONE VS QUETIAPINEXR STUDY**

*Chair: Krithika Rajagopalan Ph.D.; Author(s): Ken O'Day, Ph.D., M.P.A.; Kellie Meyer, Phar M.D., M.P.H.; Jay Hsu, Ph.D.; Andrei Pikalov, M.D., Ph.D.*

**SUMMARY:**

Objective: To model the economic impact of annual relapse-related hospitalizations among adults with schizophrenia treated with lurasidone (LUR) or quetiapine extended-release (QXR). Method: A probabilistic model, estimating per-patient-per-year (PPPY) direct mental-health-care-cost differences due to relapse-related hospitalizations, was developed using data from a multi-regional, 12-month, double-blind, parallel-group comparison study of LUR vs QXR (all patients previously treated with LUR or QXR for 6 weeks). Observed relapse-related hospitalization rates at 12 months were used to model the costs for two cohorts: 1) ALL patients receiving LUR (7.3%, n=151) and QXR (17.6%, n=85), and 2) Clinical Responders (CR) to either LUR 80 or 160 mg/day (7.2%, n=139) or QXR 600 mg/day (16.5%, n=79) that showed  $\geq 20\%$  improvement in PANSS total score and CGI-S score  $\geq 4$  at Day 42. Total direct mental-health-care-costs (inflated to 2011 USD) for relapsing and non-relapsing patients were calculated for categories including psychiatric hospitalizations, emergency services, medication management, and outpatient individual therapy per Ascher-Svanum 2010. Model robustness was tested using a uni-variate sensitivity analysis and a probabilistic sensitivity analysis of 1000 simulations using distributions of model parameters from reported 95% confidence intervals (CI). Results: Model estimated PPPY direct mental-health-care-costs for: 1) ALL LUR patients of \$21,025 (95% CI: \$20,059, \$21,979) and ALL QXR patients of \$24,301 (95% CI: \$22,479, \$26,295); and for 2) CR LUR patients of \$21,069 (95% CI: \$20,051, \$22,040) and ALL QXR patients of \$23,956 (95% CI: \$22,181, \$25,799). PPPY cost savings for ALL patients (LUR compared with QXR) were -\$3,277 (95% CI: -\$4,658, -\$2,111) and for CR patients (LUR compared with QXR) were -\$2,888 (95% CI: -\$4,256, \$1,696). Sensitivity analyses suggest cost savings with LUR were primarily driven by cost of hospitalizations and that LUR had lower PPPY costs than QXR in 100% of simulations for both ALL and CR patients. Conclusions: Adults with schizophrenia treated with LUR have lower annual direct mental-health-care-costs than those treated with QXR due to fewer relapses and relapse-related hospitalizations in this study. Model results may help payers in differentiating the real-world economic value of these agents. Funded by Sunovion Pharmaceuticals Inc.

**NR6-46****SWITCHING TO LURASIDONE IN PATIENTS WITH SCHIZOPHRENIA: TOLERABILITY****AND EFFECTIVENESS OF THREE SWITCH STRATEGIES**

*Chair: Joseph Mcevoy M.D.; Author(s): Joseph P. McEvoy, M.D.; Leslie Citrome, M.D, M.P.H.; David Hernandez, B.A.; Joseph Severs, M.S.; Josephine Cucchiaro, Ph.D.; Antony Loebel, M.D.*

**SUMMARY:**

Objective: To evaluate the effectiveness of switching clinically stable, but symptomatic non-acute patients with schizophrenia or schizoaffective disorder to lurasidone. Method: Non-acute patients who met DSM-IV criteria for schizophrenia or schizoaffective disorder and who were considered to be appropriate candidates for switching current antipsychotic medication to lurasidone, were randomized to three switch strategies: a 40/40 group (n=74) was started on a dose of 40 mg/d for 2 weeks; a 40/80 group (n=88) was started on a dose of 40 mg/d for 7 days, then increased to 80 mg/d for 7 days; and an 80/80 group (n=82) was started on a dose of 80 mg/d for 14 days. All patients were then treated for an additional 4 weeks with lurasidone 40-120 mg/d, flexibly dosed. The prior antipsychotic agent was tapered and discontinued over the initial 2-week study period. Patients were stratified based on whether the primary pre-switch antipsychotic was sedating (olanzapine, quetiapine) or non-sedating (all others). Time to treatment failure was evaluated, defined as insufficient clinical response, exacerbation of underlying disease or discontinuation due to an adverse event (AE). Safety parameters were also assessed. Results: Switching to lurasidone was well-tolerated with 81.1% completing the 6-week study. No clinically relevant differences in efficacy or tolerability were noted when comparing the 3 different switch strategies. Time to treatment failure numerically differed among patients who had been receiving a sedating antipsychotic (35.8% of the total) immediately prior to the switch to lurasidone compared to those who were receiving a non-sedating antipsychotic (log rank p=0.101), with a treatment failure rate of 11.6% vs. 5.8%, respectively. Treatment with lurasidone was associated with LS mean within-group improvement at endpoint on the PANSS of -5.8 (95% -CI, -7.0, -4.5; Cohen's d, 0.5). For the total sample, treatment with lurasidone was associated with -0.3 kg mean decrease in weight, and a median reduction in both cholesterol (-1.0 mg/dL) and triglycerides (-6.0 mg/dL). Conclusions: Switching to lurasidone was well-tolerated using a cross taper strategy regardless of initial dose used or rate of titration. Patients switching to lurasidone demonstrated clinically relevant improvement in efficacy measures, and reduction in weight and lipids. This research was funded

by Sunovion Pharmaceuticals, Inc.

#### NR6-47

### ASSESSING MEDICATION ADHERENCE AND HEALTHCARE UTILIZATION AND COSTS PATTERNS AMONG HOSPITAL DISCHARGED PATIENTS WITH SCHIZOAFFECTIVE DISORDER

*Chair: Michael Markowitz M.D.; Author(s): Sudeep Karve, Ph.D. Dong Jing Fu, M.D., Ph.D. Jean-Pierre Lindenmayer, M.D. Chi-Chuan Wang, Ph.D. Sean D. Candrilli, Ph.D. Larry Alphas, M.D., Ph.D.*

#### SUMMARY:

Educational Objectives: At the conclusion of this presentation, the participant should be able to understand patterns in medication adherence and healthcare utilization at various clinically relevant pre-admission and post-discharge periods among patients experiencing schizoaffective disorder-related inpatient admission. Purpose: Following hospital discharge, patients with schizoaffective disorder have a high likelihood of rehospitalization. The objective of this study was to assess patterns in psychotropic medication adherence and healthcare utilization and costs during clinically relevant pre-admission (in 60-day intervals, over 6-months) and post-discharge periods (in 60-day intervals, over 12-months) among patients with schizoaffective disorder. Methods: We conducted a retrospective cohort analysis of the MarketScan Medicaid database (2004-2008). Patients with an inpatient admission for schizoaffective disorder and continuous health plan enrollment were included. Medication (antipsychotics, antidepressants and mood stabilizers) adherence (proportion of days covered [PDC]) and all-cause and schizoaffective disorder-related healthcare utilization and costs were assessed during the pre-admission and post-discharge periods. Healthcare utilization and costs (2010 US\$) were compared between each adjacent 60-day post-discharge period using univariate and multivariate regression analyses. No adjustment was made for multiplicity. Results: Among 1,193 patients included, 39% were male, 43% black, and 92% were 'discharged to home for self-care' following an inpatient admission. Medication adherence rates declined in the pre-admission periods (182-121 days:65%; 120-61 days:49%; 60-0 days:46%). Compared to the 60-day pre-admission period (46%), the adherence rate increased in the initial 60-day post-discharge period (80%) and remained relatively stable in the remaining five 60-day post-discharge periods (range: 58%-63%). Both schizoaffective disorder-related (mean: \$2,370 vs.

\$1,765;  $p < 0.001$ ) and all-cause (mean: \$5,277 vs. \$4,310;  $p < 0.001$ ) healthcare costs were significantly higher in the initial 0-60 day post-discharge period compared with the adjacent 61-120 day post-discharge period. The primary drivers of schizoaffective disorder-related costs in the 0-60 day post-discharge period were rehospitalization (mean: \$860; SD: \$3,923) and pharmacy (mean: \$954; SD: \$926). Both all-cause and schizoaffective disorder-related costs declined and remained stable after the initial 60-day post-discharge period. Conclusion: We observed a high rate of rehospitalization during the initial 60-day post-discharge period compared with the 61-120 day post-discharge period among patients with schizoaffective disorder. The medication adherence and resource utilization patterns outlined in our study should help identify high-risk patients and aid in the designing of interventions that may help reduce the likelihood of inpatient admissions and the associated downstream

#### NR6-48

### I-FANS STUDY DESIGN TO EVALUATE ILOPERIDONE 12-24MG/D AFTER GRADUAL OR IMMEDIATE ANTIPSYCHOTIC SWITCH IN SUBOPTIMALLY TREATED SCHIZOPHRENIA PATIENTS

*Chair: Peter Weiden M.D.; Author(s): Leslie Citrome, M.D., M.P.H., Farid Kianifard, Ph.D., Linda Pestreich, Adam Winseck, Ph.D., Marla Hochfeld, M.D.*

#### SUMMARY:

Objective: Completing a successful switch in atypical antipsychotic treatments to achieve optimal therapeutic outcomes for the patient with schizophrenia is a frequent but not fully understood issue. We describe the design of an ongoing 12-week randomized, multicenter, open-label trial evaluating clinical outcomes with iloperidone following 2 switching approaches (gradual or immediate) in adults with schizophrenia exhibiting suboptimal efficacy and/or safety/tolerability from their current antipsychotic treatment of olanzapine, risperidone, or aripiprazole. Iloperidone is a D2 and 5-HT<sub>2A</sub> antagonist antipsychotic indicated for the treatment of schizophrenia in adults. Methods: A total of 501 patients were randomized (1:1 to gradual or immediate switch) in 3 approximately equally sized cohorts that were defined by patients' current antipsychotic treatment (olanzapine, n=157; risperidone, n=174; aripiprazole, n=170). Patients are adults (aged 18-64 y) diagnosed with schizophrenia and experiencing inadequate efficacy and/or poor tolerability due to extrapyramidal symptoms (EPS)/akathisia, elevated prolactin, weight gain, somnolence/sedation, agitation, or anxiety on current treatment

with olanzapine, risperidone, or aripiprazole for =30d. Key exclusionary criteria are: other current primary Axis I disorder, pregnancy, chemical dependency within 6 months, failed drug screen, QTcF >450 ms for men or >470 for women, risk of suicide, and/or nonstable antidepressant dose. Patients in these cohorts will be switched to iloperidone either by (a) immediate discontinuation of current treatment at baseline (BL; Day 0) or (b) gradual discontinuation by reducing current treatment to 50% on Day 1, 25% at Week 1, and 0% at Week 2. Patients will receive open-label iloperidone 1 mg twice daily (BID) on Day 1 titrated over 4 days to 6 mg BID, followed by increases up to 12 mg BID, if needed, during Weeks 2–12. The primary variable is the Integrated Clinical Global Impression of Change (I-CGI-C) and the primary analysis time point is Week 12. The secondary variables are changes from BL in Efficacy CGI of Severity (E-CGI-S), Safety and Tolerability CGI of Severity (ST-CGI-S), and Integrated CGI of Severity (I-CGI-S). Additional safety evaluations will consist of adverse event reporting (Weeks 1–12), vital signs (Screening–Week 12), weight (Screening–Week 12), ECGs (Screening and Week 1), physical exams (Screening and Week 12), and clinical laboratory evaluations (Screening and Week 12), with fasting glucose, lipids, and prolactin additionally assessed at Week 7. The Treatment Satisfaction Questionnaire for Medication (TSQM) will be assessed at BL and Week 12. Conclusion: This study design aims to contrast immediate and gradual switching approaches to inform clinicians of the efficacy, safety, and tolerability of iloperidone 12–24 mg/d in patients with schizophrenia requiring a change in therapy. Research support by Novartis Pharmaceuticals Corporation.

**NR6-49**  
**THE SCHIZOPHRENIA WITH CRIMINAL HISTORY SUBGROUP: ASSOCIATED CLINICAL AND NEUROCOGNITIVE CHARACTERISTICS**

*Chair: Giovanna Musso Ph.D.; Author(s): Pamela DeRosse, Ph.D.; Sherif Abdelmessih, MA; James Riley, MA; Katherine Burdick, Ph.D.; Jean-Pierre Lindenmayer, M.D.; Anil Malhotra, M.D.*

**SUMMARY:**

Despite the wealth of empirical data characterizing patients diagnosed with schizophrenia, few studies have attempted to characterize the subgroup of schizophrenia patients with a criminal history. The present investigation aims to characterize this subgroup by using a sample of 137 relatively stable outpatients with a documented history of criminal activity. Subjects

were characterized based on a wide-range of variables, including clinical symptoms, diagnostic comorbidity, neurocognitive function, history of childhood trauma, and community functioning. Results were then compared to commonly reported findings for the general schizophrenia population. Statistical analyses showed that, when compared to empirical reports in the general schizophrenia population, schizophrenia patients with a criminal history had a higher comorbidity rate of substance use disorders and lower comorbidity rates of anxiety and mood disorders. They also performed significantly worse on several areas of neurocognitive function. Secondary analyses were conducted to examine possible differences between subjects with a violent criminal history versus a non-violent criminal history. Additional characteristics are examined. These data as well as the similarities versus differences observed are discussed.

**NR6-50**  
**SAFETY AND TOLERABILITY OF CARIPRAZINE IN THE LONG-TERM TREATMENT OF SCHIZOPHRENIA: RESULTS FROM A 48-WEEK EXTENSION STUDY**

*Chair: Andrew Cutler M.D.; Author(s): Anjana Bose, Ph.D., Suresh Durgam, M.D., Raffaele Migliore, MA, Qing Wang, Ph.D., Adam Ruth, Ph.D., György Németh, M.D., István Laszlovszky, M.D.*

**SUMMARY:**

Objective: Cariprazine is an orally active, potent dopamine D3-preferring D3/D2 receptor partial agonist under development for the treatment of schizophrenia. This open-label extension study evaluated the long-term safety, tolerability, and pharmacokinetics of cariprazine in patients with schizophrenia. Methods: Male and female patients with schizophrenia who completed 6 weeks of double-blind treatment with placebo, cariprazine 1.5, 3.0, 4.5 mg/day, or risperidone 4.0 mg/day in the lead-in study (NCT00694707) and responded to treatment (Clinical Global Impressions-Severity [CGI-S] <=3 and >=20% reduction in Positive and Negative Syndrome Scale [PANSS] total score at endpoint of the lead-in study) were eligible to enroll in this extension study (NCT00839852). The extension study comprised open-label treatment with flexible-dose cariprazine 1.5–4.5 mg/day for 48 weeks. Efficacy evaluations included PANSS and CGI-S scales. Safety evaluations included adverse events (AEs), vital signs, laboratory measures, ECG, ophthalmology examinations, and assessments on the Barnes Akathisia Rating Scale (BARS) and the Simpson-Angus Scale (SAS). Results: A total of 93 patients entered the

open-label extension study and received cariprazine; 49.5% completed 48 weeks of open-label treatment with cariprazine. The mean duration of treatment with cariprazine (days  $\pm$  SD) was  $221.7 \pm 132.7$ ; 46 patients (49.5%) were exposed to cariprazine for at least 1 year. In patients entering the extension study, PANSS and CGI-S scores decreased over the course of the study. Serious AEs (SAEs) were reported in 12 patients (12.9%) including 1 death (suicide) during the open-label treatment period. The most common SAEs were worsening of schizophrenia (4.3%) and psychotic disorder (2.2%). Treatment-emergent AEs (TEAEs) were reported in 77 patients (82.8%). TEAEs reported in at least 10% of patients were akathisia (14.0%), insomnia (14.0%), and weight increased (11.8%). Mean changes in clinical laboratory values, blood pressure and pulse rate, and ECG parameters were generally small. No potentially clinically significant (PCS) changes in ECG parameters were observed and no patients had a QTc increase  $>60$  msec. The incidence of treatment-emergent parkinsonism (SAS  $>3$ ) was 8.6% and the incidence of treatment-emergent akathisia (BARS  $>2$ ) was 17.2%. No patient discontinued because of movement disorder-related TEAEs. Conclusions: Cariprazine 1.5-4.5 mg/day administered for up to 1 year was generally well tolerated, with relatively few new AEs associated with long-term administration and no clinically meaningful changes in the majority of safety parameters. Supported by funding from Forest Laboratories, Inc. and Gedeon Richter Plc.

**NR6-51**  
**EFFICACY OF LURASIDONE IN**  
**SCHIZOPHRENIA: FACTOR ANALYSIS OF**  
**SHORT-TERM TRIALS**

*Chair: Josephine Cucchiaro Ph.D.; Author(s): Robert Silva, Ph.D.; Yongcai Mao, Ph.D.; Antony Loebel, M.D.; Stephen R. Marder, M.D.*

**SUMMARY:**

Objective: The 5-factor model derived from the PANSS scale is one of the most widely accepted approaches to a more differentiated evaluation of the efficacy of antipsychotic medication (Marder SR et al, J Clin Psychiatry 1997;58:538-546), and provides a comprehensive assessment of symptom domains relevant to functional status and long-term outcome of schizophrenia. The aim of the current analysis was to evaluate the efficacy of lurasidone across five previously validated PANSS factors (positive, negative, disorganized thought, hostility, and depression/anxiety). Method: A post-hoc factor analysis was performed on pooled data from 5 positive six-week, double-blind,

placebo-controlled trials of subjects hospitalized with an acute exacerbation of schizophrenia who were randomly assigned to fixed, once-daily doses of lurasidone 40 mg (n=290), 80 mg (n=334), 120 mg (n=290), 160 mg (n=121), or placebo (n=497). Data were analyzed using a mixed model repeated measures (MMRM) model with an unstructured covariance matrix. Effect sizes (ES) were calculated from an ANCOVA analysis (LOCF-endpoint) as the between-treatment group difference in LS mean change scores divided by the pooled standard deviation of the change scores. Results: Baseline characteristics were highly similar in the pooled lurasidone (n=1035; mean PANSS total score, 96.1) and placebo (n=497; mean PANSS total score, 96.1) groups. At endpoint, treatment with lurasidone was associated with significantly greater improvement in the PANSS total score compared with placebo (-22.6 vs. -12.8;  $P<0.001$ ; ES, 0.42). Significantly greater endpoint improvement ( $P<0.001$  for all comparisons) was observed for lurasidone versus placebo across all five PANSS factors. Changes for lurasidone vs. placebo were -8.4 vs. -6.0 (ES, 0.35) in the PANSS positive factor; -5.2 vs. -3.3 (ES, 0.32) in the PANSS negative; -4.9 vs. -2.8 (ES, 0.40) for disorganized thought; -2.7 vs. -1.6 (ES, 0.34) for hostility; and -3.2 vs. -2.3 (ES, 0.29) on depression/anxiety factors. Lurasidone 160 mg dose was consistently associated with the highest effect size for each factor. Conclusions: In this pooled, post hoc factor analysis of lurasidone placebo-controlled trials, treatment with lurasidone across the daily dosing range of 40-160 mg, was effective in improving all 5 PANSS factors, suggesting efficacy across the spectrum of symptoms associated with schizophrenia. Funded by Sunovion Pharmaceuticals Inc.

**NR6-52**  
**SAFETY AND TOLERABILITY OF**  
**LURASIDONE IN SEVEN SHORT-TERM**  
**SCHIZOPHRENIA TRIALS: A**  
**COMPREHENSIVE DATABASE ANALYSIS**

*Chair: Andrei Pikalov M.D.; Author(s): Josephine Cucchiaro, Ph.D.; Robert Silva, Ph.D.; Jay Hsu, Ph.D.; Jane Xu, Ph.D.; Peter Werner, Ph.D.; Antony Loebel, M.D.*

**SUMMARY:**

Objective: To evaluate the safety of lurasidone in short-term studies using a comprehensive analysis of pooled Phase 2/3 data. Methods: These analyses were based on combined multiregional data from seven 6-week, double-blind, placebo-controlled lurasidone trials of subjects who met DSM-IV criteria for schizophrenia with an acute exacerbation. The analysis sample consisted of subjects treated with

lurasidone (daily dose range, 20-160 mg; total N=1508); haloperidol 10 mg/d (N=72); olanzapine 15 mg/d (N=122); risperidone 4 mg/d (N=65); quetiapine XR 600 mg/d (QXR; N=119); and placebo (N=708). Results: The mean change at LOCF-endpoint in weight (kg) was +0.4 for lurasidone, +0.02 for haloperidol, +4.2 for olanzapine, +2.1 for QXR, +0.2 for risperidone, and -0.02 for placebo. Median changes (mg/dL) in metabolic parameters were: total cholesterol, -5.0 for lurasidone, -8.0 for haloperidol, +9.0 for olanzapine, +6.5 for risperidone, +6.0 for QXR, and -5.0 for placebo; triglycerides, -4.0 for lurasidone, -3.0 for haloperidol, +25.0 for olanzapine, +4.0 for risperidone, +9.5 for QXR, and -6.0 for placebo; and glucose, 0.0 for lurasidone, +2.0 for haloperidol, +4.0 for olanzapine, +3.0 for risperidone, +3.0 for QXR, and 0.0 for placebo. Median changes in prolactin (ng/mL) were: +0.4 for lurasidone, +8.5 for haloperidol, +3.7 for olanzapine, -0.3 for QXR, +14.0 for risperidone, and -1.9 for placebo. Short-term treatment with lurasidone was not found to be associated with clinically significant effects on ECG parameters, vital signs, or other laboratory parameters. There were no subjects with QTcF =500 msec in any study group. Discontinuation due to adverse events (AEs) were 7% on lurasidone, 15% on haloperidol, 7% on olanzapine, 3% on QXR, 2% on risperidone, and 5% on placebo. AEs for lurasidone (=5% & =2-times placebo) were akathisia (12.9%), somnolence (8.6%), sedation (8.5%), schizophrenia (6.8%), anxiety (5.1%), and constipation (5.0%). Dose-related effects of lurasidone on AEs was not evident. The proportion of subjects receiving concomitant anticholinergic drugs was 24% for lurasidone, 53% for haloperidol, 18% for olanzapine, 8% for QXR, 48% for risperidone, and 13% for placebo. Conclusions: Lurasidone 20-160 mg/d dosed once-daily was associated with a low potential for weight gain, adverse metabolic changes, or effects on prolactin or QTc.

#### NR6-53

### THE UTILITY OF MMPI-2 FOR ASSESSMENT IN PATIENTS WITH SCHIZOPHRENIA AND DEPRESSION

*Chair: Min-Cheol Park M.D.; Author(s): Yun-Hwa Ko, MA Sang-Woo Oh, Ph.D.*

#### SUMMARY:

This study aims to compare the symptoms of disorders in patients with schizophrenia and depression to evaluate them and calculate the effect size using MMPI-2. The study subjects analyzed were 40 male and female schizophrenia patients and 40 male and female depression patients at the age of 19 to 60 visiting the

department of psychiatry at university hospitals located in countryside from January of 2006 till December of 2009 and a control group with 40 normal males and females. As a study method, first, a symptom checklist was used to conduct frequency analysis and chi-square test (?2). And as dependent variables of MMPI-2, 18 scales were utilized to verify that the profile forms of the three groups were different through MANOVA. Lastly, Pearson's correlation coefficient was used to apply it to the formula of the effect size and figure out the index of the effect size. According to the result of comparing the psychiatric group (schizophrenia + depression) and normal control group, there was significant difference in their sense of worthlessness, sense of inappropriateness, sexual difficulty, sleep disorder, eating disorder, sad/depressed, and suicide accident or trial. However, there was no significant difference in their having of much worry. When the schizophrenia group and depression group were compared, there was significant difference in their sense of worthlessness, sad/depressed, and suicide accident and trial. Meanwhile, there was no significant difference in their having of much worry, sense of inappropriateness, sexual difficulty, sleep disorder, and eating disorder. Next, according to the result of MANOVA analysis, there existed difference between the groups. And the result of calculating the effect size of MMPI-2 showed that the scale indicating the greatest effect size in the psychiatric patient group and depression patient group was LSE(d=2.34). And it was also found that the scales showing the biggest effect size in schizophrenia and depression patient groups were D (d=-1.07) and BIZ (d=1.01). In the end, this paper discusses the limitations of this research and future directions for further study. Key words : Schizophrenia, Depression, MMPI-2, Effect Size

#### NR6-54

### SWITCHING FROM OLANZAPINE TO LURASIDONE: RESULTS FROM A 6-MONTH OPEN LABEL EXTENSION STUDY

*Chair: Stephen Stahl M.D.; Author(s): Vamsi K. Bollu, Ph.D.; Krithika Rajagopalan, Ph.D.; Andrei Pikalov, M.D.; Jay Hsu, Ph.D.; Antony Loebel, M.D.*

#### SUMMARY:

**Objective:** In recent longer-term treatment studies of schizophrenia, all-cause treatment discontinuation has been used as a clinically meaningful composite measure of treatment efficacy, safety and tolerability. The aim of this post-hoc analysis of a 6-month lurasidone open-label extension (OLE) study was to compare the efficacy, safety, and all-cause discontinuations among patients switching to lurasidone from olanzapine or

placebo vs. patients continuing on lurasidone during a 6 month OLE study. Methods: The core study for this 6-month OLE was a 6-week, double-blind (DB), placebo-controlled trial of lurasidone 40mg and 120mg fixed doses, with olanzapine 15mg as an active-treatment arm (for assay sensitivity). Eligible patients continuing into the OLE received lurasidone fixed dose (80mg) for 1-week followed by flexible dose (40-120mg). Assessments included for analysis were: efficacy (PANSS total score changes); safety (changes in cardio-metabolic parameters), rates of all-cause discontinuation and reasons for discontinuation. Results: From 246 evaluable patients in the OLE, 115 patients continued on lurasidone, 69 and 62 patients switched from olanzapine or placebo to lurasidone, respectively. Mean total PANSS scores decreased from 66.6 (OLE baseline) to 54.9 (OLE endpoint); with similar PANSS score improvements seen among those switching to lurasidone and those continuing on lurasidone. While no significant weight changes were observed among lurasidone patients during DB or when they continued on lurasidone in OLE, patients switching from olanzapine to lurasidone showed significant and sustained weight loss during OLE. Improvements in lipids and other cardio-metabolic parameters were also observed among patients switching from olanzapine to lurasidone. Total all-cause discontinuations were 54% (n=133) at OLE endpoint; with similar rates of discontinuations between those who stayed on lurasidone (n=60, 52%) and those switching from olanzapine (n=38, 55%) or placebo (n=35, 56%), respectively. Discontinuation rates due to lack of efficacy (14%, 8%, and 11%, respectively) or adverse effects (14%, 10%, and 12%, respectively) were also similar among patients staying on lurasidone or switching from olanzapine or placebo, respectively. Discussion: In this post-hoc analysis, patients with schizophrenia who switched from olanzapine (DB phase) to lurasidone (OLE) maintained efficacy improvements at 6-months and experienced similar rates of all-cause discontinuations as those who continued on lurasidone. In addition, significant weight loss and improved lipid and other cardio-metabolic parameters were observed after switch to lurasidone. Funded by Sunovion Pharmaceuticals Inc.

**NR6-55**  
**PERSONALITY DISORDERS IN PSYCHIATRIC**  
**INPATIENTS IN SWEDEN**

*Chair: Emma Bjorkenstam B.S.C.; Author(s): Charlotte Bjorkenstam MSc Lisa Ekselius M.D. Ph.D. Herman Holm M.D.*

**SUMMARY:**

Background: An estimated 6-10 % of the adult population has a personality disorder, and persons with a personality disorder are heavy users of both primary care and mental health services constituting a considerable public health burden. Aim: To describe the utilization of mental health treatment in patients hospitalized for personality disorder in Sweden, and to analyze whether there are differences due to age, sex, and use of compulsory treatment. Methods: The Swedish National Patient Register was used to identify patients hospitalized at least once between and including the years 2000 and 2010 with a primary diagnosis of a personality disorder. Use of compulsory treatment due to a personality disorder was analyzed from national register data for the year 2010. Data is presented as morbidity rates per 100 000 inhabitants. Results: In total 8 127 women and 4 558 men were hospitalized at least once within the studied time period. Women had more hospitalization periods than men (4.2 vs. 2.3). Sixty-one % of the women and 47 % of the men were aged 18-34 years. During the 10-year period, the number of hospitalization periods increased for women and decreased slightly for men in this age group, but was stable for those older than 35 years. Cluster B disorders, in particular borderline personality disorder (63 %) were most common in women aged 18-34 years, while an unspecified personality disorder diagnosis (36 %) was most common in the corresponding male group. In this age group, 329 out of 1 194 women, corresponding to 33 women per 100 000 inhabitants were given compulsory care in the year 2010, compared to 79 of 328 men, corresponding to 8 men per 100 000 inhabitants. Conclusion: Hospitalization due to a personality disorder was more frequent among women than in men, and the number also increased during the time period in women 18-34 years, but not in men 18-34 years. Women were given compulsory treatment to a larger extent than men regardless of age.

**NR6-56**  
**PERSONALITY DISORDERS AND SUICIDE IN**  
**YOUNG INDIVIDUALS IN SWEDEN**

*Chair: Charlotte Bjorkenstam M.S.C.; Author(s): Emma Bjorkenstam BSc; Lisa Ekselius M.D., Ph.D.; Herman Holm M.D.*

**SUMMARY:**

Background: Aim: To study all-cause mortality and suicide in patients aged 18-34 years hospitalized for a personality disorder in Sweden. Additional aims were to analyze differences between the sexes and to study utilization of psychiatric care prior to death in this patient group. Methods: Suicides between and

including the years 2001 and 2010 were obtained from the Swedish Causes of Death Register. The Swedish National Patient Register was used to identify patients hospitalized with a primary diagnosis of a personality disorder. Data is presented as mortality rates per 100 000 inhabitants. Results: Of the 772 women within the age group 18-34 years who committed suicide within the time period, 14% had been hospitalized for a personality disorder at least once five years prior to the suicide. The corresponding figure for men was 3 % out of 2 160 suicides. When compared to the general population, patients hospitalized for a personality disorder had higher mortality rates. Thus, in 2010 men with a personality disorder had a mortality rate of 858 per 100 000 compared to expected 66 per 100 000. Women with a personality disorder had a mortality rate of 789 per 100 000 compared to expected 27 per 100 000. Those with a hospitalization history for a personality disorder also had significantly higher suicide rates compared to the general population. Such hospitalizations were more common among women with a personality disorder, who on average had 6.8 hospitalizations compared to approximately 2.3 hospitalizations for men. Conclusion: Patients who have been hospitalized for a personality disorder have higher suicide and all cause mortality rates compared to the general population. Furthermore, women with a personality disorder who subsequently commit suicide have used more in-patient care than corresponding males.

**NR6-57  
DECREASED PLASMA METHIONINE-  
ENKEPHALIN LEVELS IN CLUSTER HEADACHE  
PATIENTS**

*Chair: Ron Mosnaim, Ph.D, Marion E. Wolf, M.D.*

**SUMMARY:**

Results from a longitudinal study (blood drawn at days 29, 64, 89, 124, 142 and 182 of the protocol) shows that the concentration of platelet-poor plasma (PPP) methionine5-enkephalin (MET) in healthy, drug-free, white male individuals (n=5) remains within a relatively narrow range, well within the experimental error of the analytical procedures used. Inter-individual differences fail to reach statistical significance [ $x \pm SD$  and range (METpg/uL PPP) of  $91.2 \pm 15.1$ , 67.1-113.5;  $69.6 \pm 7.5$ , 66.1-90.1;  $76.6 \pm 12.6$ , 58.5-93.1;  $86.8 \pm 10.9$ , 76.3-107.4 and  $84.5 \pm 11.4$ , 68.9-103.4; for subjects 1 through 5, respectively]. MET levels were similar to those recorded from single samples obtained from a group of 24 white male, age-comparable, drug-free healthy volunteers [ $x \pm SD$  and range (pgMET/uL PPP) of  $83.3 \pm 15.1$  and 57.4-119.1]. Controls range for all subjects (n=29)

of 57.4-119.1 pgMET/mL PPP. When compared to controls, individual cluster headache patients show a much wider variation in PPP MET levels (blood drawn at different time intervals, at least 10 samples per patient, over a period of 221-298 days), with many (slightly over half) of single values below the controls range; no single MET level was above the controls range [ $x \pm SD$  and range (pgMET/uL PPP) of  $56.4 \pm 27.7$ , 6.1-100.5;  $72.6 \pm 20.5$ , 43.0-113.0;  $46.0 \pm 28.5$ , 10.0-92.6;  $53.6 \pm 27.5$ , 13.0-101.0;  $52.0 \pm 26.1$ , 17.5-83.6;  $63.5 \pm 22.3$ , 21.7-91.3 for individuals A through F, respectively]. Whereas inter-individual differences within the patient's group were not statistically significant, their peptide levels were significantly lower than those of controls. Neither presence of unspecified "headaches between clinic visits" and "daily headaches" (patients E and F, respectively), nor use of a number of drugs known to lack inhibitory activity upon the aminopeptidase-MET degradation reaction, appeared to significantly influence MET concentration. These results could lead to a better understand of the etiology of the pain associated with CH, with the relative changes in plasma peptide perhaps reflecting patient's vulnerability to such condition. Use of drugs to modulate MET function may prove useful in the treatment of CH associated pain; whether development of such drugs could find useful pharmacological applications remains to be explored.

**NR6-58  
NON-EPILEPTIC SEIZURES VS. PANIC  
DISORDER IN PATIENT WITH PERVASIVE  
DEVELOPMENTAL DISORDER**

*Chair: Lidija Petrovic-Dovat M.D.; Author(s): Aggarwal, R M.D.; Mabry, F M.D.; C Petersen M.D.; Ulmen, P LCSW; Gupta, N M.D.*

**SUMMARY:**

Introduction: Pervasive Developmental Disorders (PDD) are group of neurodevelopmental disorders that present, with qualitative impairment in the area of social interaction, communication and restricted repetitive patterns of behavior. Non-epileptic seizures (NES) resemble epileptic seizures in presentation but do not involve abnormal electrical brain wave activity. In this report we present the unusual case of Panic Attacks and Non-epileptic seizures in a patient with PDD. Diagnosis of Panic Disorder (PD) in a patient with PDD could be a major challenge due to possible misinterpretation of symptoms by the patient and similar presentation of epileptic seizures and NES. Case presentation: A seventeen year old male with diagnosis of PDD and no history of seizures, presented multiple times to an Emergency Room with episodes of hyperventilation,

rhythmic and thrashing body movements, staring, unresponsiveness, impairment in sensation and speech, but no loss of consciousness. The patient could not recall the events. After multiple hospitalizations and negative extensive medical work, a seizure disorder was ruled out (EEG was negative during the episodes) and the patient was diagnosed with NES and referred for Psychiatric evaluation. The patient was diagnosed with Panic Disorder and Generalized Anxiety Disorder. Somatization and Conversion disorders were considered in differential diagnosis. The patient could not tolerate a number of medications but showed marked decrease in anxiety and NES, after the start of psychotherapy and a trial of citalopram. Risperidone was added after the patient became increasingly aggressive and he was able to return to school. Discussion: Differentiating seizures from NES and in this case Panic Attack could be very challenging in patients with PDD who could often misinterpret the significance of bodily sensations and have history of repetitive, stereotypic behavior, difficulties with mood, and emotions regulation. It is not understood how NES originate, but one hypothesis is that they occur in the context of anxiety, stress, and conflicts but the stressors cannot always be identified. Conclusion: This case emphasizes the importance of being vigilant when evaluating seizures-like events in patients with diagnosis of PDD. Diagnosis of nonepileptic seizures can only be reached after a complete neurological and medical work up is performed and after confirmed negative epileptic episode with electroencephalography. The treatment should include a multidisciplinary approach and involve counseling, medications, and close medical supervision.

#### NR6-59

### THE IMPACT OF SHIFT DURATION ON THE EFFICACY AND TOLERABILITY OF ARMODAFINIL IN PATIENTS WITH EXCESSIVE SLEEPINESS ASSOCIATED WITH SHIFT WORK DISORDER

*Chair: John Harsh Ph.D.; Author(s): Steven G. Hull, M.D., Ronghua Yang, Ph.D.*

#### SUMMARY:

**Objective:** A recent study demonstrated that armodafinil significantly improved clinical condition and wakefulness specifically during the last 4 hrs of the night shift, as well as overall functioning in patients with shift work disorder (SWD). This post-hoc analysis examined whether the length of the night shift worked (=9 hrs vs. >9 hrs) affected the efficacy and tolerability of armodafinil in patients with SWD. **Methods:** Patients in this study had diagnosed SWD (DSM-IV and ICSD-2

criteria), worked at least five 6-12 hr night shifts/month, had mean Karolinska Sleepiness Scale (KSS) score >6, and Global Assessment of Functioning (GAF) score <70. Following randomization, patients received 150mg armodafinil or placebo on nights worked for 6 weeks. For the current analysis, patients were divided into 2 groups: those working =9 hr shifts and those working >9 hr shifts. Efficacy assessments included change in Clinical Global Impression-Change (CGI-C) score related to excessive sleepiness late in the shift (including commute home [0400 to 0800]), GAF, late-in-shift KSS, and modified Sheehan Disability Scale (SDS-M) from baseline to final visit. SDS-M was modified to capture the effect of shift work on work, family, and social life. Final visit data included last observation carried forward. **Results:** Of the 383 patients enrolled in the study, 279 (73%) worked shifts =9 hrs (n=132 armodafinil; n=147 placebo) and 104 (27%) worked shifts >9 hrs (n=61 armodafinil; n=43 placebo). At final visit, a significantly greater proportion of armodafinil patients demonstrated an improvement in late-in-shift CGI-C score from baseline compared to placebo regardless of shift duration (=9 hrs:78% vs. 60% [p=0.0017]; >9 hrs:77% vs. 46% [p=0.002]). Significantly greater improvements with armodafinil were also observed in both shift duration groups for the GAF (=9 hrs:+9.5 vs. +5.4 [p<0.0001]; >9 hrs:+9.6 vs. +4.3 [p=0.0019]) and late-in-shift KSS scores (=9 hrs:-2.9 vs. -1.9 [p=0.0002]; >9 hrs:-2.8 vs. -1.6 [p=0.0028]) at final visit. However, armodafinil treatment led to significantly greater improvement in composite SDS-M scores at final visit only in patients working >9 hr shifts (=9 hrs:-6.8 vs. -5.0 [p=0.0536]; >9 hrs:-6.8 vs. -2.7 [p=0.0086]). The most common adverse events were nausea and headache. A greater proportion of patients working >9 hrs had at least 1 adverse event compared with those working =9 hrs. Conclusion: These findings indicate that shift duration did not affect the improvement with armodafinil over placebo in terms of late-in-shift clinical condition and wakefulness and overall functioning in patients with SWD. Only those patients working >9 hrs demonstrated improvements over placebo in disability following armodafinil treatment. A greater proportion of patients working >9 hrs reported adverse events associated with armodafinil although the types of events reported were similar between shift duration groups. This study was funded by Cephalon, Inc.

#### NR6-60

### BEHAVIORAL ACTIVATION THERAPY IN MEDICATION-RESPONSIVE CHRONIC DEPRESSION WITH PERSISTENT PSYCHOSOCIAL DYSFUNCTION: A PILOT STUDY

*Chair: David Hellerstein M.D.; Author(s): Gregory Erickson, MA; Donna O'Shea, MS; Jonathan W. Stewart, M.D.; Patrick J. McGrath, M.D.; Deborah Deliyannides, M.D.; Ying Chen, M.D.; Amy Withers, BA, and Sarah K. Reynolds, Ph.D.*

#### **SUMMARY:**

**Background:** Chronic depression is associated with significant psychosocial impairment (including work, relationships, and health status) which often persists following medication-induced remission of depression. We have adapted Behavioral Activation Therapy to treat persistent social dysfunction in patients whose chronic depression has responded to medication treatment.

**Methods:** 21 patients with dysthymic disorder (DD) or chronic major depression (M.D.D)( $>6$  month duration) responsive to medication (HDRS-17 score =10) but persistent psychosocial dysfunction (SAS score =1.9) were enrolled in once-weekly 12 week Behavioral Activation Therapy adapted to improve social functioning (BA-S). We report on the first 19 subjects. Patients continued antidepressants during BA-S treatment. Assessment instruments included: Hamilton Depression Rating Scale (HDRS); Cornell Dysthymia Rating Scale (CDRS); Beck Depression Inventory (BDI); Social Adjustment Scale (SAS); Quality of Life Enjoyment Satisfaction Questionnaire (Q-LES-Q); Behavioral Activation for Depression Scale (BADs); and Environmental Reward Observation Scale (EROS). Statistical analyses for ITT sample included dependent groups t-tests to examine differences between intake and the end of active treatment at week 12. Results: 14/17 (82.35%) subjects had DD, of whom 11 had early onset DD. 4/17 had current M.D.D, and 14/17 had history of 2.71+3.16 prior M.D.D episodes. Of the first 19 subjects, 17 completed  $\geq 10$  sessions. One subject completed 3 sessions, 1 completed 6, and 2 completed 10 sessions. 78% (15/19) completed 12 sessions. Scales measuring depression symptoms all decreased significantly following BA treatment, including both clinician rated (HDRS, CDRS) and patient-rated (BDI) scales. The HDRS, ( $t=-3.08$ ,  $p=.006$ ), CDRS ( $t=-5.75$ ;  $p=.001$ ) and BDI ( $t=-2.40$ ;  $p=.023$ ) showed statistically significant drops. On scales of psychosocial functioning, scores on the Q-LES-Q ( $t=3.11$ ;  $p=.006$ ), the SAS ( $t=-2.96$ ,  $p=.008$ ), EROS ( $t=3.55$ ;  $p=.002$ ) showed significant changes from intake to week 12, indicating that subjects experienced better quality of life and greater environmental reward post-treatment. Significant improvement in the BADs scale ( $t=2.24$ ;  $p=.038$ ) was also observed, showing that participants evidenced greater levels of behavioral activation at the completion of the therapy. Other scales (TCI Harm

Avoidance, CBAS) did not show significant change in this sample. Conclusions: Results of this pilot study suggest that BA-S is a feasible treatment modality in this patient population, with good face validity and a high degree of retention in treatment. In this pilot sample, ITT analyses suggest positive outcomes on various symptom, behavioral, and social functioning measures. BA-S thus appears to be a feasible treatment approach to supplement antidepressant medication in improving psychosocial outcomes, and worthy of further development, possibly including comparative outcomes studies.

**MONDAY MAY 07, 2012**

#### **New Research Poster Session 7**

#### **TREATMENT AND SERVICES**

##### **NR7-01**

#### **ATTACHMENT SECURITY INDEPENDENTLY PREDICTS PROBLEMATIC DRUG USE IN LOW INCOME, SUICIDAL, ABUSED, AFRICAN AMERICAN WOMEN**

*Chair: Suena Massey M.D.; Author(s): Suena H. Massey, M.D., Michael T. Compton, M.D., M.P.H., Nadine J. Kaslow, Ph.D., ABPP*

#### **SUMMARY:**

**Objective:** Converging evidence suggests that secure attachment, measurable from infancy, may buffer the effects of early adverse experiences such as childhood maltreatment, and also may be a protective factor in the developmental trajectory of substance use disorders. Whether secure attachment continues to have this protective effect in adulthood, particularly in the context of severe psychosocial stress, is unknown. The goal of this study was to determine the relationship between secure attachment and problematic drug use in the context of recent suicidality, exposure to intimate partner abuse, and other psychosocial risks. **Method:** Participants were 358 low-income African American women who sought treatment for either medical or psychiatric reasons at a large, urban, university-affiliated, public hospital, and endorsed exposure to intimate partner abuse and at least one suicide attempt in the past year. Problematic drug use was defined as a Drug Abuse Screening Test (DAST) score of  $\geq 6$ , consistent with clinical guidelines for referral to substance abuse treatment. Attachment security was assessed using the secure subscale of the Relationship Style Questionnaire (RSQ). We determined the relationship between hypothesized predictors (age,

education, homelessness, childhood maltreatment, depressive symptoms, and attachment security) and the dependent variable, problematic drug use using logistic regression. We found no evidence for multicollinearity among independent variables in bivariate correlations analyses. Results: Participants averaged  $35 \pm 10$  years of age; 86% were unemployed, 40% had less than a 12th grade education, 54% were homeless, 48% had a history of previous psychiatric hospitalization, and 53% endorsed problematic drug use according to the DAST. Secure attachment independently predicted a lower likelihood of problematic drug use (OR = .504; 95% C.I. (.336 - .755);  $p = .001$ ), whereas education, childhood maltreatment, and depressive symptoms did not. Furthermore, secure attachment, along with age and homelessness, accounted for 23% of the variance in problematic drug use. Conclusions: Attachment security may provide unique resilience to problematic drug use in adulthood, even in the face of lifelong exposure to victimization and severe psychosocial adversity. Results support the importance of future research on the developmental etiology, potential buffering effects, and modifiability of attachment security to inform both preventive and therapeutic interventions. This research was supported by grant R49 CCR421767-02 from the Centers for Disease Control and Prevention National Center for Injury Prevention and Control entitled, Group interventions with suicidal African American women, awarded to the last author (Kaslow).

**NR7-02**  
**FACTORS DETERMINING SUCCESSFUL**  
**SMOKING CESSATION IN BIPOLAR**  
**DISORDER: INTERIM LOOK**

*Chair: Annette Matthews M.D.; Author(s): Vanessa B. Wilson, BS and Suzanne H. Mitchell Ph.D.*

**SUMMARY:**

Background: Persons with Bipolar I have a 44.4% lifetime prevalence of nicotine dependence but it is not known if the topographic style of their smoking is related to mood state. They are also thought to be “impulsive,” particularly when manic, but how impulsivity measures might relate to their smoking topography has not been investigated. In this study we are looking at mood state, impulsivity, and smoking topography and how those factors might affect smoking and smoking cessation. Methods: We are in the process of enrolling 30 euthymic and 30 depressed male US Veterans with bipolar I. All participants complete a baseline visit: measures of mood (YMARS, MADRAS, MINI), impulsivity (Delay discounting, Stop Task), personality measures (BIS, TPQ, & EIS), smoking

questionnaires, and a smoking topography session. The subjects are then counseled on smoking cessation and return for a second visit after their quit date to repeat measures of mood and impulsivity. Results: At this time, 28 patients have enrolled in this study (9 depressed ; 19 euthymic). Of these, 1 subject did not complete the smoking cessation and 14 subjects have completed visit #2. There were no differences in delay discounting, perceived risks and benefits of smoking cessation, smoking topography between the depressed and euthymic groups. However, there were significant differences in some of the subscales of the personality measures. The depressed group had a higher score on the BIS attention scale, motor impulsiveness, and cognitive instability scale, and the TPQ the harm-avoidance scale at the first visit. Preliminary analyses also indicate relationships between impulsivity measures and smoking topography. Discussion: Initial results do not demonstrate a difference between mood state groups, except for the personality measures. It has been shown before for persons with unipolar depression that TPQ harm avoidance scores are higher than population norms and this study seems to suggest that they are also elevated in bipolar depression compared to a euthymic bipolar state. Interpretation of the BIS is limited due to the interim nature of the data.

**NR7-03**  
**ONLINE SOCIAL NETWORKING SITES**  
**ARE DRUG USE TRIGGERS AMONG**  
**ADOLESCENTS IN SUBSTANCE ABUSE**  
**TREATMENT**

*Chair: David Tran B.A.; Author(s): Keith Heinzerling, M.D., M.P.H.; James McCracken, M.D.*

**SUMMARY:**

OBJECTIVES: Exposure to environmental cues previously associated with drug use (“people, places, and things”) is a common precipitant of drug relapse among persons receiving treatment for drug addiction. Social networks also influence substance use and this effect may be mediated via environmental cues. Use of online social networking sites has increased dramatically especially among youth. Yet the extent to which online social networking may be a source of exposure to drug cues (“people, places, things”) among youth in substance abuse treatment is not known. This study surveyed youth in substance abuse treatment on their use of online social networking and potential exposure to drug cues. METHODS: A 20-question questionnaire was administered to 37 youth, aged 12 to 18, who are receiving substance abuse treatment at an adolescent treatment center in East LA. The proportion of youth

who report use of online social networking sites, as well as, the proportion who report exposure to drug-related cues was calculated. Demographics of youth who do and do not report use of social networking sites and, among those who do, exposure to drug-cues will be compared via t-tests and chi square analysis. RESULTS: (1) On youth in substance abuse treatment: 92% use online social networking sites, with a majority using Facebook. 89% report marijuana as his/her drug of choice. (2) On level of exposure to drug-related information from use of social networking sites: 88% of boys and 100% of girls reported that his/her friends on Facebook/ MySpace/Twitter use drugs ( $p = 0.145$ ). 94% of adolescents reported his/her friends post on drug-related content whereas 22% reported his/her friends post on recovery-related content ( $p = 0$ ). 77% of girls and 53% of boys report that something on Facebook/ MySpace/Twitter made them feel like they wanted to use drugs ( $p = 0.169$ ). CONCLUSION: A majority of youth in treatment use social networking sites. Their drug of choice is marijuana. Drug cues via online social networking exist and influence youth to use drug while in treatment. These results will be used to design an intervention to mitigate online risks to substance abuse treatment outcomes.

#### NR7-04

### STUDY OF INTERFACE BETWEEN ALCOHOL DEPENDENCE AND DEPRESSION: DIAGNOSIS AND PHENOMENOLOGY

*Chair: Amresh Shrivastava, M.D.; Author(s): Milan Balakrishnan, M.D., Danny Vincent, M.D., S R Parkar, M.D., Ph.D*

#### SUMMARY:

Milan Balakrishnan, M.D., Danny Vincent, M.D., S R Parkar, M.D., Ph.D, Amresh Shrivastava Introduction Mood disorders and alcoholism share a complex relationship and often pose diagnostic dilemma for primary depressive disorder vs. appearance of depressive syndrome as a consequence of dependence. A number of patients of alcoholism have pre-existing and co morbid independent depressive disorder and others exhibit depressive syndromes in withdrawal states. We report finding of a follow-up study of patients with alcohol dependence to examine course of withdrawal state and time –line to establish definitive diagnosis of major mood disorder. Methods: The open level, cohort study was conducted in drug-de-addiction program of a teaching general hospital in Mumbai, India. The study sample was selected using DSM-IV criteria for major depression as well as alcohol dependence. The two groups, one consisting of patients with alcohol

dependence with depression and the other with alcohol dependence only were assessed using semi-structured clinical interview HDRS and HARS. The subjects were studied for phenomenology, depression, anxiety and stressful life events for 5 weeks after onset of withdrawal state. Data was analyzed using SPSS. Results: We recruited 200 patients and 40% had severe depression after one-week of abstinence. However presence of depression decreased to 5% after additional 3 weeks of abstinence. The findings suggest that that intense depression that mimic major depressive episodes appear to be common in the context of heavy drinking but are likely to improve markedly over a matter of days or week and remain untreated Conclusion: The distinction between depressive episodes that occur only in the context of heavy alcohol or drug use and those depressive episodes that appear to be independent is made through a fairly simple time line. More research is required to address this issue if diagnostic variability of depression in alcoholism

#### NR7-05

### RECOMMENDATION-CONCORDANT MANAGEMENT OF METABOLIC SIDE EFFECTS ASSOCIATED WITH ANTIPSYCHOTIC USE IN VETERANS

*Chair: Dinesh Mittal M.D.; Author(s): Richard Owen, M.D. Chengbui, Li, Ph.D. Kristin Viverito, Ph.D. Silas Williams, BA*

#### SUMMARY:

BACKGROUND: Treatment with newer antipsychotic medications is associated with increased risk of weight gain, diabetes, and hyperlipidemia. Expert consensus recommendations for monitoring and managing these metabolic side effects have been issued by various professional organizations. Previous studies have documented low monitoring rates of these metabolic side effects but whether these side effects have received recommendation-concordant management is unknown. OBJECTIVES: The specific aims of this study are to: 1) determine the extent to which patients who develop metabolic side effects during antipsychotic treatment receive recommendation-concordant management of these side effects; 2) identify patient characteristics (e.g., age, race, comorbid medical conditions) that affect the likelihood of receiving recommended side effect management. METHODS: This study is a retrospective cohort analysis of patients receiving care in 32 VA medical centers in VISNs 18-22. We identified veterans who received a new (“index”) prescription for an antipsychotic agent between April 1, 2008 and March 31, 2009. Among those who developed metabolic

abnormalities during antipsychotic treatment, we examined the proportions of patients who received recommendation-concordant management defined as an occurrence of any of the following: appropriate medication use to treat the metabolic abnormality, a weight management program encounter, a primary care visit, or a diabetes or endocrine clinic visit within 60 days of the abnormal result. As a sensitivity analysis, management actions occurring within 30 days of the abnormal results were also examined. The association of patient characteristics with indicators of side effect management was examined using multivariate logistic regression models, adjusting for patient demographics, pre-existing diagnoses of medical comorbidities, and mental health diagnoses (schizophrenia, bipolar disorder, other psychosis, non-psychotic mental health diagnosis). RESULTS: Between April 1, 2008 and March 31, 2009, 12,009 patients who had a new antipsychotic prescription and satisfy other inclusion and exclusion criteria were identified. Results of analyses of the proportion of patients with abnormal results, and the proportion with abnormal results that had management actions, are ongoing, and will be presented during the session.

**NR7-06**  
**LOW DOSE NALTREXONE-CLONIDINE**  
**TREATMENT AND TOBACCO SMOKING**  
**DURING OPIOID DETOXIFICATION**

*Chair: Paolo Mannelli M.D.; Author(s): Kathleen Peindl Ph.D., Haresh Tharwani M.D., Li-Tzy Wu ScD*

**SUMMARY:**

Objective: Cigarette smoking is highly prevalent in opioid dependence (OD), it is a significant predictor of morbidity and mortality, and is difficult to treat among OD individuals. While using opioid agonist medications has been shown to increase smoking rates, the effects of their discontinuation deserve further study. Methods: We examined smoking behavior and outcomes of 106 opioid dependent, tobacco dependent (OD-TD) patients who had access to cigarette smoking during inpatient methadone taper. Subjects received in addition low dose naltrexone (VLNTX 0.125 mg or 0.25 mg/day), or placebo, and symptomatic ancillary medications with or without clonidine (0.3 mg-0.6 mg/day). Results: Heavier smoking during treatment was associated with reduced detoxification completion ( $p=0.02$ ). Cigarette smoking did not significantly increase during methadone taper and was not associated with more intense opioid withdrawal or craving. VLNTX addition, but not clonidine, was associated with significantly less intense opioid withdrawal ( $p=0.03$ ) and smoking urges

( $p=0.02$ ), though the number of cigarette smoked was not significantly different compared with methadone treatment alone. OD-TD patients receiving clonidine in combination with VLNTX during methadone taper showed better completion rates ( $p=0.03$ ), lower smoking urges ( $p=0.02$ ) and fewer cigarettes smoked ( $p=0.02$ ), coupled with reduced smoking satisfaction and reward ( $p=0.01$ ), compared to other treatments. There were no significant differences among treatment groups in demographic and clinical measures at admission, or use of ancillary medications and adverse events during detoxification. Conclusions: The combination low dose naltrexone-clonidine was efficacious in reducing smoking among OD-TD patients during opioid detoxification and should be tested as part of smoking cessation interventions. Future investigations will determine whether opioid detoxification offers a window of opportunity for the combined treatment of opioid and tobacco dependence. References Mannelli P, Patkar AA, Peindl K, Gorelick DA, Wu LT, Gottheil E. Very low dose naltrexone addition in opioid detoxification: a randomized, controlled trial. 2009 Apr;14(2):204-13. Berrendero F, Robledo P, Trigo JM, Martin-Garcia E, Maldonado R. Neurobiological mechanisms involved in nicotine dependence and reward: participation of the endogenous opioid system. Neurosci Biobehav Rev. 2010 Nov;35(2):220-31.

**NR7-07**  
**ORGANIZATION OF STOP SMOKING UNITS**  
**IN TURKEY; PREPARATIONS AND RECENT**  
**DECISIONS BY MINISTRY OF HEALTH FROM**  
**2008-2012**

*Chair: Derya Iren Akbiyik M.D.*

**SUMMARY:**

Turkish Ministry of Health had stepped up efforts against smoking as one of the most important priorities for the last 6-8 years. In July 2009, inside smoking was prohibited as one of the very first steps. A while ago, the drugs including varenicline and bupropion were started to be given for free to the high risk smoking patients by a country wide program. However, a formal statute was not put forward to establish standardized units for stop smoking programs. Every clinic was working independently from each other with different conditions. Finally in November 2011, official organization of Stop Smoking Units was defined by a governing statute prepared and published by Ministry of Health. This was one of the biggest concrete steps towards a smoke free environment. The obstacles and/or facilitators will be discussed. This presentation will try to summarize the successful efforts of Turkish Ministry of Health from a

developing country perspective and the content of the formal statute.

#### NR7-08

### HOT AND SPICY: A LOOK INTO THE PROFOUND DISINHIBITION, AGGRESSION, AND PARANOIA OF A PREVIOUSLY HIGH FUNCTIONING SAILOR FOLLOWING “SPICE” USE

*Chair: Robert Lovern M.D.; Author(s): Kevin Holleman, M.D. Paul Hahn Andrew S. Ob Robert McLay, M.D., Ph.D.*

#### SUMMARY:

A 23-year-old Caucasian male active duty US Navy sailor admitted to the Naval Hospital inpatient psychiatry ward, after presenting to his duty station with acute new onset persecutory delusional beliefs that people were trying to hurt him after admitting to “Spice,” a synthetic cannabinoid smoking product. The patient’s stressors consisted of a recent divorce and a job reassignment. His mental status exam was disorganized with persecutory delusions, little insight and poor impulse control. Routine admission labs were all within normal limits, but a specific urine drug screen for synthetic cannabinoids was positive. Further research into the patient’s adolescence revealed a remote diagnosis of paranoid schizophrenia at age 15; briefly treated with Abilify although abruptly stopped due to side effects from medication and a lack of persisting symptoms and insufficient data to support a continued diagnosis. He also had a history of regular teenage cannabis abuse. After his presentation to the Naval Hospital, the patient remained hospitalized for a total of three weeks before being transferred to an outside civilian inpatient facility that could more fully contain and manage his disruptive and aggressive behavior. While on our ward, the patient displayed a rapidly alternating course between insightful appropriate behavior and overt disinhibition with hyperaggression and hypersexuality marked by several severe physical assaults on staff members and openly masturbating in the milieu, along with profound flight of ideas, alogia, and persecutory paranoid ideation of being followed by the CIA and rumination about specific staff members trying to harm him. The patient suffered from acute dystonia following a brief one week trial with risperidone. This regimen was changed in favor of a progressive combination regimen of IM chlorpromazine 200mg and olanzapine 10mg by mouth twice a day with adjunct PRN IM ziprasidone 10mg available every 6 hours for acute agitation. The patient was also treated with IM clonazepam, PO trazadone, and valproic acid for augmentation. Toward the end of his treatment,

the patient displayed intermittent insight into his past actions. The patient was eventually stabilized on the above mentioned medications, but has yet to achieve full remission, and is currently in outpatient care with a diagnosis of schizophrenia. It is possible that the patient experienced an acute exacerbation of a previously remitted psychotic disorder or that his lasting psychosis was a direct result of synthetic cannabis abuse. The correlation is clear, but the cause is not. His present symptoms and time course meet the symptom criteria for schizophrenia, but his unreliable history make it difficult to pinpoint an etiology for his lasting psychotic presentation. That said, with this patient’s apparent psychotic predisposition and recent Spice use and prior regular cannabis abuse, he runs an increased risk for the development of schizophrenia.

#### NR7-09

### THE COST EFFECTIVENESS OF TREATMENT WITH EXTENDED-RELEASE NALTREXONE: A STRUCTURED REVIEW ACROSS FOUR STUDIES

*Chair: Dennis McCarty Ph.D.*

#### SUMMARY:

**Objective:** The aim of this structured review was to compare results among the four published studies that evaluated the overall healthcare costs of injectable, once-monthly, intramuscular XR-NTX for the treatment of alcohol or opioid dependence. **Methods:** The structured review examined four retrospective analyses of large US commercial insurance claims databases of healthcare costs and utilization associated with treatment with either no medication (psychosocial treatment only) and all four FDA-approved medications in each disease category. Each study employed rigorous case-mix adjustment (multivariate analysis, propensity score matching with inverse probability weighting and/or instrumental variable analysis). Three studies compared alcohol dependence treatments and one compared opioid dependence treatments. Patients typically were receiving concurrent psychosocial treatments. **Results:** The overall number of cases treated across all four studies with the various treatments was: psychosocial (i.e., non-medication) treatment alone 33,043 patients; XR-NTX 1,323; oral naltrexone 6,708; disulfiram 6,611; acamprosate 16,505; buprenorphine 7,596 and methadone 1,916. The greatest reductions in healthcare expenditures (inpatient + outpatient) were found among patients using pharmacotherapy and were strongest among patients who initiated extended release naltrexone. Among the pharmacotherapies, all four studies suggested that the key driver of higher costs

appeared to be increased utilization of hospitalization with oral agents vs. the once-monthly injectable XR-NTX. In the three alcohol dependence studies, increased utilization of hospitalization appeared to be related to decreased adherence to prescription refills with the oral agents compared to XR-NTX. Limitations include the retrospective, naturalistic study designs, absence of substance use data and 6-month observation period. In conclusion, these four studies characterize the current real-world state of alcohol and opioid dependence treatment in the insured U.S. population and represent the largest and most comprehensive picture of approved treatments to date. Conclusions: A consistent pattern emerges in which patients who received only psychosocial treatment emerged over the next 6 months with the highest healthcare costs, and those treated with oral agents had significantly and substantially higher rates of hospitalization, at no net cost advantage vs. treatment with XR-NTX. The study was funded by Alkermes, Inc. The Medisorb preparation used in XR-NTX was developed with support from the National Institute on Drug Abuse (grant R43DA013531) and National Institute on Alcohol Abuse and Alcoholism (grant N43AA001002). OHSU received research funding for this study from Alkermes.

**NR7-10**  
**SAFETY AND EFFECTIVENESS OF**  
**TREATMENT WITH A ONCE-MONTHLY,**  
**INJECTABLE FORMULATION OF**  
**NALTREXONE IN A REAL-WORLD CLINICAL**  
**PRACTICE SETTING**

*Chair: Bernard Silverman Ph.D.; Author(s): David R. Gastfriend, M.D.*

**SUMMARY:**

Objective: Opioid dependence costs >\$50-billion/year in the US (Lobmaier, Cochrane Database Syst Rev 2008 Apr 16:CD006140; Birnbaum, Pain Med 2011;4:657-67). In 2010, the FDA approved once-monthly, injectable extended-release naltrexone (XR-NTX; VIVITROL®), for prevention of relapse to opioid dependence following detoxification, after a large double-blind, 6-month placebo-controlled trial (Krupitsky, Lancet 2011;377:1506-13). Sustained safety and efficacy was subsequently shown in an open-label 12 month extension study. The current registry study is assessing clinical, health economic, and health-related quality of life (HRQoL) outcomes in opioid-dependent patients receiving XR-NTX in a real-world clinical practice setting. Methods: The study is an observational, open-label, single-arm, multi-center registry of adult outpatients who have initiated

treatment with XR-NTX for prevention of relapse to opioid dependence, following opioid detoxification. Efficacy outcomes include the Opioid Craving Scale, the EuroQol 5-dimension health-related quality of life tool (EQ-5D), the 12-item Short Form Health Survey (SF-12), the Clinical Global Impression, severity and improvement scales (CGI-S, CGI-I), and the Global Assessment of Functioning (GAF) scale. Results: To date, 40 patients have been enrolled (57.5% male; mean age, 30.2 years; mean duration of opioid dependence, 60.4 months). At baseline, global illness was rated as borderline-to-markedly ill in 60.5% of patients, with a mean CGI-Severity score of 2.3, a mean Opioid Craving Score of 40.2 (scale range: 0-100), a mean EQ-5D visual analog scale score of 66.7 (scale range: 0-100), a mean GAF score of 68.3, and mean SF-12 mental health and physical component summary scores of 35.9 and 47.5, respectively (US norm=50). Conclusions: Although limitations include the uncontrolled, open design and the fact that data collection remains ongoing, registry studies provide an important test of the effectiveness, safety, and tolerability of patient populations that are more heterogeneous and treated with greater variability than in research settings. These early recruitment results show some meaningful differences from the Phase III clinical trial sample, including a greater proportion of women, shorter dependence duration, and higher craving scores. The current ongoing Registry study will add to clinical trial and health economic studies regarding the role XR-NTX will play and the population suited for this pharmacologic option. The study is funded and conducted by Alkermes .Extended-release injectable naltrexone (VIVITROL®) was developed with support from National Institute on Drug Abuse Grant R43DA013531 and National Institute on Alcohol Abuse and Alcoholism Grant N43AA001002. Dr. Silverman and Dr. Gastfriend are employees of Alkermes, Inc.

**NR7-11**  
**OPEN-LABEL STUDY OF**  
**EXTENDED-RELEASE INJECTABLE**  
**NALTREXONE (XR-NTX) IN HEALTHCARE**  
**PROFESSIONALS WITH OPIOID**  
**DEPENDENCE**

*Chair: Paul Earley M.D.; Author(s): David R. Gastfriend, M.D.; Asli Memisoglu, Sc.D.; A. Thomas McLellan, Ph.D.; Bernard L. Silverman, M.D.*

**SUMMARY:**

Objective: Opioid dependent healthcare professionals, at risk of relapse due to access to prescription opioids, are rarely prescribed medications such as

naltrexone. The aim of this pilot study was to evaluate the long-term safety, tolerability and efficacy of injectable, once-monthly, intramuscular XR-NTX in this at risk patient population. Methods: DSM-IV opioid-dependent healthcare professionals who had detoxified off opioid agonists for =2 weeks (confirmed by negative urine drug screen and by negative naloxone challenge) were offered IM XR-NTX once-monthly for 24 months. Monthly assessments included urine opioid drug tests, routine safety assessments, SF-36 Health Survey and the Opioid Craving Questionnaire. Results: 38 of 49 screened patients (77.6%) were started on XR-NTX treatment. The majority of these (N=31; 81.6%) were female and most worked as nurses. 19 patients (50%) were retained in treatment at least 12 months. No patients died or overdosed, but 20 discontinued treatment due to an adverse event (3 anxiety, 1 headache, 1 injection site reaction, 1 derealization); 7 were lost to follow-up; 5 withdrew consent; and 2 withdrew for other reasons. The most common adverse events were injection site pain (39.5%), nausea (36.8%), anxiety (26.3%), and headache (23.7%). During this one-year period 3 patients had at least one opioid-positive urine drug test. Two of these patients ultimately discontinued but the third continued in the study with no further opioid-positive urine tests. In all, 98% of a total of 501 monthly urines collected on patients during the year were opioid negative. Baseline to 12-month change scores on common status measures revealed a 46.3% reduction in mean opioid craving; and 33% improvement on the SF-36 Mental Component Score. The SF36 Physical Component Score was in the normative range at both baseline (53.4) and 12-months (51.5). Study limitations include the open design and the small sample size, due in part to the fact that the study is not yet completed. Conclusions: These results in at-risk healthcare professionals indicate that long-term XR-NTX was associated with good retention, with no new safety concerns and high rates of opioid negative urines, reduction in opioid craving, and improvement in mental health functional quality of life. The study was funded by Alkermes, Inc. Extended-release injectable naltrexone (VIVITROL®) was developed with support from National Institute on Drug Abuse Grant R43DA013531 and National Institute on Alcohol Abuse and Alcoholism Grant N43AA001002. Drs. Gastfriend, Memisoglu and Silverman are employees of Alkermes, Inc. Dr. Earley is a consultant to Alkermes, Inc.

#### NR7-12

### INJECTABLE EXTENDED-RELEASE NALTREXONE (XR-NTX) FOR OPIOID DEPENDENCE: LONG-TERM SAFETY AND EFFECTIVENESS

*Chair: David Gastfriend M.D.; Author(s): Evgeny M. Krupitsky, M.D.; Edward V. Nunes, M.D.; Walter Ling, M.D.; Asli Memisoglu, Sc.D.; Nicole Amador Ph.D.; Bernard L. Silverman, M.D.*

#### Summary:

**Objective:** To evaluate the long-term safety and efficacy of injectable, once-monthly, intramuscular XR-NTX for the treatment of opioid dependence. **Methods:** Patients who completed an initial 24 week randomized, double-blind (DB), placebo-controlled trial of XR-NTX were either continued on XR-NTX or, if they had received placebo, were switched to XR-NTX for 52 weeks of open-label (OL) treatment. Patients received I.M. injections every 4 weeks in addition to biweekly individual drug counseling. Efficacy outcomes included the rate of monthly opioid-negative urine tests (primary endpoint), the Opioid Craving Scale, and health-related QoL scores such as the SF-36 scale, and responder rates (much/very much improved on the Clinical Global Impression, Improvement scale (CGI-I)). **Results:** In the DB phase (N=250), the median proportion of abstinent weeks was 90% for XR-NTX vs. 35% for PBO (P=0.024) during weeks 5-24; total 6-mo abstinence was 36% for XR-NTX vs. 23% for PBO (P=0.0002). In the OL extension (n=114), 67 continued, i.e., XR-NTX continued on XR-NTX, whereas 47 patients switched, i.e., PBO to XR-NTX. Overall, 71 patients (62.3%) completed 1-year of open-label XR-NTX and 58 patients (50.9%) were completely abstinent (based on opioid-negative urines). The XR-NTX continued on XR-NTX group experienced sustained improvements in: craving (i.e., “need for opioids”); the CGI-Improvement scale (at the end of OL treatment, 97.0% were CGI-I responders, and 89.4% of PBO switched to XR-NTX patients were responders); the SF-36 mental health component score (which had improved from a mean of 34.8 to 50.6 during DB treatment, and maintained this level of improvement through the end of 52 weeks of OL treatment (mean, 50.2)); and the EQ-5D Health Status. Common adverse events were LFT elevations, toothache and flu; 2.6% reported injection site pain. No meaningful between-group differences occurred in ALT, AST or GGT. All safety events observed during the open-label extension were consistent with the events previously described in the approved product labeling. No patients died, overdosed or discontinued due to severe adverse events. **Conclusions:** Once-monthly XR-NTX combined with counseling for opioid dependence maintained safety & effectiveness for up to 18 months. The study was funded by Alkermes, Inc. The Medisorb preparation used in XR-NTX was developed with support from the

National Institute on Drug Abuse (grant R43DA013531) and National Institute on Alcohol Abuse and Alcoholism (grant N43AA001002).

**NR7-13****VARENICLINE IN OUTPATIENT PSYCHIATRIC HEAVY SMOKERS**

*Chair: Faruk Abuzzabab M.D.; Author(s): F. S. Abuzzabab, Sr, M.D., Ph.D., K. B. Abuzzabab, RN, JD, LLM, P. Dorsen, M.D.*

**SUMMARY:**

**Introduction:** Smoking cessation is a challenge for psychiatric patients. The possible emergence of suicidal ideation, hallucinations, nightmares, insomnia and increase in anxiety has limited the application of denicotinezation. **Methods:** Ten outpatients with DSM IVR diagnosis of schizoaffective bipolar, and unipolar depressive disorders with nicotine dependence were given varenicline for smoking cessation. Starting dose followed the recommended guideline of 0.5 mg per day for 3 days then 0.5 mg twice per days for 4 days. On day 8, 1 mg. twice a day, was prescribed for a month. The dose was increased up to 4 mg. per day after the first month which is above the approved recommendation.\* **Results:** The average amount of cigarettes per day was 32. This dropped to 8 cigarettes per day at the end of the study. These patients were closely monitored for any worsening of their psychiatric symptoms which did not occur. These patients tolerated Varenicline well even at 4 mg. **Conclusions:** In this very small sample open label study, Varenicline was effective in reducing cigarette smoking when it was used above the recommended dose in outpatient psychiatric heavy smokers. \*The use of Varenicline above 2 mg. per day is considered off label not approved by the FDA. Supported in part by Psychopharmacology Fund and Minnesota Medical Foundation.

**NR7-14****BUPROPRION SR AND HARM REDUCTION VS. ABSTINENCE-FOCUSED TREATMENT FOR PROBLEM GAMBLING**

*Chair: Nitigna Desai M.D.; Author(s): Barbara Elaine Rofman, RN, MS, CNS; Kendra King, MA; Christopher Waltrous, MA; Christopher Krebs, Ph.D.; Marc Potenza, Ph.D., M.D.; Charles Drebing, Ph.D.*

**SUMMARY:**

Abstract Relatively few investigations into safe and effective pharmacotherapies for the treatment of PG have been performed to date and no FDA-approved

pharmacotherapies exist for PG at the present time. This study evaluates the impact of the combination of medication and psychotherapy compared to abstinence-focused treatment for problem gambling on gambling frequency and intensity, treatment compliance, global functioning, disability, and treatment motivation. Veterans who met inclusion criteria were randomized to one of four treatment groups: Bupropion and Harm Reduction, Bupropion and Gamblers Anonymous, Placebo and Harm Reduction, or Placebo and Gamblers Anonymous. Psychotherapy treatment consisted of a 12-week, 1 session per week, harm-reduction protocol adapted from similar published substance abuse treatment protocols/manuals or Gamblers Anonymous. Patients met with a member of the research team on a weekly basis for 12 weeks to participate in the psychotherapy intervention, to obtain medication refills and to have their general clinical status monitored. An additional follow-up visit was scheduled at week 26, following the active phase. Preliminary findings suggest that there is a high rate of co-morbidity for problem gamblers with other disorders such as substance dependence, mood disorders, and anxiety disorders. In addition, the amount of money and time spent on gambling decreased from the time of baseline interviews to the completion of the study. **Relevance** This poster is relevant to "Revolutionary Changes and Emerging Innovations" because the rising prevalence rate of Pathological Gambling has caused a great need for effective evidence based treatment for people with pathological gambling. There is limited research investigating medication and psychotherapy for treatment of Pathological Gambling. This study examines the effectiveness of harm reduction therapy compared to GA in combination with bupropion versus placebo. **Impact** A greater understanding of how effective psychopharmacology and a form of harm-reduction psychotherapy is on treatment outcomes for problem gamblers is essential to providing better care to individuals who suffer from the condition, as well as making the clinical and public world more aware of the struggles associated with the illness. **Objectives:** Identify factors that may improve treatment retention and adherence; Understand how treatment can be effective in reducing the amount of time and money spent gambling; And describe the basic demographics of the study sample as well as comorbid disorders.

**NR7-15****EFFECTIVENESS OF ADDICTION PHARMACOTHERAPY IN A COMMUNITY TREATMENT PROGRAM**

*Chair: David Lott M.D.*

**SUMMARY:**

Several medications are FDA approved for prevention of relapse in addictive disorders. Each of these medications has been shown efficacious in randomized controlled clinical trials for reducing substance use as well as improving a variety of other outcomes. Previous studies have examined adoption of medication use in community treatment programs, but few studies have evaluated the effect of medication use in structured community programs on treatment outcomes. This study hypothesizes that addiction medications will improve a variety of outcomes including treatment retention, substance use rates, and cravings for drugs. Data were collected from participants (n=103) in a community adult addiction day treatment program regarding use of addiction medications during treatment (buprenorphine, naltrexone oral, naltrexone extended-release injection, acamprosate, and disulfiram). The program involves 3-5 hours per day of structured therapy programming and includes methods of 12-step facilitation, cognitive behavioral therapy, and motivational enhancement. Subjects provided self-report data about substance use frequency and quantity as well as cravings. Data were analyzed using t-tests and chi-square tests. 45% of participants were prescribed 1 or more addiction medication during treatment. In the overall sample, use of any addiction medication was not associated with a significant difference in any outcome measure, but there was a trend toward increased length of stay ( $p=0.07$ ). Subset analyses revealed that use of any alcohol-related medication resulted in significantly larger reduction in drinking amount ( $p<0.05$ ) and use of buprenorphine resulted in significantly lower frequency of heroin use and lower intensity of cravings ( $p<0.05$ ). In this treatment program sample, addiction medications are frequently used and improve some of the measured outcomes. Additional study will help clarify the potential benefits of addiction medication in community treatment programs.

**NR7-16****COGNITIVE TASK PERFORMANCE AND ALCOHOL USAGE IN YOUNG ADULTS**

*Chair: Arit Harvanko B.A.; Author(s): Brian L. Odlaug, M.P.H., Liana R.N. Schreiber, B.A., Jon E. Grant, M.D., J.D., M.P.H.*

**SUMMARY:**

**Objective:** Research has shown a variety of cognitive deficits in individuals after the onset of an alcohol use disorder but less is known about cognitive deficits in sub-syndromal alcohol use or of cognitive deficits

preceding alcohol use disorders. Looking at measures of cognitive impulsivity using well validated, translational, computerized cognitive tests we explored differences in non-drinkers, at-risk drinkers and individuals with an alcohol use disorder. We also followed a sub-sample of participants for one-year to observe relationships between baseline scores and onset of at-risk drinking and/or an alcohol use disorder. **Method:** Demographic and cognitive test scores were taken from subjects in a longitudinal study of non-treatment-seeking young adults aged 18-29 years who were recruited for a study examining impulsivity. Participants were given a general psychiatric interview, self-report scales (Eysenck Impulsivity Questionnaire, Barratt Impulsivity Scale and Tri-Dimensional Personality Questionnaire), and cognitive tests from the Cambridge Neuropsychological Automated Test Battery. Subjects were also administered the same tests after one year. **Results:** 155 young adults (mean age:  $21.15 \pm 3.092$  years; 25.8% female), free from non-alcohol-related psychiatric diagnoses and drug use, were used in this sample. At baseline at-risk drinkers (n=82) and individuals with alcohol use disorders (n=25) bet significantly more overall on the Cambridge Gambling Task than nondrinkers (n=48). Individuals with alcohol use disorders also endorsed higher impulsivity than at-risk and nondrinkers on the Barratt Impulsivity Scale and Eysenck Impulsivity Questionnaire. Individuals with alcohol use disorders and at-risk drinkers also endorsed higher venturesomeness than nondrinkers on the Tridimensional Personality Questionnaire. Individuals who progressed to meet criteria for at-risk drinking, or an alcohol use disorder, after one year, bet more overall on the Cambridge Gambling Task. Other measures of impulsivity showed no association with increased alcohol consumption after one year. **Conclusions:** This represents one of few studies to examine cognition and the construct of impulsivity in sub-syndromal alcohol use. Our results indicate that individuals with sub-syndromal alcohol use may possess similar cognitive characteristics as at-risk drinkers and those with an alcohol use disorder. Our results may also indicate that some, but not all, types of impulsivity found in at-risk drinkers may be associated with the development of an alcohol use disorder.

**NR7-17****ANTIPSYCHOTIC DOSE ESCALATION PRIOR TO THE DEVELOPMENT OF NEUROLEPTIC MALIGNANT SYNDROME (NMS)**

*Chair: Julie Langan Other Author(s): Dr Daniel Martin MBChB, BMSC (Hons) Dr Polash Shajaban MBChB, M.P.H.il, MRCP(UK,) FRCPsych*

**SUMMARY:**

Background: “Neuroleptic malignant syndrome” (NMS) which derives from the French “syndrome malin des neuroleptiques” was first described in 1960 by Delay and colleagues in association with haloperidol. It is a potentially fatal idiosyncratic reaction to antipsychotics. Pathophysiology remains enigmatic. Mortality rates may be as high as 55%. Rapid alteration and escalation of anti-psychotic dose is thought to be an important risk factor. “Rapid escalation of dose” as a phenomenon has been difficult to define. Aims: To identify cases of NMS, review risk factors and focus on changes in antipsychotic dose in the 30 days prior to NMS onset. We also attempt to scientifically define “rapid escalation of antipsychotic dose.” Methodology: Retrospective analysis to identify NMS cases using DSM-IV criteria within NHS Lanarkshire, Scotland was undertaken. Once identified, demographics, risk factors for NMS and the episode were described by 2 independent psychiatrists. A 30 day antipsychotic dose trajectory prior to NMS onset was recorded. Cumulative antipsychotic dose was calculated using chlorpromazine equivalence to allow comparison of total cumulative dose of different anti-psychotics. In the UK the British National Formulary (BNF) contains information regarding maximum licensed doses of antipsychotic medication. Cumulative antipsychotic dose as a percentage of total maximum BNF dose was also calculated. Dose trajectories were compared to inpatient and outpatient clozapine titration schedules. Results: 12 cases were identified. Sex distribution was equal. Average age was 47.8 years. The most common diagnosis was Schizophrenia (295){50%, (n=6)}, followed by Mood (Affective) Disorders (296){25% (n=3)}. 33.3% (n= 4) received parenteral antipsychotics within 30 days of NMS onset. Antipsychotic polypharmacy rates were high 41.7% (n=5). Individual 30 day dose trajectories prior to NMS onset were plotted and means obtained. Mean dose trajectory was compared to standard clozapine inpatient and outpatient titration regimens. NMS patients had higher total daily chlorpromazine dose and more rapid dose escalation, particularly in the 10 days prior to NMS onset, compared to individuals titrated on clozapine. Differences in cumulative dose and dose escalation using percentage maximum BNF were less marked. Discussion: It would appear that using higher doses and titrating anti-psychotics faster than standard clozapine titration schedules may be associated with the development of NMS. Converting antipsychotic medication received to a cumulative chlorpromazine equivalent and monitoring this over time may be useful in early detection and prevention of NMS. Chlorpromazine equivalence as a measure of

total anti-psychotic dose received may better predict NMS compared to percentage BNF.

**NR7-18**

**EFFECTIVENESS VS EFFICACY RANKINGS BY A MODIFIED PRECIS TOOL FOR SCHIZOPHRENIA TRIALS OF LONG-ACTING INJECTABLE VS DAILY ORAL ANTIPSYCHOTIC TREATMENTS**

*Chair: Larry Martinez Ph.D.; Author(s): Larry Alphs, M.D., Joseph F. Hulihan, M.D.*

**SUMMARY:**

Introduction: Several prospective studies have compared long-acting injectable versus daily oral antipsychotic treatments for patients with schizophrenia. While many hypothesize an advantage for the former, few studies have shown meaningful benefit. This may be partly linked to the need for a true comparative effectiveness (pragmatic or real world) approach to demonstrate the advantage for a long-acting agent over a daily oral medication. This pilot project explored the feasibility of retrospectively rating the “effectiveness” of relevant study designs, and to ultimately assess the relationship of that rating to outcome. Methods: PRECIS (Pragmatic: Explanatory Continuum Indicator Summary) is a tool designed to assist researchers in the study development process and help ensure that designs meet the intended objective of being a pragmatic (effectiveness) vs. explanatory (efficacy) study (Thorpe et al, 2009). This pilot project employed PRECIS to rate a completed study comparing long-acting injectable risperidone to other antipsychotics for schizophrenia (Grimaldi-Bensouda et al, 2012 [In press]). The study concluded an advantage for long-acting injectable risperidone on rates of hospitalization. PRECIS consists of 10 domains representing study features relevant to the pragmatic: explanatory continuum. PRECIS was modified for this project so each domain is rated as 0=extremely explanatory, 1=very explanatory, 2=explanatory, 3=elements of both designs, 4=pragmatic, 5=very pragmatic, 6=extremely pragmatic (total score range 0 to 60). Each author of this abstract independently rated the study design and documented the rationale for domain scores. Domain scores were added for a total score per rater, and then averaged across raters for the average total study score. Results: The study’s average total PRECIS score was 48.7 (rater scores: 46, 48, 52). The study design was rated more pragmatic than explanatory on the domains of intervention flexibility (both experimental and comparison), follow-up intensity/duration, primary trial outcome, participant compliance, and practitioner

adherence. The average ratings on each of these domains ranged from 5.3-6.0. Other domains showed elements of both pragmatic and explanatory designs, with average ratings of 3.7 for: participant eligibility, practitioner expertise for the interventions (both experimental and comparison), and primary analysis. Radar graphs are used to clearly illustrate these results. Limitations include that ratings are not absolute or validated. Conclusion: This pilot project demonstrated the feasibility of using a modified PRECIS to rank completed studies on the pragmatic: explanatory continuum. Follow-up work will include using PRECIS to rate the designs of published studies comparing long-acting and daily oral antipsychotics to ultimately test the hypothesis that a comparative effectiveness (pragmatic) approach is related to outcome. Supported by Janssen Scientific Affairs, LLC.

#### NR7-19

### CAN A COMPUTER ADMINISTER THE MADRS? COMPARISON WITH SITE-BASED RATERS IN THREE GLOBAL CLINICAL TRIALS

*Chair: Gary Sachs M.D.; Author(s): Michelle Arkow, BA and Dan DeBonis, BA*

#### SUMMARY:

**Background:** Determining the reliability of clinical rating scales across the range of circumstances of its proposed use is key to establishing the acceptability of any measure proposed as study outcome variable. Scales such as the Montgomery Asberg Depression Rating Scale (MADRS) are well established but can be cumbersome and expensive to use especially in large clinical trials with many raters. If the psychometric properties of the MADRS with computer administration are comparable to site-based ratings, computer administration may provide a useful alternative. **METHODS:** Three multicenter placebo controlled double blind studies were identified in which the MADRS was administered independently by site based raters (MADRS-SBR) and by a computer (MADRS-COMP) as part of a quality management program. Internal scale consistency was assessed using Cronbach's alpha calculated for the MADRS-SBR and MADRS-COMP at baseline, the first post randomization visit, study endpoint, other visits, and all visits. Comparisons of the MADRS-SBR and MADRS-COMP were made at overall and at four study time points Baseline, First Post-randomization visit, Study Endpoint and all other visits. At each time point, the variance observed by site based rater was compared to that observed by the computer and

expressed as a percentage of the variance observed for the computer administered MADRS. (MADRSSBR/MADRSCOMPx 100). Results: The sample included 7544 pairs of MADRS-SBR and MADRS-COMP ratings from 1 unipolar depression and 2 bipolar and randomized controlled trials. There were no significant differences between MADRS-SBR and MADRS-COMP on any measure at anytime point. Mean Scores (SD) for MADRS-SBR vs MADRS-COMP respectively were Baseline 30.3(5.8) vs 30.4(8.6); 1st-post randomization visit 24.4 (8.2) vs 23.4 (10.2); Study end point 14.3(10.4) vs 15.0 (11.6); and overall 20.1(10.7) vs 20.3(11.9). Cronbach's Alpha Across Study Visits for MADRS-SBR and MADRS-COMP respectively were Baseline .674 vs .688; 1st-post randomization visit .809 vs .776; Study end point .891 vs .854 and overall .889 vs .847. Similar results were found in the individual studies. Conclusion: Close agreement between MADRS-COMP and MADRS-SBR across study visits and therapeutic indications during actual clinical trials supports the validity and reliability of computer administered MADRS in studies of Unipolar and Bipolar Depression. The MADRS-SBR and MADRS-COMP may also be useful benchmarks against which to judge the performance of other scales proposed for use in global multisite studies. The similar drop in performance observed for both the MADRS-SBR and MADRS-COMP at study baseline visits suggests that factors other than rater behavior may play an important role undercutting the reliability of baseline scores. Strengths and weaknesses of MADRSSBR and MADRSCOMP should be considered in the selection of outcome measures.

#### NR7-20

### EXTRAPYRAMIDAL SYMPTOMS IN RECOVERED FIRST EPISODE SCHIZOPHRENIA PATIENTS AT TEN YEARS

*Chair: Amresh Shrivastava M.D.; Author(s): Nilesb Shah, M.D.,DPM.DNB, Megan Johnston MA, Larry Stitt, Ph.D.*

#### SUMMARY:

Amresh Shrivastava, Nilesb Shah, Megan Johnston, Larry Stitt Introduction: Side effects of Extrapiramidal symptoms (EPS) are main argument against prescribing first generation antipsychotics. EPS are distressing and interfere with recovery and functioning of patients. Some of these symptoms are persistent over long period of time, even after antipsychotics have been stopped. It was believed that second generation drugs are less likely to cause EPS, which may help in better functioning. We examined a cohort of patients of first episode schizophrenia in a ten-year follow up study for presence

of EPS. Method. We assessed patients who had shown clinical recovery at the end of ten years treatment. These patients were assessed for psychopathology, (by PANSS) level of functioning (by GAF), cognition (by WMS) and presence of EPS by Abnormal Involuntary movement scale (AIMS). Details of clinical assessment were recorded. Result We examined 60 patients who had shown recovery as per CGIS. EPS was found in 35% patients at the ten years follow up. Only 5% patients were having abnormal movement at the initial contact of first episode schizophrenia. Fine bilateral tremor and akathisia were the commonest abnormalities present in more than half of the sample Presence of EPS was significantly associated with lesser level of functioning. 89% subjects were on atypical antipsychotics at the time of assessment. Majority of patients had treatment with second-generation medication during the ten years course. Presence of EPS did not differ with age of onset of illness, though there was slight correlation with younger age of onset. Presence of EPS was not associated with persisting psychopathology or cognitive functioning. Discussion: In the era of first generation antipsychotic tardive dyskinesia was observed in about 25 to 40% subjects in long-term follow up. These symptoms were very incapacitating. In the present times when these patients are treated with SGAs, EPS still persists, however its severity in lesser and most of the patients remain functioning at a reasonable level. EPS appears to be a distinct reality with antipsychotics. Art of prescribing needs to be more refined in order to minimize these symptoms. Conclusion: 35% clinically recovered patients in ten years follow up are found to have EPS.

**NR7-21**  
**ATYPICAL ANTIPSYCHOTICS USAGE IN LONG-TERM, TEN YEAR'S FOLLOW UP OF FIRST EPISODE SCHIZOPHRENIA**

*Chair: Amresh Shrivastava M.D.; Author(s): Megan Johnston MA, Larry Stitt Ph.D, Nilesh Shah. M.D.,DPM,DNB*

**SUMMARY:**

Amresh Shrivastava, Megan Johnston, Larry Stitt, Nilesh Shah Abstract: Background: The role of antipsychotics in long-term recovery from schizophrenia remains questionable. It is not clear if the effect of these medications is correlated with levels of clinical and functional recovery. The pattern of antipsychotic medication use is a major aspect of pharmacotherapy in long term follow ups of schizophrenia. Aim: The aim of this study was to examine patterns of antipsychotic usage in patients with long standing psychosis and

their relationship with social outcome. Methods: We recruited 116 patients who had more than 80% compliance as reported by relatives from the cohort of a long-term outcome study. These patients were assessed on antipsychotic medication use and on clinical and functional parameters in a cross-sectional study design in a naturalistic setting. Results: There was high compliance rate (72%). Most patients (77%) used atypical antipsychotics, 81 (69%) used a single medication, 35 (30%) used more than one [21 (18.1%) two and 14 (12%) three] atypical antipsychotic drug. Only 10 (8.6%) were taking typical antipsychotics. There were no among-drug differences in the percentage of patients meeting the recommended dose ( $p=.056$ , Fisher's exact test). Chlorpromazine equivalent dosage did not differ amongst any atypical antipsychotics subgroup. We also did not find any significant difference in recovery on CGIS nor on QOL or GAF between groups of different antipsychotic drugs. Conclusion: This study from Mumbai, India shows that most patients of schizophrenia in a long term follow up use atypical antipsychotics which are prescribed within recommended limits. The chlorpromazine equivalence dosages do not differ across antipsychotic medications. The outcome on clinical and functional parameters is also similar across all second generation antipsychotics

**NR7-22**  
**USE OF LISDEXAMFETAMINE DIMESYLATE IN TREATMENT OF COGNITIVE IMPAIRMENT AND FATIGUE: A DOUBLE-BLIND, PLACEBO-CONTROLLED STUDY**

*Chair: Joel Young M.D.*

**SUMMARY:**

Objective: To assess the safety and efficacy of lisdexamfetamine dimesylate (LDX) in the treatment of cognitive impairment, fatigue, and chronic pain in adults (ages 18 – 60) with chronic fatigue syndrome (CFS). Methods: Adults with CFS were randomly assigned to a flexible morning dose (30, 50, 70 mg/day) of placebo or LDX for a six-week trial. Symptom assessments were administered at each visit. Cognitive impairment was assessed using the Behavior Rating Inventory of Executive Function—Adult (BRIEF-A). Fatigue and pain were assessed with the Fatigue Severity Scale, the McGill Pain Questionnaire, and the Fibromyalgia Impact Questionnaire. The Clinical Global Impression, AD/HD Rating Scale, and Hamilton Anxiety Scale were also administered. Safety was assessed through the measurement of vital signs at each visit. Results: Relative to the placebo group, participants in the LDX

group showed statistically significant improvement on the BRIEF-A, Fatigue Severity Scale, McGill Pain Inventory, Clinical Global Impression, and AD/HD rating scale. Statistically significant differences between LDX and placebo were not observed on the Fibromyalgia Impact Questionnaire or the Hamilton Anxiety Scale. Changes of clinical importance were not noted in vital signs. Conclusions: Relative to placebo, LDX improved executive functioning and reduced fatigue, pain, and AD/HD symptoms. The results suggest the safety and efficacy of LDX as a treatment for impaired cognitive functioning, chronic fatigue, and pain in patients with CFS. Furthermore, the study detected high rates of AD/HD in this CFS population, suggesting a link between the two conditions. LDX should be studied more comprehensively in CFS and fibromyalgia.

**NR7-23**  
**IMPROVEMENTS IN CITALOPRAM SEXUAL DYSFUNCTION BY SWITCHING TO ESCITALOPRAM**

*Chair: Andres Avellaneda Ojeda M.D.; Author(s): Liliana Lopez M.D. Asim A. Shah, M.D.*

**SUMMARY:**

Case: 33 year old man with history of Hypothyroidism has first episode of anxiety and depressive symptoms including depressed mood, lack of sleep, loss of interest, low energy level, decreased appetite and mild psychomotor retardation. He did not experience suicidal ideations, and had no problems with concentration. He was started on Citalopram 20 mg daily. After one week of starting the medication, he presented excessive sweating at night, decreased sex drive, loss of interest in sex, weak morning erection and increased latency for erection. After taking Citalopram for 6 weeks, his PCP switched him to Escitalopram 10 mg due to these sexual side effects, as he was otherwise responding well to Citalopram. After one week he noticed significant improvement in sexual symptoms but continued to present night sweats. Recently, the Escitalopram dose was increased to 20 mg daily. He started to have sweating and decreased sexual drive and delayed orgasm, he reports that the symptoms are not as severe when compared he was on Citalopram 20 mg. Social: Computer engineer, drinks 3-5 alcohol drinks per night, about 1 month ago decreased to 2 drinks per night. No tobacco or drug use. Discussion: The last studies report between 30 to 60% of SSRIs treated patients may experience some form of treatment induced sexual dysfunction, significantly higher with Paroxetine, fluoxetine and in some reports with Citalopram among other SSRIs. Some clinicians consider to switch therapy

to an agent with a lower incidence of sexual side effects, which offers the advantage of removing the offending agent from the patient's treatment regimen altogether and replacing it with an agent that offers similar efficacy and fewer sexual adverse effects. However, one of the risks that clinicians should consider is that any required tapering period between ending one treatment and initiating another would place a particular patient at risk for relapse of depressive symptoms. Ashton 2006 reported that average of 68.1% of patients experienced improvement in sexual dysfunction by discontinuing their SSRIs and switching to Escitalopram 10mg. Also, 73.1% of patients on 10 mg showed mild or marked improvement in sexual functioning versus 63.2% of patients on 20 mg and 50% patients on 30 mg of Escitalopram. Because sexual dysfunction is thought to be a dose related side effect, a lower dose is less likely to cause sexual dysfunction than a higher dose. Conclusion: SSRIs may not have the same potential for sexual side effects development, even small differences in molecular configuration like in case of isomers, may make a difference on side effect profile. There is increased association with Citalopram 20 mg dose and sexual side effects in this patient, which seemed to decrease with equivalent dose of Escitalopram 10mg. This effect also seem dose dependent, since increasing dose of Escitalopram showed slight increase in sexual side effects, but still lower if compared with Citalopram subjective

**NR7-24**  
**CURTAILING ANTIPSYCHOTIC POLYPHARMACY IN A STATE INSTITUTION:REVISITING AN INTERVENTION AFTER TEN YEARS**

*Chair: Jeffry Nurenberg M.D.; Author(s): Schleifer, Steven, S. Becker, Robert*

**SUMMARY:**

Antipsychotic polypharmacy is becoming a norm and has occasioned much controversy. We had undertaken a performance improvement initiative at a state psychiatric hospital to reduce polypharmacy in late 2001. Documentation of antipsychotic prescribing practices for 14 psychiatrists in November, 2001 was shared with each by the chief of psychiatry, comparing individual data with that of anonymous peers. Suggesting that some polypharmacy may have been unnecessary, a goal of reduced antipsychotic polypharmacy of 10 percent was suggested, with, however, no sanctions implied. Antipsychotic polypharmacy fell significantly ( $p < 0.01$ ), from 40 percent of patients treated with antipsychotics in November, 2001 to 31 percent in August, 2002.

Based on the perception that polypharmacy had increased substantially subsequently, we undertook a similar intervention in February, 2011 to determine if similar clinical conditions and behaviors would apply. Antipsychotic polypharmacy was found for 49.2% of 465 patients treated with antipsychotics in December, 2010, with feedback by the medical chief provided in February, 2011 (and no other formal interventions). Overall hospital polypharmacy rates declined to 44%, 39.6%, and 40.8% in May, August, and October, 2011, respectively. There were significant overall time effects ( $F=3.25, p<0.025$ ), with significant differences between the baseline and the August and October levels ( $p<0.05$ ). Patterns of polypharmacy medications and factors contributing to the reduction, including that of the intervention, require consideration. The findings suggest that despite a shift in inpatient characteristics, clinical practice, and staffing, initiatives requiring only modest effort may lead to significant change in hospital-wide prescribing practices.

**NR7-25**  
**DRUG UTILIZATION PATTERNS FOR**  
**PALIPERIDONE PALMITATE IN MEDICAID**  
**PATIENTS**

*Chair: Erik Muser Phar M.D.; Author(s): Elizabeth Campagna, MS, Joseph Parks, M.D., Paul Stuve, Ph.D., Deborah Thomas, Ph.D., Hai Fang, Ph.D., Eva Dilbert, MHA, Dilesh Dosbi, Phar M.D., John W. Newcomer, M.D., Elaine H. Morrato, DrPH*

**SUMMARY:**

**Objective:** Paliperidone palmitate (PP) is a once-monthly atypical antipsychotic approved for the treatment of schizophrenia. The long-acting formulation is designed to improve patient adherence to therapy; however, data on real-world utilization are limited. This retrospective cohort study aimed to describe PP utilization patterns within the Missouri Medicaid system. **Methods:** Healthcare claims (08/2009 to 04/2011) from the Missouri Medicaid system were analyzed for 1531 patients starting PP. Patients newly initiated on PP with at least 12 months of continuous Medicaid eligibility before and after PP initiation (index date) were included ( $N=943$  [61.6%]). Patients dually eligible for Medicaid and Medicare were excluded (24.7%), resulting in a final study cohort of 355 patients. Descriptive statistics were calculated to characterize PP use in the 12 months following the drug index date (first outpatient prescription recorded in the pharmacy claims). Dosing patterns were described using modal dose and days between prescriptions. Treatment adherence for this injected medication was described using number of

prescription claims per patient and derived days supply (using the labeled dosing schedule). **Results:** The modal dose for the index PP prescription claim was 234 mg (46.5% of patients), for the second PP prescription claim 156 mg (56.0%), and for the third and subsequent prescription claims (maintenance) 156 mg (42.9%). The second most common maintenance dose was 117 mg (33.5%). The median number of PP prescription claims per patient was 9 (interquartile range [IQR]: 4-15); 42.0% of patients had 12 or more PP claims, whereas 23.9% had 3 or fewer PP claims. The median (IQR) derived days of supply dispensed per patient was 270 (90-450) days. The median (IQR) days between index and second prescriptions was 21 (4-31) days; 38.9% of patients had their second PP prescription claim within 10 days of their index claim date. The median (IQR) days between second and third prescriptions was 28 (25-35) days and between all subsequent prescriptions was 30 (28-35) days per patient. **Conclusion:** This is one of the first analyses examining real-world utilization of PP in a Medicaid population. The majority of patients were therapy adherent, and dosing appears to have been generally consistent with labeled instructions. Funded by Janssen Scientific Affairs, LLC

**NR7-26**  
**N-ACETYL CYSTEINE REDUCES**  
**AGGRESSIVE BEHAVIOR IN CHRONICALLY**  
**HOSPITALIZED MENTALLY ILL PATIENTS**

*Chair: Swapnil Gupta M.B.B.S Author(s): Richard McCarthy, M.D., Ph.D. Jatinder Mohan Chawla, M.D. Lama Bazzi, M.D.*

**SUMMARY:**

**Objective/Hypothesis:** N-acetyl cysteine (NAC) is a little understood, acetylated amino acid with an emerging usefulness in psychiatry. N-acetyl cysteine has been shown to reduce the symptoms of both schizophrenia (Berk et al, 2008) and bipolar disorder (Berk et al, 2008) in two placebo controlled trials. It is thought to act via modulation of NMDA glutamate receptors or by increasing levels of glutathione, thereby acting as an anti-oxidant. We aim to study the effect of N-acetyl cysteine as an adjunctive medication, on aggressive behavior in chronically hospitalized, mentally ill patients, irrespective of index psychiatric diagnosis. **Method/Proposed Methods:** Patients with severe mental illnesses, irrespective of diagnosis, who were chronically hospitalized at Kingsboro Psychiatric Center and whose aggressive behavior was refractory to treatment with conventional psychotropic medications including antipsychotics, mood stabilizers antidepressants and benzodiazepines were started on N-acetylcysteine in

an open label fashion by the primary treatment team. All patients started on N-acetylcysteine between the period of February and December 2010 were identified using pharmacy records. The number of aggressive incidents, types of aggressive incidents (verbal, aggression directed against property, peer or staff) and the interventions used to manage these incidents (verbal redirection, intra-muscular or oral emergency medications, seclusion and restraint) were counted using an electronic event monitoring system that is used in the hospital. These data were obtained for each patient for a period of six months before and six months after the addition of N-acetylcysteine to the standard treatment regime (mirror image design). The data will be both qualitatively and quantitatively analyzed, looking for trends in aggressive behavior before and after the addition of NAC. Furthermore, we will collect clinical data, including subjects' diagnoses on other axes, thus allowing for confounding variables as well as the influence of comorbid personality disorders in our analysis. Discussion/Significance: If found effective, NAC may provide a more tolerable option for treating aggression, as an adjunct to other medications that have more serious adverse effects such as lithium and antipsychotics including clozapine. Moreover, it is also available as an over the counter medication unlike other psychotropic medication. In addition, the effects of NAC on other causes for chronic hospitalization, including positive and negative symptoms, extrapyramidal symptoms, and inappropriate sexual behaviors, remain to be explored.

**NR7-27**  
**EFFECT OF MODAFINIL COMPARED WITH**  
**CAFFEINE ON PREATTENTIVE AUDITORY**  
**PROCESSING AS REFLECTED BY MISMATCH**  
**NEGATIVITY (MMN)**

*Chair: In Won Chung M.D.; Author(s): Tak Youn, M.D., Kyungmi Jang*

**SUMMARY:**

The mismatch negativity (MMN) as an auditory evoked potential is thought to reflect an early, preattentive, preconscious attention process. We investigated the impact of modafinil as a CNS stimulator on MMN with high density electroencephalography (EEG). Method: A group of 12 healthy subjects was studied in randomized double blind trials under the following 4 conditions: after 200mg Provigil, 100mg caffeine, 200mg caffeine or placebo. The MMNs resulting from auditory stimuli with passive oddball paradigm in 12 normal subjects, were recorded by 64 channel EEG. The latency and power of MMN were analysed by SCAN

program. Results: A latency of MMN after Provigil and caffeine 100mg and 200mg were shortened than placebo significantly. An amplitude of MMN of Provigil, caffeine 100mg, and 200mg were also increased significantly. Conclusion: Modafinil is a psychostimulant appeared to have multiple effects on catecholamine systems in the brain, including dopamine and norepinephrine. Our study showed modafinil improved informational processing in normal subjects.

**NR7-28**  
**TREATMENT PATTERNS, HEALTHCARE**  
**UTILIZATION AND COST AMONG PATIENTS**  
**WITH MAJOR DEPRESSIVE DISORDER**  
**(M.D.D) TREATED WITH ANTIDEPRESSANTS**

*Chair: Keith Isenberg M.D.; Author(s): Debra Eisenberg, Ph.D., Tao Gu, Ph.D., Jennifer Wang, Ph.D., Jeff T White, Ph.D.*

**SUMMARY:**

Selective Serotonin Reuptake Inhibitors (SSRIs) and Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) are effective treatment of Major Depressive Disorders (M.D.D). This study evaluated treatment patterns, healthcare resource utilization, and cost associated with use for treatment of M.D.D. The retrospective cohort study used administrative medical and pharmacy claims data from the HealthCore Integrated Research Database (HIRD). Patients aged 18-64 with 1 or more medical claim for M.D.D and one or more pharmacy claim for SSRIs and SNRIs were identified between January 1, 2009 and November 30, 2009. Patients were excluded if they had a claim for bipolar disorder (ICD-9 CM=296.0x, 296.1x, 296.4x-296.9x) or were not continuously enrolled for at least 1 year during the study period. Adherence patterns (e.g. proportion of days covered [PDC]), and healthcare utilization and cost (M.D.D-specific and total cost of care) were assessed using descriptive statistical analyses. Generalized linear model (GLM) with the log link function and a gamma distribution was used to examine the association between health care cost while controlling for patient demographic and clinical characteristics. 81,197 patients were identified. Escitalopram (26%) was prescribed most frequently, followed by sertraline (16%), duloxetine (14%), venlafaxine (12%), fluoxetine (12%), citalopram (10%), paroxetine (6%) and desvenlafaxine (4%). PDC was highest for venlafaxine (66%) followed by duloxetine and paroxetine (62%), sertraline (60%), fluoxetine (59%), escitalopram (57%), desvenlafaxine (55%) and citalopram (54%). Post-index rates of M.D.D-related inpatient admission were similar among the groups (desvenlafaxine 3%, escitalopram

3%, duloxetine 5%, venlafaxine 4%, citalopram 3%, fluoxetine 3%, paroxetine 3%, and sertraline 3%). These trends were also noted in the ER, office visit and outpatient setting for both M.D.D-specific and total cost of care. M.D.D-specific healthcare costs were lowest for citalopram (\$858) followed by sertraline (\$1,128), fluoxetine (\$1,295), paroxetine (\$1,406), desvenlafaxine (\$1,948), escitalopram (\$2,065), duloxetine (\$2,867) and venlafaxine (\$2,893). Controlling for variables including age, gender, region, pre-index comorbidity and treatment pattern indicated a significant difference in M.D.D-related (hazard ration=1.33;p<.0001) and total cost (hazard ration=1.138;p<.0001). Conclusions: PDC rates were less than desirable but similar to that observed in clinical practice. Differences in the costs associated with SSRIs and SNRIs are not explained by variation in treatment pattern, comorbidity, region, gender and age.

**NR7-29****A SURVEY OF PATIENT'S MEDICATION KNOWLEDGE AT TIME OF DISCHARGE: A BENCHMARK AND AN UPDATE**

*Chair: Ronald Rosenberg M.D.; Author(s): Mark Russ M.D., John Kane M.D.*

**SUMMARY:**

At or near time of discharge 113 consenting patients were interviewed by auxiliary staff regarding knowledge of their medications. Patients demonstrated accuracy for an average of 58.3 % of their psychotropic medications.. Scores of their knowledge of regime and intent to adhere to their regime were also made. Patients who could name their diagnoses had better knowledge of their medications, including patients who named the wrong diagnosis. Schizophrenic patients tended to have less knowledge than those with affective illnesses. The study emphasizes the need to teach patients about their illnesses and raises questions regarding cognitive issues that could impair patients with schizophrenia.

**NR7-30****EVALUATING THE SAFETY AND METABOLIC PROFILE OF VYVANSE FOR THE TREATMENT OF ADHD IN EUTHYMIC ADULTS WITH BIPOLAR I/II DISORDER**

*Chair: Roger McIntyre M.D.; Author(s): Mohammad Alsuwaidan, M.D., Isaac Szpindel, M.D., Timothy Bilkey, M.D., Doron Almagor, M.D., Hanna Woldeyobannes, HBSc., Alissa Powell, BA, Laura Ashley Gallaugher, HBSc., Joanna Soczynska, HBSc., Sidney Kennedy, M.D.*

**SUMMARY:**

Background: Individuals with bipolar disorder (BD) cluster risk factors for metabolic syndrome and have significantly higher rates of overweight/obesity, diabetes mellitus (DM), and dyslipidemia when compared to the general population and select psychiatric control groups. Moreover, attention deficit hyperactivity disorder (ADHD) differentially affects adults with BD. ADHD, comorbid in BD, is associated with a more complex illness presentation, earlier age at onset, substance use comorbidity, and poor functional outcomes. There remains a dissensus in the field as to the role of psychostimulants in bipolar disorder. There is a paucity of empirical evidence guiding treatment decisions as to the appropriate use of this class of agents in the adult BD population. Objective: The primary objective of the present study was to evaluate the effect of lisdexamfetamine dimesylate on weight, BMI, and waist circumference parameters in euthymic individuals with primary diagnosis of BD I/II and ADHD. The secondary objective of this study was to evaluate the safety and efficacy of lisdexamfetamine dimesylate in the treatment of ADHD in adults presenting with syndromal ADHD phenomenology. Methods: A total of 45 subjects with a primary diagnosis of BD and adult ADHD were enrolled. Subjects received open label adjunctive lisdexamfetamine dimesylate for four weeks, initiated at 30 mg/day and titrated to 30-70 mg/day based on efficacy and tolerability. Results: This study has now been completed (last patient last visit January 2012). Results from the analysis of this study will be presented.

**NR7-31****EFFECT OF LURASIDONE ON DEPRESSIVE SYMPTOMS IN PATIENTS WITH SCHIZOPHRENIA**

*Chair: Henry Nasrallah M.D.; Author(s): Josephine Cucchiaro, Ph.D. Jay Hsu, Ph.D. Peter Werner, Ph.D. Antony Loebel, M.D.*

**SUMMARY:**

Objective: Clinically significant depressive symptoms are common in schizophrenia, and are associated with greater functional impairment and worse outcomes (Zisook et al, Am J Psych 1999;156:1736-43; Mulhollan et al, Adv Psych Treatment 2000;6:169-77). The goal of this study was to evaluate the efficacy of lurasidone in patients with a DSM-IV diagnosis of schizophrenia who were experiencing clinically significant depressive symptoms. Methods: A post-hoc analysis was performed on pooled data from 4 six-week, double-blind, placebo-controlled trials, for which MADRS data were available. Subjects hospitalized with an acute

exacerbation of schizophrenia were randomly assigned to treatment with fixed, once-daily doses of lurasidone 40 mg (n=236), 80 mg (n=322), 120 mg (n=232), 160 mg (n=112), or placebo (n=439). LOCF-endpoint data were analyzed based on an ANCOVA model. Remission was defined as an endpoint MADRS <10 (Hawley et al, J Aff Disord 2002;72:177-84). Results: Baseline characteristics were similar for lurasidone (n=938; mean MADRS, 11.5) and placebo (n=448; mean MADRS, 11.9) subjects. At baseline, 45.0% of subjects had a MADRS >12, 33.0% >14, 24.5% >16, and 18.8% >18. Treatment with lurasidone was associated with significantly greater LOCF-endpoint improvement in the MADRS compared with placebo in the total sample (-2.8 vs. -1.4; p<0.001), and in each baseline depression severity subgroup: MADRS >12 (-6.7 vs. -4.8; p<0.005), MADRS >14 (-7.8 vs. -5.3; p<0.005), MADRS >16 (-9.3 vs. -6.3; p<0.005), and MADRS >18 (-9.7 vs. -6.8; p<0.05). The largest effect size was observed for the 160 mg dose of lurasidone (0.43). Conclusion: The results of this pooled post hoc analysis show a relatively high frequency of concurrent depressive symptoms in subjects hospitalized for acute schizophrenic exacerbation. In these pooled studies lurasidone produced significant improvement in depressive symptoms associated with schizophrenia throughout the daily dose range of 40-160 mg, with an efficacy advantage for the 160 mg dose. These results warrant further evaluation of lurasidone in patients with schizophrenia and co-morbid depression

**NR7-32**  
**VENTRICULAR FIBRILLATION ARREST**  
**WITH THERAPEUTIC VENLAFAXINE**  
**DOSING: A CASE REPORT**

*Chair: Mayuri Hassano M.Psy.; Author(s): Crepaldi A. L.; Vieira, M.E. B*

**SUMMARY:**

Introduction Venlafaxine is a widely prescribed drug to treat anxiety and depressive disorders. Its cardiovascular side effects include clinically significant blood pressure increase, orthostatic hypotension and tachycardia. Life-threatening arrhythmias are extremely rare even in overdose, except possibly in larger doses (>8 grams) of the medication. Case presentation We present a case of a 42-year-old man without pre-existing cardiac disease, who started on venlafaxine 75 mg/day to treat a severe agoraphobia and panic disorder as well as a moderate major depressive episode (DSM-IV criteria). He was already taking diazepam 10 mg/day without symptoms improvement. Two months later he was brought to hospital's emergency room in ventricular fibrillation arrest, and was successfully resuscitated and

fully recovered. After complete cardiologic evaluation and investigation, all possible causes of the ventricular arrhythmia were excluded, except for the daily use of venlafaxine combined with diazepam. An implantable cardioverter defibrillator was placed in his heart in order to prevent future life-threatening arrhythmias. At present the patient is taking sertraline 150 mg per day and he is in cognitive and behavioral therapy with significant symptoms improvement. Discussion The authors discuss antidepressant cardiovascular side effects and the precautions that should be taken into account when deciding the antidepressant class. Conclusion This case represents the first report of ventricular fibrillation in a patient using low doses of venlafaxine.

**NR7-33**  
**USING AN EMR TO IMPROVE METABOLIC**  
**MONITORING FOR PATIENTS ON**  
**ANTIPSYCHOTIC MEDICINES: AN**  
**INTERDEPARTMENTAL INTERDISCIPLINARY**  
**QUALITY PROJECT**

*Chair: Ronit Dedesma M.D.; Author(s): Matthew Davis M.D., Abbie Ewell M.D., David Baron M.D., Jessica Goren Ph.D., Hilary Worthen M.D., Miranda Balkin M.D., Nadine Palermo DO, Clinton Pong M.D., Carleen Riselli RN, Michael Soliman M.D., James Yeh M.D., and Robert Joseph M.D.*

**SUMMARY:**

Purpose: Patients with Serious Mental Illness are known to have shorter life expectancy than the general population. A significant amount of the mortality is due to preventable cardio-vascular complications of antipsychotic medicine. These medicines, especially second generation antipsychotics (SGA) are known to cause many metabolic changes associated with cardiovascular disease. These include weight gain, and disturbances of glucose and lipid metabolism. Monitoring metabolic changes in patients placed on SGA has been recommended by many professional groups including the APA and ADA. Despite these recommendations systematic monitoring of metabolic changes has rarely been accomplished. We will describe a joint effort by the Departments of Family Practice (FP), Internal Medicine (IM), Psychiatry, Pharmacy and IT to monitor metabolic syndrome in patients placed on AM at Cambridge Health Alliance, a safety net primary care network in the northern suburbs of Boston. Method: Baseline and rates of metabolic monitoring for patients newly started on SGA during 2010 were obtained from our EMR. An educational program about the morbidity associated with SGA and the recommended guidelines was developed for all

members of Departments of Psychiatry, FP and IM. The monitoring program was promoted through a series of Grand Round presentations by residents in IM and FP and through a number of educational sessions throughout all three departments. The EMR was then used to prompt prescribers at the time they were prescribing of the recommended monitoring guidelines. EMR Tools using Epic software such as smart phrases and flow sheets were developed to facilitate and promote metabolic monitoring. Results: Baseline data notes that 798 patients were started on a SGA during 2010. Sixty-one % of the prescriptions were written by psychiatrists, 27 % by IM and FP providers and 12% of patients had prescriptions written by both a psychiatric provider and a primary care provider. Baseline metabolic measures were obtained in 30-40% of patients without significant differences in rates between psychiatric and medical providers. Among all prescribers 23% of prescriptions were for "Other Mood" Disorders; 15% for psychotic disorders; 19 % for Bipolar Disorder; 11% for anxiety disorders; 26 % for unlisted diagnoses and 4% for substance use disorders. Monitoring rates increased over the months following the educational efforts and the implementation of the EMR prompts. These data will be reported. Conclusion: Monitoring for metabolic side effects of AM according to guideline recommendations was poor (30-40%) at baseline (usual care). An institutional wide quality improvement program involving internal medicine, family medicine, psychiatry, pharmacy and IT was developed, implemented and led to an improvement in these rates.

**NR7-34**  
**TREATMENT OF CLOZAPINE INDUCED**  
**SIALORRHEA WITH BUPROPION: A CASE**  
**SERIES**

*Chair: Robert Stern M.D.; Author(s): Judy Springer, DM.D., Scott W. Podell, DM.D., Natarajan Elangovan, M.D.*

**SUMMARY:**

Background: Clozapine is the treatment of last resort for patients with "treatment refractory" schizophrenia. Clozapine produces several difficult to manage side effects, including sialorrhea, which occurs at a rate of approximately 50%. Severe or even moderate sialorrhea can reduce clozapine's tolerability and may lead to treatment discontinuation. Currently there is no established treatment for CIS. Objectives: This Performance Improvement project assessed two therapeutic options for CIS: scopolamine transdermal patch - 1.5 mg post-auricular, replaced every 72 hours (as per Gaftanyuk and Trestman 2004) or bupropion -

150 mg/p.o./daily (as per Stern et al. 2009). Methods: Patients who experienced sialorrhea in the course of their treatment with clozapine were offered to participate in the PI project; patients completed a pre- and post CIS treatment evaluation consisting of a questionnaire and salivation rate measurement (cc/5 min). Pre" and "post" intervention findings were compared. Results: Bupropion resulted in superior improvement in day time CIS, and by comparison in strikingly higher improvements in night time drooling. Clinicians and patients found the bupropion treatment to be effective. No adverse drug reactions were reported with either bupropion or scopolamine. Discussion: These findings suggest that further controlled trials to assess the safety and efficacy of bupropion in the treatment of clozapine induced sialorrhea are warranted.

**NR7-35**  
**RATES OF MONITORING FOR METABOLIC**  
**SIDE EFFECTS OF ANTIPSYCHOTICS AT 32**  
**VA MEDICAL CENTERS**

*Chair: Richard Owen M.D.; Author(s): Dinesh Mittal, M.D. Chenghui Li, Ph.D. Silas Williams Kristen Viverito, Ph.D.*

**SUMMARY:**

Objective: This study examined current practices for monitoring metabolic side effects among outpatients receiving an antipsychotic medication at 32 Veterans Affairs (VA) Medical Centers. Methods: In a retrospective cohort analysis using data extracted from national and regional VA data sources, we examined the extent to which patients beginning treatment with a new antipsychotic medication (not prescribed in the prior six months) had monitoring of weight, glucose (or hemoglobin A1c), and low-density lipoprotein cholesterol (LDL) monitored at baseline and 90-day follow-up monitoring as recommended by an American Psychiatric Association/American Diabetes Association consensus panel. We selected outpatients beginning a new antipsychotic treatment episode in the 32 facilities in Veterans Integrated Service Networks (VISNs) 18-22 between April 1, 2008 and March 31, 2009 (N=12,009). Monitoring of the metabolic parameters was examined within 30 days before or after the new prescription (baseline) and between 60 and 120 days thereafter (follow-up). Multivariate logistic regression models examined the association of patient characteristics with the likelihood of receiving recommended baseline and follow-up monitoring. Results: Frequency of monitoring for each of the three metabolic parameters (weight, glucose/hemoglobin A1c, LDL) was significantly greater (p<0.001) at baseline than at 90-day follow-up. Overall, 74.6% patients received monitoring of at least

one of the metabolic parameters at baseline and 55.2% received some follow-up monitoring. Weight was the most frequently monitored metabolic parameter at both baseline (66.6%) and 90-day follow-up (49.5%), whereas baseline and follow-up monitoring were less frequently performed for glucose (45.8% and 27.1% respectively) and LDL (32.1% and 16.2%, respectively). Having diagnoses of diabetes or dyslipidemia were the most consistently significant predictors for both baseline and follow up monitoring of the metabolic parameters. Monitoring did not significantly differ between patients with schizophrenia and patients with non-psychotic mental disorders. However, patients with no mental health diagnosis had significantly lower rates of monitoring. There were also significant differences in monitoring rates for patients prescribed antipsychotics with different propensity to cause metabolic side-effects. For example, patients prescribed an antipsychotic agent in the highest risk category (e.g., olanzapine or clozapine) were more likely to have weight monitored at baseline than those in the lowest risk category (e.g., aripiperazole or ziprasidone; adjusted odds ratio = 1.2, 95% CI 1.01-1.42,  $p < 0.05$ ). Conclusions: Quality improvement efforts are needed to improve monitoring for metabolic side-effects of antipsychotics.

#### NR7-36

### EVALUATION OF METABOLIC LABORATORY MONITORING AND CO-MORBID METABOLIC CONDITIONS IN MEMBERS OF A MANAGED MEDICAID PLAN USING ATYPICAL ANTIPSYCHOTICS

*Chair: Lisa Werner D.O.; Author(s): Phil Hanus, Phar M.D., Thomas Wolfe, Phar M.D., Martin Giannamore, Phar M.D.*

#### SUMMARY:

Objectives: 1) To evaluate compliance of laboratory monitoring for metabolic effects (glucose and lipids) of second-generation antipsychotic (SGA) medications according to published national guidelines, 2) to evaluate the prevalence of co-morbid metabolic conditions (dyslipidemia, hypertension, heart disease and diabetes) and medication treatment for these conditions, and 3) to determine predictors of metabolic monitoring. Methods: A retrospective analysis of pharmacy and medical claims from 6/1/07 to 5/31/09 for adult members with at least 1 prescription for an SGA between 6/1/08 and 5/31/09. For assessment of laboratory monitoring, only patients continuously enrolled for at least 12 months inclusive of the first SGA prescription were evaluated. Medical claims were used to assess metabolic lab monitoring and the occurrence

of psychiatric and co-morbid metabolic conditions. Pharmacy claims were used to determine number of patients being treated for co-morbid metabolic conditions. A subset of SGA new starts, defined as no prescriptions for a SGA during the 6 months prior to the index prescription, was also evaluated. Results: 8285 patients were identified with 66% female and age  $39 \pm 12$  years. Bipolar disorder (36%), depression, other (35%) and schizophrenia (13%) were the most common psychiatric diagnoses. Quetiapine (35%), aripiperazole (25%) and riperidone (18%) were the most commonly used SGAs. Patients were identified with at least one diagnosis code for the following medical conditions: hypertension (35%), dyslipidemia (29%), diabetes (16%), CVD (12%) and obesity (8%). Antihypertensive (40%), antihyperlipidemic (22%) and anti-diabetic (12%) medications were commonly used in these patients. 3235 of these patients were evaluated for laboratory monitoring. Laboratory monitoring during at least a 12 month period occurred in 55% of patients for cholesterol, 70% of non-diabetic patients for glucose, and 55% of diabetic patients for A1c. A subset of patients newly started on an SGA ( $n=1043$ ) were evaluated for lab monitoring. 42% of these patients had a cholesterol assessment, 70% of non-diabetic for glucose and 45% of diabetics for A1c. Patients with a primary care visit were more like to have an assessment of cholesterol (OR 3.52, 95% CI 2.58-4.8) and glucose (OR 4.34, 95% CI 3.29-5.72). New starts were less likely to have cholesterol assessment (OR 0.49, 95% CI 0.41-0.58). Conclusions: These results suggest that opportunities exist to enhance the monitoring for patients on SGAs. The greatest opportunity exists for those patients newly started on therapy. Enhanced care transition and communication with a PCP may facilitate improved monitoring, recognition and treatment of co-morbid metabolic conditions.

#### NR7-37

### GINSANA-115 EFFECT ON FRAMINGHAM RISK SCORE IN SCHIZOPHRENIA PATIENTS MAINTAINED ON ATYPICAL ANTI-PSYCHOTICS:A POSTHOC ANALYSIS OF RCT

*Chair: Simon Chiu M.D.; Author(s): Zack Cernovsky, Ph.D.; Yves Bureau, Ph.D.; Robbie Campbell, M.D., FRCP(C); Mariwan Husni, M.D., FRCP(C); John Copen, M.D., FRCP(C); J Houicin, Ph.D.*

#### SUMMARY:

Introduction: Recently, accumulating evidence suggests that schizophrenia carries higher cardiovascular and metabolic risks. The role of atypical antipsychotics

in mediating the health risks remains controversial. Very few studies focus on risk reduction strategies. Objective: Test whether the phyto-neurosteroid, PanaxGinseng adjunct treatment is efficacious in reducing the cardiovascular risks as measured with Framingham Risk score (FRS) in schizophrenia. Framingham risk score encompasses smoking history, age, gender, blood pressure, lipid profile (LDL-cholesterol, total cholesterol) in ranking the risk score. Method: We conducted a post-hoc study of the action of a standardized formulation of PanaxGinseng : Ginsana-115 (Boehringer-Ingelheim, Switzerland) in modifying FRS in a randomized controlled study of the Ginsana-115 in a cohort of schizophrenic subjects exhibiting significant negative symptoms. Schizophrenics with SANS (Scale for Assessment of Negative symptoms) score > 24 entered into the study. The subjects were Randomized into 3 groups: placebo-controlled; Ginsana-115 100 mg, and Ginsana-115 200 mg group. The FRS was evaluated at week 0 and week 8 along with SANS score. The subjects were maintained on atypical antipsychotic. Safety was monitored with adverse events checklist, AIMS, vitals and metabolic screen Results: We recruited total of 28 subjects for post-hoc study: age 37,8 yrs; Male/female ratio 21:7. As compared to the baseline, the placebo group (n=14) did not show any significant change in the FRS score (16.3 % decrease p >0.05). Both the Ginsana-115 groups (100 mg n=8; 200 mg n=6) showed significant reduction in FRS score (24.1 % decrease for combined group (P < 0.05). Lipid level changes contributed largely towards the alterations in FRS scores. The risk factor decreased in parallel with the response rate of Improvement in negative symptoms Between-subject t-test showed PG 200 mg significantly (p< 0.05) reduced Flat Affect of SANS: effect size rpb =0.43 The side effects were highly tolerable and no adverse events were noted.. Conclusion: We interpreted the Ginsana cardiovascular protective effects in the light of its action at the PPAR (Peroxisome Proliferating Activating Receptor) complex modulating cardiovascular and metabolic cascade events . Ginseng warrants a larger controlled study to confirm the cardio-metabolic risk reduction in schizophrenia. Supported by SMRI USA

**NR7-38**  
**CONCORDANCES IN NORMAL CLINICAL PRACTICE WITH THE SPANISH CLINICAL CONSENSUS RECOMMENDATIONS FOR IMPROVING TREATMENT ADHERENCE IN SCHIZOPHRENIA**

*Chair: Mario Pena M.D.; Author(s): Alex Pons, M.D., Psy.D. Miquel Roca, M.D., Psy.D.*

**SUMMARY:**

Introduction: Non-adherence to treatment is extremely prevalent among patients with schizophrenia, reaching rates as low as 50% to 60%. This causes increased risk of exacerbations and relapses, more visits to the mental health center, frequent hospitalizations, and suicidal behavior. Furthermore, as the quality of life of both the patients and their environment worsen and the patient's social abilities diminish, more health resources are warranted. Despite the importance of this issue, in Spain few studies have evaluated the degree of adherence to treatment and analyzed the strategies used to improve compliance in patients with schizophrenia. Objective: To assess the degree of correlation between normal clinical practice and the theoretical recommendations outlined in the Spanish Clinical Consensus for the management of adherence failure in schizophrenia after a new therapeutic strategy had been initiated. Patients and methods: A six-month prospective, epidemiological and multicenter study was conducted in 2,433 patients aged 18-75 years of both sexes diagnosed with schizophrenia according to the DSM-IV criteria, with unsatisfactory pharmacological adherence and those who had a new therapeutic strategy established to improve compliance at the baseline visit. 295 psychiatrists from acute and mental health units throughout Spain participated. The study was of a non-intervention nature, and the treatment prescribed was determined by the clinical judgment of the physician responsible for the patient's management. Other assessments included socio-demographic and clinical characteristics, pharmacological treatment compliance and therapeutic strategy carried out in the management of adherence failure according to patient's profile. Results: Among study patients the most frequent cause of failure of pharmacological compliance was lack of insight (55.8%), followed by lack of efficacy (15.5%), adverse events (9.9%), and lack of family support (9.3%). The therapeutic strategies implemented to improve the lack of drug compliance by 241 (81.7%) psychiatrists that participated in this study did not match up with the Consensus recommendations. Regarding those patients whose management was in accordance with the first-line Consensus recommendations corresponded to patient groups with profile 6 (drug and alcohol consumers) (83.9%), followed by profile 1 (lack of insight) (76.0%). Conclusions: Our results point towards a possible inadequate management of Spanish schizophrenic patients with an unsatisfactory pharmacological adherence. In the majority of cases, the clinical management did not match up with the first-line Consensus recommendations and only 4 out of 10 patients included were managed according to

these. The deepest non-concordances with Consensus recommendations were the strategies preferred to evaluate compliance, the non-pharmacological therapies employed, and the lack of use of atypical injectable drugs.

#### NR7-39

### ANTIPSYCHOTIC DRUG ADHERENCE CORRELATES WITH HOSPITALIZATION RATES AND LENGTH OF STAY AMONG MEDICARE AND NON-MEDICARE SCHIZOPHRENIA POPULATIONS

*Chair: Ross Baker Ph.D.; Author(s): Bruce Wong, M.D.; Steve Offord, Ph.D.; Dario Mirski, M.D.; Jay Lin, Ph.D.*

#### SUMMARY:

**Background:** Non-adherence to antipsychotic medications is due to multiple factors including, in part, disease state and tolerability of currently available antipsychotic medications. Both compound the more general reasons for non-adherence to medication often seen in other conditions. **Objective:** To determine whether there is a relationship between medication adherence, all-cause hospitalization rates, and hospital length of stay (LOS) in Medicare and non-Medicare patients with schizophrenia. **Methods:** Patients with schizophrenia who were  $\geq 13$  years of age and used antipsychotic medications between 1/1/2005 and 9/30/2010 were identified from the MarketScan Medicare and Commercial health care claims databases. Antipsychotic medication adherence was estimated with a medication possession ratio (MPR) for the first year of medication use. Patient demographics and comorbidities were measured at baseline. All-cause hospitalization rates and LOS were determined for the follow-up period and their relationship to MPR was assessed using generalized linear models. Statistical analysis was carried out by SAS. **Results:** 1462 schizophrenia patients were identified from the non-Medicare population and 354 from the Medicare population who received a new prescription for an antipsychotic agent, the most common being risperidone, aripiprazole, and quetiapine. Non-Medicare patients were 50% female with a mean age of 39.1 years. Medicare patients were 65% female with a mean age of 71.4 years. Medicare patients were sicker, with Charlson comorbidity index (CCI) mean scores of 1.77 compared with non-Medicare patients who had a mean CCI score of 0.50 ( $p < 0.05$ ). During the first year after the initiation of an antipsychotic agent, the mean  $\pm$  standard deviation MPRs were  $0.43 \pm 0.35$  and  $0.49 \pm 0.37$  for the non-Medicare and Medicare populations, respectively. Hospitalizations for schizophrenia occurred at a mean rate of 0.23 hospitalizations per patient year

in non-Medicare patients and 0.18 hospitalizations per patient year in Medicare patients. Among non-Medicare patients, an increased MPR was associated with a lower hospitalization rate ( $-0.195$  hospitalizations;  $p = 0.011$ ) and shorter LOS ( $-2.11$  days;  $p = 0.018$ ). Similarly, among Medicare patients, higher adherence was associated with fewer hospitalizations ( $-0.261$  hospitalizations;  $p = 0.044$ ) and shorter LOS ( $-4.77$  days;  $p = 0.021$ ). **Conclusions:** We find an inverse relationship between antipsychotic medication adherence and hospitalization rates and LOS in both Medicare and non-Medicare schizophrenia patients. This relationship provides evidence that improving medication adherence in schizophrenia can reduce hospitalizations, LOS, and thus reduce overall healthcare costs. Antipsychotic medications are the mainstay for treating schizophrenia and thus, there is a significant challenge for health care professionals and patients to manage medication adherence to reduce the burden of schizophrenia on patients and health care resources.

#### NR7-40

### DRUG COMPLIANCE AND ASSOCIATED OUTCOMES IN SCHIZOPHRENIA PATIENTS BEFORE AND AFTER THE INITIATION OF DEPOT ANTIPSYCHOTIC AGENTS

*Chair: Steve Offord Ph.D.; Author(s): Dario Mirski, M.D.; Jay Lin, Ph.D.; Bruce Wong, M.D.*

#### SUMMARY:

**Background:** Depot antipsychotic agents are primarily used to manage poor drug compliance in the treatment of schizophrenia. Compliance behavior surrounding the use of depot agents in monitored clinical practice such as registries or clinical trials is difficult to quantify because of the bias introduced by the monitoring (Hawthorne effect). We studied the magnitude of non-compliance in patients prior to the receipt of depot agents and the subsequent healthcare outcomes of compliance using healthcare claims data. The results may aid clinical practice decisions in schizophrenia management. **Method:** Schizophrenia patients were identified from the MarketScan Commercial database, a US national health plan database, between 1/1/2005 and 9/30/2010. Index events were patients initiating treatment with depot antipsychotics compared to patients initiating oral antipsychotics. New oral antipsychotic users were chosen as the comparison group since it is the cohort most likely to exhibit good compliance, creating a conservative comparison cohort. Patients were required to be  $\geq 13$  years at the index event and have  $\geq 12$  months of continuous health plan coverage prior to (baseline) and after (follow-up) the index event.

Medication compliance was estimated with a medication possession ratio (MPR), which represents the time each patient possessed a drug compared to the total expected duration of therapy. MPR are expressed as median  $\pm$  standard deviation. A lower MPR indicates lower drug compliance. Statistical analysis was undertaken in SAS. Results: 3,004 patients met inclusion criteria. 394 patients initiated depot agents and 2,610 oral agents with a mean age of  $41.7 \pm 15.5$  and  $37.1 \pm 15.9$  years, respectively. Prior to depot initiation, median MPR was  $0.28 \pm 0.37$  which improved to  $0.79 \pm 0.34$ , while on depot agents, a relative increase of 182%. The median MPR during follow-up periods was significantly higher in the Depot vs. Oral cohort,  $0.79 \pm 0.34$  vs.  $0.58 \pm 0.35$ ,  $p < 0.0001$ . Hospital visits fell from  $1.6 \pm 1.66$  in the baseline period to  $0.7 \pm 1.20$  admissions per patient following the initiation of depot agents ( $p < 0.0001$ ). The total length of stay also decreased significantly from  $16.9 \pm 20.7$  days to  $6.6 \pm 14.4$  days ( $p < 0.0001$ ). There was no significant change in overall outpatient resource usage including the number of emergency room visits. Conclusions: Upon initiation of depot antipsychotics, patients had significantly improved drug compliance. In addition, patients initiating depot antipsychotic agents for schizophrenia treatment have significantly better drug compliance in comparison with patients initiating oral agents. The improvement in compliance is associated with reduced hospital admissions and short hospital length of stay.

**NR7-41****PATIENT CHARACTERISTICS OF PALIPERIDONE PALMITATE USERS AND ORAL SECOND GENERATION ANTIPSYCHOTIC USERS IN SOUTH CAROLINA MEDICAID**

*Chair: Meera Narasimhan M.D.; Author(s): Suzanne Hardeman, MSN, PMHNP Maria Butkus, M.P.H. Heather Kirby, BS Wally Altman, BS Michael Durkin, MS Andrew Howe, Phar M.D., BA*

**SUMMARY:**

Background: Paliperidone Palmitate (PP) is an injectable long-acting second generation antipsychotic approved for the treatment of schizophrenia. Limited information on utilization and patient considerations outside of clinical trials is available. Objective: To describe the clinical characteristics of patients initiated on PP or oral second generation antipsychotics (SGAs) in a Medicaid population. Methods: Retrospective pharmacy and medical claims (3/2009 to 6/2011) from the South Carolina Medicaid and Department of Mental Health programs were analyzed. Patients newly initiated on

PP or oral SGAs (aripiprazole, iloperidone, olanzapine, paliperidone, quetiapine, risperidone or ziprasidone) with 6 months continuous Medicaid eligibility were included for analysis. Medicare dual-eligible patients were excluded. The index date was defined as the first outpatient prescription/inpatient order for PP or oral SGA. Patients were followed 6 months pre- and post-index date. Baseline patient characteristics evaluated included: demographics (age, sex, and ethnicity), mental health (SMI) and comorbid concomitant diagnoses and PP or SGA medication utilization. Descriptive statistics were used to summarize the data. Results: 1,195 patients met the study eligibility criteria (185= PP, 1,010= oral SGA). The mean (SD) age of PP patients and oral SGA patients was 37.6 (11.8) years, and 36.3 (12.2) years, respectively. Patients treated with PP were more likely (59.4% versus 38.2%) to be male as compared to patients using oral SGAs. Patients receiving PP were more likely (60.9% versus 35.2%) to be African American than patients receiving oral SGAs. The mean (SD) Charlson Comorbidity scores were 0.43 (1.0) and 0.60 (1.3) for the respective PP and oral SGA patient populations. The mode (median) dose of the first observed PP claim was 117 (156) mg and the dosing distribution was 37.3% for 117mg, 23.2% for 156mg, 37.3% for 234mg, 1.1% listed <117mg and 1.1% initial dose not indicated. The mode (median) number of claims during the outpatient study period was 8 (6) injections for PP patients and 1(2) prescriptions for oral SGA patients in the post 6 month period. Conclusion: These preliminary results suggest that patients receiving PP differed from patients receiving oral SGAs on important demographic and clinical measures of comorbidity. These findings suggest that further research is needed to examine additional patient factors and outcomes associated with the differing treatment modalities.

**NR7-42****IMPROVEMENT IN THE LANGUAGE FUNCTION OF A PATIENT WITH AUTISM SPECTRUM DISORDER AFTER TREATMENT WITH TRANSCRANIAL MAGNETIC STIMULATION: A CASE REPORT**

*Chair: Matisyabu Shulman B.A.; Author(s): Giovanni Caracci M.D., Ye-Ming J. Sun M.D. PH.D.*

**SUMMARY:**

Transcranial magnetic stimulation (TMS) has been used experimentally to improve language in patients with language deficits. We hypothesized that TMS would provide language improvement in patients suffering from autism spectrum disorder. Thus we assessed the

language function of a patient with autism spectrum disorder under repetitive TMS (rTMS) treatment for her depression. The patient is a 20 year old female with depression and autistic disorder. Standard rTMS was delivered with NeuroStar magnetic stimulation system. After 15 sessions of treatment the patient showed improvement in the areas of communication and social interaction as assessed by the Autism Diagnostic Observation Schedule (ADOS) (6 to 4 and 13 to 11 respectively.) The patient's depression was also improved as evidenced by decreases in her HAM.D. (31 to 8) and Beck scores (39 to 13). To determine whether the improvement in language has been due to treatment of her depression or the direct action of TMS on the language center further research is needed.

**NR7-43****DEPRESSION AND HISTORY OF SUICIDE ATTEMPTS ARE RISK FACTORS FOR PREGNANCY AMONG ADOLESCENT GIRLS IN BOLIVIA: A CASE-CONTROL STUDY**

*Chair: Rosario Martinez-Saravia M.D.; Author(s): Rocabado-Michel I. M.D., Vaca-Martinez A. Ph.D., Castilla-Puentes W. M.D., Sanchez-Russi C. Ph.D., and Castilla-Puentes R. M.D., DrPH*

**SUMMARY:**

**Objective.** To examine if depression and history of suicide attempts are risk factors for pregnancy among adolescent girls in Bolivia. Our hypothesis is that depression and suicidality may be key factors accounting for the relationship between pregnancy in adolescents. **Methods.** A matched case-control study with cases and controls identified within a community-based demographic and health survey was conducted in La Paz Bolivia, from January 2010 to November 2011. A questionnaire focused on suicide behaviors, socioeconomic status, family structure, education, reproductive health, and childhood-adolescent trauma was applied to 645 adolescent girls (9-19 years of age). Depressive symptoms were measured by the Center for Epidemiological Studies Depression Scale (CES-D), with scores > 16 indicative of elevated depressive symptoms. Conditional logistic regression was used to adjust for potential confounders. **Results.** Respondents included 99 cases and 546 controls. Through multivariate analysis, depression [odds ratio (OR) 2.16, 95% confidence interval (CI) 1.24-3.77 ], the history of a prior suicide attempt 12 month and lifetime (OR 2.98, 95% CI 3.70-11.27 and OR 6.23, 95% CI 1.12-64.90 respectively) were factors associated with increased risk of adolescent pregnancies. As expected, another factors statistically associated in the multivariate analysis were:

physical and sexual abuse during childhood-adolescence (OR 2.13, 95% CI 1.35-3.38; OR 2.07, 95% CI 0.95-4.49 respectively ); being use of contraception (OR 5.31, 95% CI 2.92-9.65); history of anxiety disorders (OR 1.69, 95% CI 0.80-3.53); being less than 6 years in school at the time of the interview (OR 2.71, 95% CI 0.82-8.93); and living in a very poor household (OR 7.67, 95% CI 3.81-15.47). **Conclusion.** These findings suggest that depression (including suicidality) may be a key mechanism accounting for pregnancy among adolescents. The study found that in addition to depression and lifetime and 12 month suicide attempts, having suffered from physical and sexual abuse during childhood-adolescence, being use of contraception, a reported history of anxiety disorders, lower education and living in a very poor household were associated with adolescent pregnancy in La Paz.

**NR7-44****THE STATUS AND PERCEPTIONS OF MENTAL HEALTH IN MARRIAGE IMMIGRANTS AND THEIR CHILDREN IN KOREA**

*Chair: Yong-Chon Park M.D.; Author(s): Sun-Hea Lee, M.D. Dong-Hyun Ahn, M.D.*

**SUMMARY:**

**Objectives:** This study was purposed to examine the mental health in international marriage immigrants and their children in Korea. Furthermore we examined maternal perceptions of child mental illness and treatments. **Methods:** Seventy four immigrant mothers (21 Vietnamese, 16 Philippines, 15 Chinese, 22 others) and 86 Korean mothers were enrolled in this study. Participants were administered symptom checklist-90(SCL-90) for mothers and child behavior checklist (CBCL) for their children to examine mental health. The data about perceptions and treatments of mental illness were taken from semistructured interview with immigrant women. **Results:** Immigrant mothers especially lower educated women or Philippines had higher rates of psychological distress. Younger children had more externalizing behavior regardless of ethnicity and older children had more social problems or somatic symptoms than control group. Immigrant perceptions of child mental illness were almost 90% and were slightly different from Korean. However rate of visiting experts was generally lower than Korean. **Conclusion:** This study highlights the psychiatric difficulties of marriage immigrant and their children. Although they can perceive child mental illness, the utilization of mental health services may be severely limited.

**NR7-45****CULTURAL MISTRUST AND PSYCHOPATHOLOGY IN AFRICAN AMERICANS**

*Chair: William Lawson M.D.; Author(s): Michael A. Gara, Ph.D., William A. Vega, Ph.D., Stephan Arndt, Ph.D., Michael Escamilla, M.D., David E. Fleck, Ph.D., Ira Lesser, M.D., Harold W. Neighbors, Ph.D., Daniel R. Wilson, M.D., Ph.D. Stephen M. Strakowski, M.D.*

**SUMMARY:**

Rates of clinical diagnoses of schizophrenia in African Americans are uniquely elevated among major US ethnic groups and contradict population rates derived from epidemiologic surveys. A 6 site study of comparing ethnicity-blinded and unblinded diagnostic ratings of African American to White and Latino subjects with severe affective disorder using a sequential assessment design showed that African Americans according to the consensus of blinded expert raters, had higher and putatively misdiagnosed rates of schizophrenia spectrum diagnoses than did non-Latino White subjects. A key contributor in several studies have been higher reported rates of psychotic symptoms in African Americans. However African Americans also show higher rates of cultural mistrust: the degree to which African Americans distrusted white society. We sought to determine from this carefully diagnosed and blinded rater study if mistrust contributed to reported psychosis. The relationship between the cultural mistrust inventory and psychopathology as measured by the SAPS, MADRS and YMRS was examined in the 244 African American patients with severe affective disorders. 104 male and 144 female (age range 18-43) from the 6 regional site study were included. We found that the cultural mistrust inventory is significantly related to total psychosis ( $r=.15$ ) hallucinations/delusions ( $r=.14$ ) and depression ( $r=.20$ ), ( $p<.05$ ), but not mania or bizarre behavior, when controlling for demographics. Cultural mistrust is presumed to be the result of negative racial experiences or awareness of historical antecedents. These findings provide limited support to a cultural basis for the greater risk of psychosis in African Americans, which may account for the overdiagnosis of schizophrenia. Additional research is necessary to better understand socio-cultural factors such as cultural mistrust and psychopathology

**NR7-46****TREATMENT OF DEPRESSION IN LATINO WOMEN: RELEVANCE OF ACTIVATION AND SELF MANAGEMENT TRAINING**

*Chair: Laura Safar M.D.; Author(s): Co-Authors: Alegria, M.*

**SUMMARY:**

**Title:** Treatment of Depression in Latino Women: Relevance of Activation and Self-Management Training  
**Background:** Depression is highly prevalent and a significant source of morbidity and disability in the United States. Latinos comprise a growing percentage of the US population. The lifetime prevalence of Major Depressive Disorder is 10-25% for women and 5-12% for men. Less power and learned helplessness are some of the psychosocial factors which may explain this gender difference. Practice guidelines recommend both pharmacological and psychological interventions for the treatment of depressive disorders. There are very limited quantitative data supporting guidelines for the treatment of depression in Latino Women. Cultural factors and the influence of vegetative symptoms and negative cognitions characteristic of depression may contribute to perpetuate low levels of activation and self-management in Latinas. Activation and Empowerment training may help depressed Latinas develop a more collaborative relationship with their mental health provider and participate more effectively in their mental health care. **Objective:** To examine if the DECIDE intervention, which teaches patients a set of skills which may facilitate a more active role in the mental health encounter and in the individual self-management, and a more collaborative provider patient relationship, provides benefits in the treatment of depressed Latino Women. **Method:** A total of 225 depressed and 76 non-depressed Latino women were enrolled in a multisite random controlled trial examining a patient activation and self-management intervention. Measurements of activation (Patient Activation Scale-PAS) and of Self-Management (Perceived Efficacy in Patient-Provider interactions and Self Management-PEPPI) were administered at baseline, 45 days, and 90 days. Demographic characteristics across control and intervention groups are comparable, which indicated successful randomization. **Preliminary results:** There was an increase in activation in both intervention groups, but only in the non-depressed group there was a significant difference between intervention and control subjects. There was an increase in Self-Management scores in both intervention groups, but only in the subgroup of depressed subjects the difference was significant between intervention and control subjects. We discuss these findings and the influence of depressive disorders in subjects' activation and self-management.

**NR7-47****PILOT SURVEY OF COGNITIVE BEHAVIORAL**

## PSYCHOTHERAPY (CBT) SUPERVISORS TO DETERMINE THEIR SUPERVISORY PRACTICE AND LEARNING NEEDS

*Chair: Diana Kljenak M.D.*

### SUMMARY:

Background: Substantial empirical support for cognitive behavioral therapy (CBT) effectiveness in treatment of various psychiatric disorders has been demonstrated. Adequate training in CBT results in improved therapist competence and patient outcomes. Effective clinical supervision is an essential part of the training in CBT. However, we do not have a complete and accurate understanding of how supervisors themselves acquire competence in CBT or of the methods of CBT supervision they use. The need for training of supervisors is widely accepted and there is evidence that it can be effective. Methods: We piloted an anonymous self-administered questionnaire survey to CBT supervisors who have attended a supervisory peer support group. The survey included questions on kind of training CBT supervisors have had both in CBT and in CBT supervision, supervisory methods they currently use and their perceived educational needs. Summary of results: 12 supervisors were invited to participate, and 7 responded (58 % response rate). Most (86%) trained CBT by attending various workshops. 57% received their training during residency in psychiatry. Only 43% have attended a formal teaching/supervision course. Modeling of the structure of CBT session during the supervision was done always or often by 57% of respondents. More than 50% of responders never or rarely observed trainee's therapy session either through direct, video or audiotape observation. 100% of the respondents were interested in receiving further training in CBT supervision with 86% of the respondents believing that this training should be done through a formal course. Conclusion and Discussion: This pilot survey has provided a baseline analysis of CBT supervisors' supervisory practice and educational needs. Surveyed CBT supervisors have expressed a strong need to receive further training in CBT supervision through a formal course. The needs assessment will serve as a platform for the development of a faculty development program for CBT supervisors. By addressing psychotherapy supervisors learning needs more successful psychotherapy supervision outcomes are likely which may positively influence therapy outcomes.

## NR7-48 TATTOOS IN THE UNITED STATES ARMED FORCES

*Chair: Bhagwan Babroo M.D.; Author(s): R. Gregory Lande, D.O. and Alyssa Soumoff, M.D.*

### SUMMARY:

Service members of the United States Armed Forces deployed to the war-zone exhibit tattoos which are more descriptive and graphic in content. Persons with tattooed body art consider these designs to be forms of identification of their persona. The authors planned a study through the use of a pre-printed questionnaire provided to the military personnel at Walter Reed Army Medical Center in Washington, D.C. from July 2010 through June 2011. The purpose was to investigate correlation between individuals, their experiences and the tattoos they obtain. The tattoo questionnaire collected information about the subject's age, gender, religion, ethnicity, particulars of any tattooed relatives, facts of the military service, deployment to the war-zones, and a description of the tattoos. The individual provided information about the tattoo, location, age obtained, reason, relationship to deployment period, influence of others or done under influence of a substance, and any regrets. They reported that about half of all tattoos were located on the upper extremities, a quarter on the back of the torso, the remainder on the front of the torso, lower extremities, head and neck. A small number of respondents regretted getting tattooed. No gender difference in the number of tattoos was found; however the mean age when they had their first tattoo was higher for women than for men. The age at which the officers had their first tattoo was also higher than that of the enlisted. The largest number had the theme of symbols, icons, messages, words and numbers, followed by images of nature, of military bearings & patriotism, of religion, of myth/lore and death. Given the five choices as reasons for getting the tattoos; a third replied as expression of self-identity, a third as either to express unity, in memoriam or as a decoration, and the remainder as other reason. One-fourth was influenced by other soldiers, friends or family to get a tattoo. Majority of service members chose professional artists to get inked. No correlation was found between the number of months of deployment and the number of tattoos. Keywords: Tattoo, Body Art, Armed Forces, Deployment

## NR7-49 A CASE OF GRAVE'S DISEASE TREATED BY A PSYCHIATRIC ACT TEAM

*Chair: Mary Woesner M.D.; Author(s): Jeremy Marsh MS4 & Daniel Kanofsky M.D., M.P.H.*

### SUMMARY:

Introduction: Physical diseases are difficult to treat in psychiatric patients, whether they are co-morbid disorders or mental disorders due to a general medical condition. The psychiatric symptoms are difficult to treat on a medical ward or clinic and the physical symptoms are difficult to treat on a psychiatric ward or clinic. For this reason, medical-psychiatric units have been developed. However, these are uncommon. It has been suggested that psychiatric Assertive Community Treatment (ACT) Teams are a place to integrate medical and psychiatric treatments. Methods: The medical and psychiatric records of an Assertive Community Treatment (ACT) Team patient with a seven year history of Grave's disease/hyperthyroidism were reviewed. The patient was followed at home by members of the ACT Team. Results: We review the case of a woman with psychiatric symptoms caused by untreated Grave's disease. Her Grave's disease remained untreated due to non-compliance with medications and due to severe symptoms of irritability, aggression, and mood variability which were not manageable by the medical teams. The patient improved through the interventions of the psychiatric ACT Team. Conclusions: We make a case for the use of the psychiatric ACT Team in the treatment of patients with mental disorders due to a general medical condition, when the psychiatric manifestations are severe and cannot be managed on a medical ward or in a medical clinic. We suggest the concept of the "medical-psychiatric ACT Team" as a corollary to the medical-psychiatric inpatient unit.

**NR7-50**  
**MEDICAL CLEARANCE FOR PSYCHIATRIC PATIENTS IN THE EMERGENCY ROOM: A LITERATURE REVIEW AND FUTURE RECOMMENDATIONS**

*Chair: Deepa Hasija M.D.; Author(s): Sadia Ghaffar M.D., Sarah Sheikh M.D., Amel Badr M.D.*

**SUMMARY:**

When an emergency room physician encounters a patient with psychiatric treatment needs, he or she must first determine whether or not a patient is medically stable before being transferred to psychiatric care. This is referred to as medical clearance which includes thorough history taking, physical examination, full set of vitals, laboratory evaluation, and in some cases additional testing. Appropriate treatment in the emergency setting is vital in avoiding morbidity from misdiagnosis of medical conditions presenting as psychiatric conditions. Patients presenting with benign complaints and normal physical exams usually have a low chance of clinically significant laboratory findings. Literature shows that

the majority of medical problems and substance abuse can be identified by vital signs and basic history and physical. Universal laboratory and toxicologic screening of all patients with psychiatric complaints is of low yield. However, determination of complete workup should be determined by the patients presentation. The purpose of this study is to summarize the literature available to provide the readers with data from the past that will help shape future medical practice.

**NR7-51**  
**UNDERSTANDING BARRIERS TO METABOLIC SCREENING FOR PEOPLE WITH SEVERE MENTAL ILLNESS: A SURVEY OF PSYCHIATRISTS AND PRIMARY CARE PROVIDERS**

*Chair: Aishat Giwa B.A.; Author(s): Martha Shumway, Ph.D., Charlene Chang, B.A., Elena Fuentes-Afflick, M.D., Dean Schillinger, M.D., Eliseo Perez-Stable, M.D., James W. Dilley, M.D., Christina Mangurian, M.D.*

**SUMMARY:**

Background: People with severe mental illnesses (SMI) die, on average, 25 years earlier than the general population. Similar to the general population, cardiovascular disease is the primary cause of death among this population (Colton et al., 2006). It has been shown that the antipsychotic medications used to treat this population result in metabolic abnormalities that may lead to increased rates of cardiovascular disease (Newcomer 2005). In 2004 the American Psychiatric Association, in collaboration with the American Diabetes Association, published national guidelines with recommendations for how best to screen this population (ADA/APA 2004). Unfortunately, nearly eight years later, the screening rates remain low. To our knowledge there have been no studies comparing the views on the barriers to care for this vulnerable population of primary care providers (PCP) and psychiatrists. Objectives: 1) Compare the PCPs' and psychiatrists' attitudes about the barriers to metabolic screening for people with severe mental illness. 2) Assess their beliefs about the role each plays in the metabolic screening of this population. Methods: Study Design: Descriptive Survey Study Subjects: Primary Care Providers and Psychiatrist who treat adults with schizophrenia and other SMI within the San Francisco County. Procedure: An anonymous survey, developed largely from previously validated surveys, was administered to primary care providers working in San Francisco County community health clinics and psychiatrists affiliated with San Francisco County Community Behavioral Health Service. Data analysis: Most of the data will be presented

as descriptive statistics. We will compare responses from PCP (160) and psychiatrists (81) by using t-tests for continuous variables and chi-square tests for categorical variables. Results: Final results are pending, but identified primary barriers are hypothesized to be similar between both groups, including, limited staff time, and severity of mental illness. It is also hypothesized that both will believe it is the primary care providers' responsibility to treat for metabolic dysfunction. References: American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, North American Association for the Study of Obesity: Consensus development conference on antipsychotic drugs and obesity and diabetes. *Diabetes Care*, 27:596–601, 2004. PMID:14747245. Colton CW, Manderscheid RW: Congruencies in increased mortality rates, years of potential life lost, and causes of death among public mental health clients in eight states. *Preventing Chronic Disease*, 3(2):A42, 2006. Newcomer JW: Second-generation (atypical) antipsychotics and metabolic effects: a comprehensive literature review. *CNS Drugs*, 19(Suppl 1):1-93, 2005.

**NR7-52****MEETING THE NEEDS OF VETERANS WITH GAMBLING PROBLEMS**

*Chair: Nitigna Desai M.D.; Author(s): Author Barbara Elaine Rofman, RN, MS, CNS; Kendra King, MA; Edward Federman, Ph.D.1.; Cynthia Yeager, MS, APRN; William Gilbert, AS; Monica Jubinsky, RN; Christopher Waltrous, MA*

**SUMMARY:**

**Abstract** The lifetime prevalence of problem and pathological gambling for people with psychiatric disorders and substance abuse is approximately 29% and has been identified as an increasing disorder among veterans that is rarely diagnosed or treated, often because clinicians are unaware of problems and lack education in assessment, diagnosis and treatment of gambling disorders. After conducting two gambling treatment studies at the ENRM VAMC, it became apparent that despite low frequency of diagnosis of pathological gambling, there were many veterans needing diagnosis and treatment, but virtually no specialty services or providers available. Clinical work supported existing literature: there is a high incidence of comorbid substance dependence, psychiatric disorders and resulting consequences, thus identifying an urgent need for treatment for this vulnerable population. **Methods & Results** Since the VA serves few veterans diagnosed with pathological gambling, we chose a strategy of increasing providers and services. The first

step was the introduction of gambling psycho-education into a process addictions group and the creation of a compulsive gambling psycho-education group in the Substance Abuse Treatment Program. While some veterans had ambivalence initially about receiving education about gambling in the Aftercare Program, they found the group to be informative, helpful and supportive and some chose abstinence as a goal. The second step was providing two conferences to VA mental health providers on identifying, diagnosing, and treating pathological gambling and two seminars about PG for peer specialists. The third step was applying for a VA Innovations Project Grant to educate and supervise mental health clinicians to facilitate their certification as Massachusetts Problem Gambling Specialists (MA-PGS). Clinicians were prepared to educate their colleagues, to screen and assess veterans for gambling problems, to treat veterans with gambling problems themselves and to become resources about gambling prevention, education and treatment to others at the ENRM VAMC. Six clinicians became certified MA-PGS. It became evident that increasing the availability of qualified providers was a successful approach to increasing treatment for pathological gambling in an organization with few diagnosed cases and services.

**NR7-53****HOMELESSNESS AND RECOVERY FROM THE PERSPECTIVES OF PEOPLE WITH DUAL DIAGNOSIS**

*Chair: Maria Mananita Hipolito M.D.; Author(s): Elizabeth Carpenter-Song, Ph.D. Rob Whitley, Ph.D.*

**SUMMARY:**

Mental health services have come to view stable housing as critical to the continued recovery of people living with psychiatric disabilities. According to the Substance Abuse and Mental Health Services Administration, half of the mentally ill homeless population in the United States also suffers from substance abuse and dependence. Minorities, especially African Americans, are over-represented in this group. The present study examines the experiences of people with co-occurring disorders of mental illness and addiction that are formerly homeless and now living in intentional recovery communities (RCs) provided by a core service agency in Washington, D.C. First person narratives collected in the context of a longitudinal qualitative study titled, *Creating Communities* were examined to determine the influence of the evolution of housing for these individuals from “having no place to stay” to living in a stable place of their own. The authors explore the

importance of stable, supportive housing for individuals recovering from mental illness and addiction through the ontological security of having a place to call “home” and a place of physical, psychological and social safety. Three domains strongly emerged in which residents convey the impact of transitioning from being homeless to being housed in a stable housing units with supportive environment. Residents felt that living in a supportive housing improved their sense of security, imparted a favorable effect in their sense of independence, and encouraged social and community participation. ‘Creating Communities’ is being conducted in the context of an ongoing collaboration between Dartmouth Psychiatric Research Center and Howard University. This five-year research and training center grant focuses on the recovery and rehabilitation of African Americans with severe mental illness funded by National Institute on Disability and Rehabilitation Research.

**NR7-54**  
**SOCIAL ADJUSTMENT OF FIRST-EPISODE SCHIZOPHRENIA PATIENTS: STABILITY DURING A YEAR OF TREATMENT**

*Chair: Swapnil Gupta M.B.B.S Author(s): Nina R. Schooler, Ph.D. Ayako Sunakawa Abdel Elmouchtari, M.D. Peter J. Weiden, M.D.*

**SUMMARY:**

Objective: Patients with schizophrenia are known to have deficits in premorbid social adjustment. In addition, the symptoms of schizophrenia cause impairment in social and occupational functioning. We aimed to study the social adjustment of patients with first episode of schizophrenia longitudinally over the first year of outpatient treatment following initial hospitalization. Method: The study was conducted at Kings County Hospital Center (Brooklyn, NY), a busy inner-city public psychiatry clinic. Out-patients with a confirmed diagnosis of schizophrenia, schizophreniform or schizoaffective disorder who were enrolled in a randomized open labeled trial of long-acting risperidone versus oral second generation antipsychotic were assessed for the level of social adjustment using the brief version of the Social Adjustment Scale (SAS II). Assessments were done at baseline, twelve, thirty-six and fifty-two weeks by resident psychiatrists who were not blind to treatment. SAS data were available for 34 of the 37 subjects in the trial. We described the time course of six items including role functioning, social contacts and patient self-appraisal. Results: The average age of the patients was 25.9. 76% were male; they had 11 years of education and over half were unemployed at study entry. Virtually all were Afro-Caribbean or African

American. Social adjustment as assessed on all items of the scale was stable over the four points of assessment. Conclusions: Social adjustment of this cohort of first episode schizophrenia patients who were in treatment remained stable during the first year after an initial hospitalization in the community. These findings should be understood in the context of the general level of social functioning seen in the community from which these patients were drawn.

**NR7-55**  
**TWO-YEAR PROSPECTIVE STUDY OF PATIENTS OF SCHIZOPHRENIA IN A COMMUNITY MENTAL HEALTH CENTER IN KOREA**

*Chair: Sohn Jee Hoon M.D.; Author(s): Maeng-je Cho, M.D., Ph.D. SuJeong, Sung, M.D. Jin Sun, Kim, M.D. Ji Min Ryu, M.D.*

**SUMMARY:**

Object : To observe a longitudinal course of patients with schizophrenia enrolled in a community mental health center (CMHC) in Seoul, Korea, and to evaluate a clinical effectiveness of case management service offered for them. Method : We recruited newly enrolled patients from a community mental health center in Seoul. Eighty-nine new patients with a DSM-IV-TR diagnosis of schizophrenia enrolled in the CMHC and qualified as study participants. Fifty-two patients of these patients opted to engage in case-management services and included in study group. The other thirty-seven patients declined to engage but agreed to participate in research based follow-ups and included in control group. Both groups were regularly evaluated by research team for three years. There was no significant difference in demographic and clinical profile between study and control group. Result : There was no follow up loss during three year follow up. For the first year of observation, the yearly durations of admission were not significantly different between the case-managed group and the control group (-1.93 weeks vs -0.81 weeks), but durations of admission of case-managed group became significantly shorter for the second year. (-3.56 weeks vs +3.92 weeks) We also found very small, yet significant improvements of BPRS and GAF scores at second yearly follow-up. There were no differences between two groups, in changes of other effectiveness indicators, including occupational functioning, quality of life, and familial burden of care. Conclusion : We found out that for our sample, at least two years of community service was needed to reduce the durations of admission as well as to improve psychopathology and functioning of patients. The community service in

Korea is standardized by the national health ministry, so there is possibility that this finding would be replicated in further Korean studies. Still, longer follow-up studies are needed for the comprehensive evaluation of the effectiveness of Korean community services.

#### NR7-56

### AN INITIAL EVALUATION OF THE INTENSIVE CASE MANAGEMENT SERVICES IN A RECOVERY-BASED PROGRAM: OPENING DOORS TO RECOVERY IN SOUTHEAST GEORGIA

*Chair: Thomas Reed B.S.; Author(s): Michael T. Compton, M.D., M.P.H., Beth Broussard, M.P.H., C.H.E.S.*

#### SUMMARY:

In the post-institutionalization society, programs are redefining treatment models for serious mental illnesses aimed at reducing recidivism of individuals into and out of hospitals, jails, and homelessness. The importance of peers in recovery has been shown in models such as the Clubhouse (Whitley et al. 2011), and intensive case management has been effective in programs such as Assertive Community Treatment (Salyers et al. 2011). For individuals with serious mental illnesses, having autonomy in constructing their recovery plan has been shown to be effective in multiple studies (Mead et al. 2000). The Opening Doors to Recovery program (Compton et al. 2011) combines these concepts into a unique case management program with three Community Navigation Specialists (or Navigators); a licensed social worker, a family member of someone with a serious mental illness, and a certified peer specialist. The Navigator team focuses on helping individuals with established recidivism access adequate treatment, develop a meaningful day, acquire safe housing, and use technology as a tool toward recovery. We conducted a curriculum evaluation of the Navigators' training program using surveys that asked participants to rate their experience in the training program to gauge its effectiveness. We also conducted a qualitative process evaluation with 25 interviews of key stakeholders, Navigators, and consumers. The interviews asked participants to identify strengths and weaknesses of the program. In evaluating the training curriculum, participants found it to be helpful and the overall training met expectations. The most helpful curriculum aspect was "goal setting and action planning." Statistically significant improvements were found for both knowledge and self-efficacy using paired-samples t-tests (before and after attending the training curriculum). In the program evaluation, common strengths were having a professional, family, and peer

Navigator to provide different perspectives. Consumers cited the importance of the peer Navigator more often while stakeholders cited the importance of the professional Navigator more often. Having a Navigator on call 24/7 was commonly mentioned as a strength. Teamwork and partnerships were stressed as vital to the success of the program. The ability for Navigators to "think outside of the box," compared to traditional case management, was commonly cited as important in implementing the recovery plan for consumers. One weakness was the large territory of the rural Navigator teams who are often several hours away from consumers. Suggestions for improvements revolved around enhancing information systems, streamlining available resources, creating a rural and urban model, and developing fidelity measures. An ongoing outcome study is assessing the effectiveness of the novel Community Navigation Specialist model in 100 participants with an established history of recidivism.

#### NR7-57

### READING IS ASSOCIATED WITH BETTER OUTCOME THROUGH INCREASED OCULAR ILLUMINANCE DURING LIGHT TREATMENT

*Chair: Aamar Sleemi M.D.; Author(s): Aamar Sleemi M.D.; Gloria M Reeves M.D.; Kelly J Roban Ph.D.; Patricia Langenberg Ph.D.; Mary Johnson, Ph.D.; Sumit R Bose, BS; Baharak Khabazghavini M.D.; Dipika Vaswani M.D.; Olaoluwa Okusaga M.D.; Timileyin Adediran BS; Thea Postolache; Hyacinth Uzoma M.D.; Teodor T Postolache M.D..*

#### SUMMARY:

Background: Bright light therapy is a safe and effective treatment for winter seasonal affective disorder (SAD). However, little is known about activities patients undertake during light treatment and if these activities are associated with outcome. During treatment, patients are instructed to only intermittently look towards the light source; other activities, such as reading, listening to music, talking on the phone, etc., are encouraged during this time, which potentially may affect ocular light exposure. We now relate, for the first time to our knowledge, different activities to outcome of bright light, hypothesizing that reading will be negatively related to outcome. We have also compared illuminance with vs. without reading. Methods: For our analysis of the relevance of different activities on outcome of light therapy, 79 patients (33 males & 45 females), aged 18- 64 with SAD were treated with daily bright light treatment for 6 weeks. Patients completed a daily activity and compliance form. Total minutes and percentage for each activity were calculated. For comparing outcome in

relationship with different activities, statistical analysis included a) t-tests to compare the duration of and percent for each activity in remitters vs. non remitters, b) logistic regression with remission as dependent variable, and activities, gender and age as independent variables, to identify a parsimonious model of outcome prediction, and c) linear regression of depression scores on average cumulative reading duration and relative percentage of reading. Then, in order to assess the effect of the reading material on illuminance, two technicians measured the illuminance of a light box (Phillips BrightLight 6, Phillips/Apollo Health, American Fork, Utah) with a light meter (Kleton K7020) directed towards the center of reading material that was placed on a table in front of the light box. The measurement was also performed after reading material was removed. The two measurements were performed in a randomized order. Friedman ANOVA with Wilcoxon posthoc tests were used to compare illuminance with vs. without reading. Results: Reading duration and percentage were greater in remitters ( $p=0.006$  and  $p=0.006$  respectively), predicted remitter status ( $p=0.010$  and  $p=0.007$  respectively), and were negatively related to depression scores at study completion ( $p=0.010$  and  $p=0.019$  respectively). We found the presence of the reading material increased illuminance by 470.93 lux (95% CI 300.10-641.75),  $p<0.0001$ . Conclusions: Activities during light treatment were quantified, and among all, reading was the only activity associated with clinical outcome. As reading materials reflect light from the lightbox, reading during light therapy may increase ocular illuminance. If this is replicated in larger studies with continuous recordings and randomized design, it may lead light treatment delivery improvement to maximize effectiveness of bright light treatment for SAD.

**NR7-58**  
**MEASURING GLOBAL MENTAL HEALTH, MULTI-MORBIDITY BURDEN, PAIN-IMPAIRMENT, AND FUNCTIONAL PERFORMANCE IN SUBJECTS WITH TBI & CHRONIC PAIN**

*Chair: Armando Miciano M.D.*

**SUMMARY:**

The study measured the global mental health (GMH), multi-morbidity burden (MMB), pain-related impairment (PRI), and functional performance status (FPS) in subjects with Traumatic Brain Injury (TBI) and chronic non-malignant pain (CNP). A retrospective study was done in a comprehensive outpatient rehabilitation facility on 29 of 100 subjects (19 men & 10 women, age 28-62). Outcome measures

used were: PROMIS-Anxiety, PROMIS-Depression, Self-Administered Co-Morbidity Questionnaire (SCQ), Pain Disability Questionnaire, from the AMA Guides to Evaluation of Permanent Impairment 6th Edition, and Berg Balance Scale. The PROMIS-Anxiety & PROMIS-Depression (AD) subscales measured the GMH, SCQ measured the MMB, PDQ measured the PRI, and BBS measured the FPS. Clinical scores ranged: PROMIS-Anxiety T-score 37-83 (average 60); PROMIS-Depression T-score 38-81 (average 59.2); SCQ 0-15 of 39 (average 7.0); total PDQ 6-150 of 150 (average 92); and, BBS 8-56 out of 56 (average 42.0); Subjects with Traumatic Brain Injury and with chronic non-malignant pain tend to have decreased global mental health, mild multi-morbidity burden, moderate pain-related impairment, but have good physical performance. The study found a trend relationship of the FPS to GMH, MMB, and PRI and supported that the health burden of TBI care to be extensive due to the clinical complexity involving both physical and psychosocial aspects. The study then recommends that the SCQ, PDQ, and PROMIS be part of the comprehensive clinical measures for these difficult-to-manage subjects who needs integrated care. Further study on the correlation of PROMIS, SCQ, PDQ, & PPS should be done.

**NR7-59**  
**RESPONSE TO PGY-1 RESIDENT PHYSICIAN SUICIDE AT AN ACADEMIC INSTITUTION**

*Chair: Christina Girgis M.D.*

**SUMMARY:**

Objectives: After a recent suicide of a PGY-1 resident physician at a large urban medical center, we offered two types of post-suicide resident debriefing sessions. Our objective was to identify useful debriefing strategies for surviving peers in an institution which openly discusses resident suicide. Methods: Two methods were employed. Within 36 hours, all surgical residents met with hospital, clinical and academic leadership for debriefing, including the chaplain. This was followed by a meeting with 17 residents within the intern's surgical subspecialty. In the internal medicine program, the training director, resident chiefs and an outside psychiatrist met with residents one week after the suicide. The psychiatrist co-led the discussion with the program director. Appropriate details that were known were discussed, and the psychiatrist discussed mental health issues in residents. Outcomes: 1) Five surgical residents initiated subsequent private discussions with the chaplain. 2) Faculty perception at the general surgery resident meeting was that some residents

appeared uncomfortable or uninterested in debriefing. 3) At the surgical subspecialty follow up meeting, however, several residents spoke about their colleague, and coping with residency stress. The chairman of the program was surprised to hear that they had not previously felt comfortable requesting help for stress. 4) In the internal medicine session, over 60 residents were present. When invited by the psychiatrist, ten questions were asked in total. Question topics included available resources to residents, cultural issues for international medical graduates, resident stress, bullying of residents, and time off for treatment. One resident publicly stated she would be comfortable asking for help if needed. Subsequently, an intern told his chief resident that he now carries the Employment Assistance Program brochure with him in order to be able to offer it to colleagues if needed. 5) Internal medicine residents later suggested that small group settings were preferred. Conclusion: Few institutions have a protocol in place to address resident survivor reactions after suicide by a colleague, and discomfort with suicide is common. We conclude: 1) Open discussion of resident suicide provides an opportunity to address this significant emotional stressor. No harmful effects of bringing suicide “out of the closet” were detected. 2) Group size and/or specialty may affect resident willingness to debrief in a public setting. 3) While initial appearances may suggest that debriefing may be uncomfortable for some residents, the incidence of individual follow up with the chaplain suggests it is beneficial nonetheless. 4) The presence of a psychiatrist allows for expert discussion of stress and suicide risk factors. 5) Involvement of the chaplain should be included in a model protocol. Research about impact of suicide and post-suicide debriefing on resident emotional wellbeing is warranted.

**TUESDAY MAY 08, 2012**

New Research Poster session 8

## PSYCHIATRIC SUBSPECIALITIES

### NR8-01

#### BRIEF RATING OF AGGRESSION BY CHILDREN AND ADOLESCENTS (BRACHA): A RELIABILITY STUDY

*Chair: Drew Barzman M.D.; Author(s): Douglas Mossman M.D.*

#### SUMMARY:

Background: Although the BRACHA has not been formally evaluated in the outpatient setting, the sum of

the 14 BRACHA items was proven to be directly related to the risk of inpatient pediatric aggression in 3 to 19 years olds. Recently, Barzman and colleagues showed that the Brief Rating of Aggression by Children and Adolescents (BRACHA) may help clinicians rapidly assess the risk of aggression by child and adolescent psychiatric inpatients. Findings from an initial accuracy study led Barzman and colleagues to suggest that the BRACHA may help admitting clinicians differentiate between patients of relatively low and high aggression risk, which could help inpatient staff members plan treatment, reduce injuries, and reduce need for restraint. Introduction: The Brief Rating of Aggression by Children and Adolescents (BRACHA) is a 14-item instrument scored by emergency room staff members to assess aggression risk during an upcoming psychiatric hospitalization. This study investigated the inter-rater reliability of the BRACHA 0.9, the latest version of the instrument. Method: After receiving training based on the BRACHA 0.9 manual, ten intake workers viewed 24 ten-minute videos in which child and adolescent actors portrayed pediatric emergency room patients with low, moderate, or high levels of risk for aggression during an upcoming hospitalization. We then evaluated inter-rater reliability for individual BRACHA items using three measures of agreement, and reliability for total BRACHA 0.9 scores using conventional (“frequentist”) methods and Bayesian techniques for calculating the intraclass correlation coefficient ICC(2,1). Results: Inter-rater reliability for individual items ranged from good to almost perfect, with Kendall’s W exceeding 0.75 for eight of 14 BRACHA items. The ICC(2,1) for the total BRACHA 0.9 score was 0.9099 using both conventional and Bayesian methods (95% credible interval 0.8530 – 0.9533), suggesting an excellent level of overall agreement. Conclusion: The BRACHA appears to be an accurate, highly reliable instrument for assessing the risk of aggression by children and adolescents who are about to undergo psychiatric hospitalization.

### NR8-02

#### ASTHMA AND SUICIDALITY AMONG ADOLESCENTS IN THE YOUTH RISK BEHAVIORAL SURVEY

*Chair: Ivan Aldea M.D.; Author(s): Erik Messias, M.D., M.P.H., Ph.D.*

#### SUMMARY:

OBJECTIVE: Asthma is one of the most common, severe, and chronic medical conditions that starts in childhood with progressively growing prevalence over the last two decades. Predominantly with an adult

population, there is growing evidence of an association between suicidality and asthma. We hypothesize that adolescents with a history of asthma will endorse higher rates of suicidality than those with no asthma history. **METHODS:** Data comes from the Young Risk Behavior Surveys (YRBS) of 2007 (n = 14,041), and 2009 (n = 16,410), which provides cross-sectional nationally representative samples of US high school students. Exposures include lifetime and current asthma. Outcomes include four suicidality variables: suicidal ideation, suicide plan, suicide attempt and attempt requiring medical treatment. Logistic regression models were used to estimate the relationship between asthma and suicidality after adjusting for confounders including age, sex, ethnicity, substance use and sadness over a two week period. **RESULTS:** While the prevalence of asthma endorsed by high school students increased (2007 with 20%; and 2009 with 22%), its association with sadness remained stable (OR = 1.4 [95% CI: 1.2 – 1.7] on both samples). Similarly, suicidality remained unchanged from 2007 to 2009 with roughly 14% reporting suicidal ideation, 11% planned suicide, 6% attempted suicide, and 2% reported an attempt requiring treatment. On both samples, adolescents who endorse having either lifetime or current asthma show significantly higher risk of all suicidality variables when compared to adolescents with no asthma. After adjustment, the most severe variables of suicidality remained significantly higher in the current asthma group. In the 2009 sample, “suicide attempts” (OR = 1.5 [1.0 – 2.1]) and “suicide requiring treatment” (OR = 2.5 [1.5 – 4.2]). This finding was also seen with the 2007 sample with “suicide attempts” (OR = 1.6 [1.2 – 2.1]) while “suicide requiring treatment” (OR = 2.0 [1.2 – 3.2]). This significance was lost with the lifetime asthma group after adjusting for all confounders. **CONCLUSION:** This data suggests that in adolescents, endorsement of either lifetime or current asthma is associated with higher levels of suicidality when compared to adolescents with no asthma history. In the current asthma group, this association persists with the most severe variables of suicidality after controlling for effects of sadness. Findings are consistent across sample years and are aligned with growing evidence linking asthma and suicidal ideation in both adults and adolescents. Therefore, suicidality and depression screening is strongly encouraged in primary care settings when an adolescent acknowledges having asthma of any type.

**NR8-03****GEOGRAPHIC MOVES AND MENTAL HEALTH SERVICE USE AMONG US MILITARY CHILDREN**

*Chair: Jeffrey Millegan M.D.; Author(s): Charles Engel, M.D. M.P.H.*

**SUMMARY:**

**Background:** Geographic moves are routine among children of members of the US military. Moving can be a stressful life event. **Objective:** Determine the effect of geographic moves on the rate of mental health service use (outpatient mental health visits, psychiatric hospitalizations, ER mental health visits) among children age 6 to 11 and age 12 to 17. **Methods:** This was a retrospective cohort study. De-identified medical administrative records of children of active duty personnel between fiscal years 2007 through 2009 were analyzed. Mental health service use was identified using ICD-9 codes. Children with geographic moves in fiscal year 2008 were compared with those without geographic moves with regard to rates of mental health service. Logistic regression was used to summarize relationships and adjust for confounding variables. **Results:** A total of 548,336 children age 6 to 17 years were included. Mean child age was 10.8 years (SD: 3.3); 51% were male. 179,486 (25%) children moved in fiscal year 2008. In fiscal year 2009, 92,226 (17%) had mental health outpatient care, 2,826 (0.5%) had psychiatric hospitalizations and 2,552 (0.5%) had a mental health ER visit. After adjusting for other variables, children age 6 to 11 with a geographic move had higher rates of mental health outpatient visits (OR 1.03 (CI 95%: 1.01 – 1.06)). Children age 6 to 11 with a geographic move had higher rates of mental health encounters for adjustment disorders (OR 1.05 (CI 95%: 1.01 – 1.10)), attention disorders (OR 1.04 (CI 95%: 1.01 – 1.07)) and intentional self-injury (OR 1.47 (CI 95%: 1.11 – 1.96)). After adjusting for other variables, children age 12 to 17 with a geographic move had higher rates of mental outpatient visits (OR 1.04 (CI 95%: 1.01 – 1.07)), psychiatric hospitalizations (OR 1.19 (CI 95%: 1.07 – 1.32)), and ER mental health visits (OR 1.20 (CI 95%: 1.07 – 1.32)). Children age 12 to 17 with a geographic move had higher rates of mental health encounters for adjustment disorders (OR 1.09 (CI 95%: 1.04 – 1.15)), impulse disorders (OR 1.07 (CI 95%: 1.02 – 1.12)) and substance use disorders (OR 1.23 (CI 95%: 1.09 – 1.38)). **Conclusion:** Children with a geographic move in the previous year have increased rates of mental health encounters compared to those without a geographic move. Among adolescents, this increased risk extends to psychiatric hospitalizations and ER visits.

**NR8-04****OVERLAPPING SYMPTOMS AND DIAGNOSTIC DIALEMMA IN AUTISM**

## SPECTRUM DISORDER VS BIPOLAR DISORDER IN CHILDREN AND ADOLESCENTS

*Chair: Garima Singh M.D.; Author(s): Dr Pamela Campbell  
Dr Sandra Vicari*

### SUMMARY:

**Objective:** Autism spectrum disorder (ASD) is a developmental childhood disorder arising in early years of life and characterized by patterns of delay and deviance in the development of social, communicative, cognitive and executive skills, whereas, Bipolar disorder (BD) is a primarily affective and cyclic psychiatric illness with episodes of Depression and Mania. A strong association has been reported in numerous studies between BD and ASD. The similarities in the clinical presentation of both the disorders and the differing medication management are an important concern and an important topic which requires further research. There is no objective medical test for BD; even the current DSM-IV does not distinguish age specific criteria for the bipolar disorder. Thus, the clinical presentation can be mistaken for other common childhood onset mental illness. Some studies have been done on the prevalence of the BD and the ASD and their correlation and management but the conclusions are conflicting and no clear cut result is available. **Method:** We did a Retrospective review of 100 patient charts seen in the inpatient setting or Southern Illinois university (SIU) Child psychiatry outpatient clinic that were diagnosed with ASD under their Axis-I diagnosis in 3 years (2009-2011). This study also examined the age, gender, clinical presentation, time of diagnosis, developmental history, family history and pharmacotherapy. The validity of the diagnosis was assessed using DSM-IV (TR) and AACAP practice parameters. Descriptive statistical analysis was done using SPSS. **Result:** Out of 100 individuals with ASD, 96 of them has history of aggression, 99 has mood lability, 54 has sleep disruption but only 2 of them has classic mania and hypomania symptoms. 20 individuals had diagnosis of Bipolar disorder or Mood disorder during their treatment. 33 patients has family history of BD and 28 has ASD. **Conclusion:** There is a high rate of mis or over diagnosis, as children diagnosed with autism spectrum disorder often has mood dysregulations, aggressive behavior, irritability and emotional lability. Thus, whether these presentations are a separate bipolar disorder or characteristics of autism spectrum disorder has become an area of controversy and scientific debate. This further raises question of diagnostic significance and overlap of symptoms

## NR8-05 GENDER-SPECIFIC ASSOCIATION OF NOREPINEPHRINE TRANSPORTER POLYMORPHISMS IN ATTENTION DEFICIT-HYPERACTIVITY DISORDER

*Chair: Yong-Ku Kim M.D.; Author(s): Yong-Ku Kim,  
So-Young Oh Department of Psychiatry, College of Medicine,  
Korea University, Korea*

### SUMMARY:

**Object** We investigated the association of three common polymorphisms of norepinephrine transporter (NET) gene SLC6A2, T-182C (rs2242446), A-3081T (rs28386840) and G-1287A (rs5569) with attention deficit-hyperactivity disorder (ADHD) and the relationships of these polymorphisms with clinical severity and characteristics in Korean population. **Method** The genotype, allele frequency and haplotype of 103 ADHD patients and 173 healthy controls were analyzed for T-182C, A-3081T and G-1287A. All participants completed the Korean version of ADHD Rating Scale (K-ARS) and the ADHD group also completed the Korean Educational Development Institute-Wechsler Intelligence Scale for Children (KEDI-WISC) and continuous performance test (CPT) in drug-naïve state. **Results** We found that AA genotype of A-3081T showed the odds ratio of 8.943 (95% CI: 1.05-76.14,  $p=0.045$ ) compared with TT genotype in female. Compared with T allele, A allele represented the odds ratio of 2.223 (95% CI: 1.081-4.570,  $p=0.030$ ). In the haplotype analysis, the most common T-A-G haplotype was related to the increased risk of ADHD ( $p=0.011$ ) and this association was stronger in female ( $p=0.002$ ). Other two haplotype T-T-G and C-T-G were protective to ADHD in female ( $p=0.021$ ,  $p=0.017$ , respectively). In addition, we found the association of A-3081T and G-1287A polymorphisms with K-ARS, CPT and KEDI-WISC. Non-T carriers (AA genotype) of A-3081T showed lower omission error than T carriers (AT + TT genotype) ( $F=4.938$ ,  $p=0.040$ ) in female. In G-1287A, boys not carrying G allele (AA genotype) showed higher K-ARS total scores than G carriers (GA+GG genotype) ( $F=4.095$ ,  $p=0.047$ ), lower verbal IQ and total IQ ( $F=4.830$ ,  $p=0.031$ ,  $F=5.225$ ,  $p=0.025$ , respectively) and girls not carrying A allele (GG genotype) showed lower omission error than A carriers (GA+AA genotype) ( $F=8.030$ ,  $p=0.011$ ). **Conclusions** We found a significant association between SLC6A2 A-3081T and ADHD in girls. The most common T-A-G haplotype was related to risk of ADHD and a stronger association was found in girls. Our result also suggested the possible role of A-3081T and G-1287A polymorphisms in clinical presentation of

ADHD. This is the first report describing gender-related association of the three common polymorphisms of SLC6A2 with ADHD in Korean sample.

**NR8-06**  
**CHANGES IN THE ICNDS BETWEEN TWO VISITS IN 762 YOUTH WITH EPILEPSY**

*Chair: Diana Lorenzo M.D.; Author(s): Prakash Kotagal M.D., Sarah Mathtys, Robert Butler and Tatiana Falcone M.D.*

**SUMMARY:**

Objective: To evaluate changes in the Impact Childhood Neurological Disability Scale (ICNDS) and Liverpool Seizure Severity Scale (LSSS) between two consecutive visits in 762 youth with epilepsy. Methods: Patients were identified from an outpatient pediatric epilepsy clinic, patient data was self entered in an electronic database, prior to their epilepsy appointment. The Knowledge Program was created with the goal to measure the patient overall outcome and quality of life over time. Patients were between 0 to 18 years of age, and with ICD-9 diagnosed coded for epilepsy. Subject completed the ICNDS and LSSS survey questionnaire which assessed general well-being and quality of life (QoL). Responses to QoL were coded Likert scales from 1= worst and 6= best QoL. The ICNDS was analyzed by 4 subscales; Behavior and inattention, cognition, physical/neurological disability and epilepsy. Results: Two of the 4 subscales of the ICNDS; Inattentiveness (p value=0.0004) and cognition (p value=0.0415) had an statistically significant impact on the QoL, especially for those subject with scores 2,3,4 during the first visit. Patients hours of activities improved when the ICNDS subscales, on physical/ neurological disability score ( p value= 0.0471), epilepsy (p value =0.0001) and oyhe neurological disability score ( p value= 0.0471)improved for visit one to two. Conclusions: The 4 subscales of the ICNDS had an impact on the quality of life in youth with epilepsy. Early intervention focusing on the number of seizures as well as the different psychosocial and physical domains ( attention, cognition, social interaction, school performance)is the key to improve the quality of life in youth with epilepsy.

**NR8-07**  
**EFFECT OF SYMPTOM SEVERITY ON AMYGDALA AND HIPPOCAMPUS VOLUMES IN YOUTH WITH AND AT HIGH RISK FOR BIPOLAR DISORDER**

*Chair: Erica Sanders B.A.; Author(s): Meghan Howe, LCSW Kiki Chang, M.D.*

**SUMMARY:**

Objective: Children of parents with bipolar disorder (BD) are at high risk for developing BD themselves, with those with ADHD and depression at particularly high risk. Past studies have shown that children with BD have reduced hippocampus and amygdala volumes compared with healthy controls, but few studies have examined subcortical volumes in children at high risk for BD before development of mania. Studies of children with parents who have major depressive disorder (M.D.D), have shown that healthy and depressed M.D.D offspring have smaller hippocampal volume than controls, thus linking reduced hippocampal volume to depression risk. However, no studies have examined the correlation between symptom severity and subcortical volumes in these at-risk populations. The goal of this study was to examine subcortical correlates of symptom severity in bipolar offspring with and at-risk for BD. We hypothesized that more severe mania and depression symptoms would be correlated with reduced amygdala and hippocampus volumes respectively. Methods: We included 75 children (mean age = 13 (2.59), 72% male) with at least one parent with BD. Of the 75 bipolar offspring, 27 had BD and 48 had prodromal symptoms (40 had M.D.D and ADHD, 8 had ADHD and mood symptoms). The WASH-U KSADS was used to assess diagnosis and symptom severity and magnetic resonance imaging (MRI) was conducted on a 3T scanner. Volumetric image analysis was performed using SPM8, BrainImageJava and manual tracing of amygdala and hippocampus volumes. A clinical variable (CV) for mood symptom severity was calculated. The mania CV was created by adding together the scores (on a scale of 0-6) of the most severe episode in the six months prior to the scan for each DSM-IV-relevant mania question on the WASH-U KSADS. The depression CV was calculated similarly. Spearman correlations were conducted between amygdala and hippocampus volumes and CV mania and depression scores respectively. Results: Total, right, and left amygdala volumes were negatively correlated with mania CV scores (tot: p=.003, R: p=.03, L: p=.009). In addition, total, right, and left hippocampus volumes were negatively correlated with depression severity (tot: p=.02, R: p=.02, L: p=.008). When we controlled for lithium exposure post hoc, the findings remained significant. As subjects with BD had significantly higher CV scores than those without BD (p<.001), we re-analyzed the data after removing these subjects and the findings remained significant. Conclusions: These findings support the idea that there is a continuum of mood symptom severity in youth before, during, and after the onset of full mania, which is inversely correlated with amygdala and hippocampus

volumes. Previous studies in at-risk youth, which did not find reduced volume in these structures, may have been affected by a small range of mild symptom severity in subjects. Mechanisms of how mood symptom severity leads to volumetric changes in the brain need to be explored.

#### **NR8-08 MORTALITY IN EATING DISORDERS**

*Chair: Jaana Suokas M.D.; Author(s): Jaana Suvisaari, Mika Gissler, Jari Haukka*

##### **SUMMARY:**

**Objective:** To determine mortality in patients treated in a specialized eating disorder unit. **Method:** The sample is based on case-control design and includes 2442 patients (2329 women and 113 men) treated in an eating disorder clinic of Helsinki University Central Hospital under the period of 1995-2010. The unit comprises of a hospital ward and an outpatient clinic. For each patient four controls were selected from the National Central Population Register and matched for age, sex and place of residence. Mortality data was from National Causes of Death Register. Diagnostic information was based on a clinical diagnosis made by the attending psychiatrists at the patient's arrival. We used Poisson regression model to calculate relative risks (RR) for mortality due to all causes, all external causes of injuries and accidents, and suicide. **Results:** Eating disorders were treated mostly (81%) in out-patient care, but about half (45%) of anorexia nervosa patients had also needed inpatient care. Eating disorder patients had an increased mortality: the RR for all cause mortality was 6.52 (95% CI 3.42-12.42) in AN, 2.97(95% CI 1.89-4.65) in BN and 1.78 (95% CI 0.55-5.77) in Binge eating disorder. Mortality risk in AN was highest during first years after admission but declined after that, while in BN the mortality risk started to rise two years after the admission. Relative risk for suicide was elevated both in AN (RR 5.10; 95% CI 1.37-18.98) and in BN (RR 6.07; 95% CI 2.48-14.86) **Conclusions:** Mortality rates in the study conform the serious nature of eating disorders. It also demonstrated an increased risk of suicide among both AN and BN patients.

#### **NR8-09 EFFECTIVENESS OF TELEPSYCHIATRY-BASED CULTURALLY SENSITIVE COLLABORATIVE TREATMENT FOR DEPRESSED CHINESE AMERICANS IN PRIMARY CARE**

*Chair: Albert Yeung M.D.; Author(s): Albert Yeung, M.D.,*

*Sc.D., Kate Hails, B.A., Aya Inamori, B.A., Trina Chang, M.D., M.P.H., Nbi-Ha Trinh, M.D, M.P.H, Maurizio Fava, M.D.*

##### **SUMMARY:**

**Objective:** To examine the effectiveness of treating less acculturated depressed Chinese Americans in primary care using telepsychiatry-based Culturally Sensitive Collaborative Treatment (CSCT). **Method:** Depressed Chinese American patients were identified through systematic depression screening in a primary care clinic and advertisement in local newspapers. Patients who screened positive (Patient Health Questionnaire-9=10) were interviewed using the Structured Clinical Interview for DSM-III Axis I Disorders-Patient Edition (SCID-I/P). Patients who met the study's eligibility criteria were randomized to receive either treatment as usual or the intervention under investigation. The six-month intervention involved: 1) an initial psychiatric interview using a culturally sensitive protocol via videoconference; 2) eight scheduled phone visits with a care manager assigned to the patient, who monitored the patient's progress, as well as medication side effects and dosage if applicable; and 3) collaboration between the patient's PCP, psychiatrist, and care manager. Treatment outcomes were evaluated by blind assessors at 1.5, 3, and 6 months using the 17-item Hamilton Rating Scale for Depression (HAM-D-17) and the Clinical Global Impression scale (CGI). Interim intent-to-treat analyses were performed on subjects who completed the 24-week intervention during the period from July 2008 to March 2010. The dependent variables were response rates and remission rates of both groups. Response rate was defined as =50% reduction of the HAM-D-17 score at the last visit completed as compared to baseline, and remission rate was defined as a HAM-D-17 score = 7 at the last visit. The independent variable was randomization status; gender and baseline HAM-D-17 score were included as covariates. **Results:** 114 subjects (female 65%, mean age 49 ± 15) completed the 24-week study, and 46% of them were randomized into the intervention group. The mean HAM-D-17 score at baseline was 20 ± 4, within the range of moderate-severe depression. Based on intent-to-treat analyses, the adjusted odds of the intervention group had approximately 3.6 times greater response rates (OR 3.6; 95% (1.5-9.0); p=0.005) and 4 times greater remission rates (OR 4.0; 95% CI 1.5-10.8; p=0.006). **Conclusion:** Telepsychiatry-based CSCT is efficacious in improving treatment outcomes of depressed Chinese Americans in a primary care setting. **Key Words:** Depression, collaborative treatment, primary care, Chinese Americans, care management. **Target Audience(s):** Psychiatrists, Psychologists, Social Workers, Primary

Care Practitioners, Trainees

**NR8-10**

**A VALIDATION STUDY OF A PROPOSED DSM-V DIAGNOSTIC ENTRY: DISRUPTIVE MOOD DYSREGULATION DISORDER**

*Chair: David Pogge Ph.D.; Author(s): Martin Buccolo, Ph.D. John Stokes, Ph.D., Philip D. Harvey*

**SUMMARY:**

Background. The DSM 5 committee has proposed a new childhood disorder, called Disruptive Mood Dysregulation Disorder (DM.D.D). This condition is proposed to be marked by intense temper outbursts superimposed on a background of persistent depressed or irritable mood. As many admissions to inpatient care for children and adolescents are due to temper outbursts and aggression, we used a large database of child and adolescent inpatient admissions to examine the prevalence and correlates of children and adolescents who had these characteristics. Methods. During a two-year period 1505 adolescent psychiatric patients were admitted to a private psychiatric hospital. Of these cases, 1351 were rated by their clinicians as having at least moderate depression at the time of admission. From this subsample, 368 cases were also rated as having severe symptoms of hostility and explosiveness at the time of admission. We created a hypothetical subgroup of DM.D.D cases on the basis of at least moderate depression and severe hostility and explosiveness and compared the depressed adolescents with and without DM.D.D on several different variables. These included the frequency of clinical diagnoses of major depression vs. NOS diagnoses; the likelihood of receiving an intervention involving restraint or seclusion during their admission; the number of restraint and seclusion episodes; global ratings of psychopathology; and length of inpatient stay. Results. Thirty-one percent of Depressed adolescents without a putative DM.D.D diagnosis received a diagnosis of major depression from their clinicians, while only 16% of the DM.D.D cases received such a diagnosis. Sixty percent of DM.D.D cases received an NOS diagnosis while 51% of the cases without a putative DM.D.D diagnosis received a diagnosis,  $X^2(1)=24.06, p<.001$ . Cases with a putative diagnosis of DM.D.D had a 28% likelihood of experiencing restraint or seclusion during their admission, compared to 14% of cases without this putative diagnosis. The number of restraints and seclusions averaged 2.2 for DM.D.D cases, compared to 0.84 for other cases,  $t(1349)=6.13, p<.001$ . DM.D.D cases had a significantly longer length of stay than other cases, 22.8 vs. 17.5,  $t(1349)=4.02, p<.001$ . However,

global psychopathology rated by their clinicians across all items in the psychiatric rating scale did not differ,  $t(1349)=1.52$ . Discussion: In this archival study based on a large database, a subgroup of explosive and hostile adolescents with concurrent depression can be identified. These cases are less likely to have major depression as their diagnosis than adolescents with less explosiveness and they have longer inpatient stays marked by greater likelihood of disruptive behaviors. While these results need to be confirmed prospectively, the data suggest that depressed adolescents with hostile and explosive features have a different presentation and course of treatment than those without explosiveness.

**NR8-12**

**LOWER RATES OF PUBLICATION ABOUT DELIRIUM IN PEDIATRICS VERSUS CHILD AND ADOLESCENT PSYCHIATRY JOURNALS FROM 2001-2011**

*Chair: Patrick Kelly M.D.; Author(s): Matthew D. Burkey, M.D.*

**SUMMARY:**

Objective Recent research on delirium reveals a low rate of recognition and frequent misattribution of delirious phenomenology (e.g., to depression or psychosis) by pediatricians. The objective of this study was to assess publication rates of articles about delirium in leading pediatrics and child and adolescent psychiatry (CAP) journals as a proxy for relative interest in and exposure to information about delirium. Method We performed a systematic analysis of articles indexed by PubMed using a keyword search for "delirium". Rates of articles published about delirium from 10/1/2001 to 9/30/2011 in the top 3 pediatrics journals and the top 3 CAP journals (selected by impact factor) were compared, with significance assessed using a 2-tailed Z-test at the 0.05 level of significance. Articles identified were reviewed and data abstracted to assess topical focus, publication type, author affiliation, and geographic location. Results In the top 3 pediatrics journals, 2 articles were found using the keyword "delirium" (out of 15,210 articles published; rate: 1.3 per 10,000 articles). Both articles were published in a single journal, whereas the other 2 journals published none. Both were observational studies primarily focused on another condition; delirium was mentioned as a consideration in the differential diagnosis or as one of many complications of the underlying condition. Both studies were carried out in the U.S.; one was authored by neurologists and the other by a combination of pediatricians, child psychiatrists, and other specialists. Among the top 3 CAP journals, 8 articles were found using the keyword "delirium" (out of

3,920 articles published). Of these, 4 had delirium as a primary subject, 2 as a secondary subject, and 2 did not mention delirium (despite the positive keyword search). Including only articles with delirium as a primary or secondary subject, the rate of publication in CAP journals was 15.3 per 10,000, significantly greater than the rate in pediatrics journals ( $p < 0.001$ ). All 6 delirium studies were published in a single journal; the other 2 journals published none. Five studies were from the U.S. and 1 was from Spain; 4 were authored by psychiatrists and 2 by a combination of psychiatrists (child and adult) and other specialists. Conclusions Very few articles about delirium were published in leading pediatric or CAP journals between 2001 and 2011. Significantly fewer articles were published in the leading pediatric journals, and none had delirium as a primary focus. These results suggest a notable gap in recent, high-quality scholarship about delirium over the past 10 years and offers evidence that there may be less interest in delirium among pediatric researchers, editorial boards, and/or readers. The lack of published articles in the pediatrics literature may also contribute to misidentification of delirium by pediatricians.

**NR8-13**  
**ADOLESCENTS' BELIEFS ABOUT**  
**MEDICATION, FAMILY BELIEFS, AND**  
**THERAPEUTIC ALLIANCE WITH THEIR**  
**DOCTORS: PREDICTORS OF ADHERENCE**  
**TO PRESCRIBED PSYCHIATRIC**

*Chair: Fayez El Gabalawi M.D.; Author(s): Mark A. Novitsky Jr., M.D. Anil Meesala, M.D. Kanthi Varagani, MBBS Abel Bumgarner, MSIV Benjamin E. Leiby, Ph.D Matthew B. Wintersteen, Ph.D James Luebbert, M.D.*

**SUMMARY:**

Purpose: Examine the relationships between adolescent/family beliefs about psychiatric medications, therapeutic alliance between adolescents and doctors, and medication adherence. Method: 81 inpatient adolescents and their families completed questionnaires that included Morisky 8-item medication Adherence Scale (MMAS-8), Beliefs about Medicines Questionnaire (BMQ), Working Alliance Inventory- short form (WAI-S), and inventory of reasons for non-adherence. Questionnaires were given upon admission, discharge, and at one month follow-up. Due to non-normality, medians and inter-quartile range (IQR) are reported for variables of interest. The Wilcoxon Signed Rank test was used to test for any change in belief over time, and the Wilcoxon Rank-Sum test was used to compare adherence groups with respect to adolescent or family beliefs. High adherence was defined as MMAS score

greater than or equal to 6. Correlation was calculated using Spearman correlation. Results: 71% of adolescents reported lower adherence (MMAS < 6) at one month follow-up. Frequently cited reasons for non-adherence included: difficulty remembering to take medication, family not in agreement with patient taking medication, and issues related to filling prescriptions. Adolescent general beliefs about medication showed a small improvement from admission to discharge (Median change of 1 unit;  $p = 0.01$ ) but did not change from discharge to follow-up. There was no evidence of change in adolescent specific beliefs about medication over time. Adolescent beliefs at admission were not associated with adherence before admission. There was some evidence that admission general beliefs and follow-up general and specific beliefs were associated with follow-up adherence with high adherence patients having (more positive) beliefs ( $p = 0.08$ ,  $p < 0.01$ , and  $p = 0.09$ , respectively). Family beliefs were marginally associated with adherence at discharge ( $p = 0.08$ ). Family beliefs were positively correlated with adolescent general beliefs at discharge ( $r = 0.28$ ,  $p = 0.01$ ) and follow-up ( $r = 0.27$ ,  $p = 0.02$ ). Therapeutic alliance was not associated with adherence. Conclusion: Most inpatient adolescents (71%) showed low adherence to medication at one month follow up. Adolescent and family beliefs about medication were positively correlated, and were associated with follow-up adherence. Thus, attention to adolescent and family beliefs about medication during hospitalization may serve as a viable clinical tool to improve follow-up adherence. More research is needed in this area.

**NR8-14**  
**HELP SEEKING BEHAVIORS AMONG**  
**ADOLESCENTS WITH SELF HARM:**  
**REPRESENTATIVE SELF-REPORT SURVEY OF**  
**18104 STUDENTS**

*Chair: Norio Watanabe M.D.; Author(s): Atsushi Nishida, Ph.D. Shinji Shimodera, M.D., Ph.D. Ken Inoue, lecturer, M.D., Ph.D. Norihito Oshima, M.D. Tsukasa Sasaki, M.D., Ph.D. Shimpei Inoue, M.D., Ph.D. Tatsuo Akechi, M.D., Ph.D. Toshi A. Furukawa, M.D., Ph.D. Yuji Okazaki, M.D., Ph.D.*

**SUMMARY:**

Objective: This study aimed to determine the prevalence and associated factors of help seeking and to explore resources for help among adolescents with self harm in the previous 12 months. Method: Representative cross sectional survey using anonymous self report questionnaire. 8620 adolescents aged 12 to 15 in 47 junior high schools, and 9484 aged 15 to 18 in 30

senior high schools were enrolled into the study in Japan. The primary outcome measure was defined as current help seeking behaviors among adolescents with self harm in the previous 12 months. Information about sociodemographic and psychological factors and complaints of physical symptoms possibly associated with help seeking was also collected. Results: Of 17671 adolescents whose responses were adequately obtained, 276 (3.3%) junior and 396 (4.3%) senior high school students reported an act of self harm in the previous year that met study criteria. Among those with self harm, 40.6% of adolescents in junior and 37.6% in senior high schools reported that they currently had psychological problems or stressful events but did not consult anyone about them (poor help seeking). In both groups, poor help seeking was significantly more common in those having none to consult about psychological problems (odds ratio 9.16, 95% confidence interval 4.55 to 18.43,  $P < .0005$  in those aged 12 to 15; 9.94, 5.52 to 17.92,  $P < .0005$  in those aged 15 to 18), and in those with current suicidal ideation (1.97, 1.04 to 3.71,  $P = .037$ ; 1.90, 1.07 to 3.40,  $P = .030$ ), revealed through a multivariate logistic regression analysis. In terms of complaints of physical symptoms among adolescents with poor help seeking, in comparison with those without self harm, those aged 12 to 15 with self harm were likely to have complaints of abdominal pain (1.66, 1.05-2.64,  $P = .032$ ), tinnitus (2.27, 1.46-3.54,  $P < .0005$ ) and fatigue (2.18, 1.37-3.47,  $P = .001$ ), and those aged 15 to 18 with self harm were likely to have complaints of tinnitus (2.38, 1.60-3.54,  $P < .0005$ ). For help, friends represented the most common resource to approach. Family members were significantly less common resource for help in those with self harm than in those without, but school nurses were more common in those with self harm. Conclusions: Around 40% of adolescents with self harm in the previous year do not seek help. School based mental health should aim at screening for school students at risk, and at educating school nurses for prevention care for self harm. Educational Objective: At the conclusion of this session, the participant should be able to identify what factors were associated with poor help seeking behaviors in students with self harm, and what resources for helping students with self harm were available.

**NR8-15**  
**DETERMINING AN OPTIMAL CUT OFF SCORE FOR THE WFIRS-P USING ROC CURVE ANALYSIS**

*Chair: Trevor Thompson Ph.D.; Author(s): Vanja Sikirica Ph.D., M.P.H., Andrew Lloyd DPhil, Juliana Setyawan Ph.D., M.S., Margaret Weiss M.D. Ph.D., M Haim*

*Erder Ph.D., Paul Hodgkins Ph.D., MSc*

**SUMMARY:**

**Objectives:** The current study employed Receiver Operating Characteristics (ROC) analysis to (i) evaluate the ability of the Weiss Functional Impairment Rating Scale- Parent Form (WFIRS-P) to discriminate ADHD and non-ADHD individuals, and (ii) identify a WFIRS-P cut-off score that optimizes correct classification. **Methods:** The WFIRS-P was completed by the parents/guardians of 678 children (476 physician-defined ADHD cases and 202 non-ADHD controls) with a mean age of 11.5 (SD=3.4; range=5-19). The WFIRS-P provides an overall rating of degree of impairment of an individual's behaviour or emotional problems on clinically-relevant domains of functioning using a 4-point Likert scale (0=never or not at all, 3=very often or very much). Although the WFIRS-P can be scored on several domains, a single mean WFIRS-P was employed for maximum parsimony. Non-parametric ROC analysis resulting from 2000 stratified bootstrap replicates was used to examine the classification performance of the overall WFIRS-P mean score and to estimate an optimal classification cut-off score. **Results:** Area Under the ROC Curve was 0.91 (95% CI=0.88-0.93) suggesting the WFIRS-P exhibits an excellent basis for accurate discrimination of ADHD and non-ADHD. Youden's J index revealed that sensitivity (0.83) and specificity (0.85) was maximal for an overall mean WFIRS-P score of 0.65. **Conclusions:** When assessing function, the WFIRS-P appears to provide a simple and effective basis for differentiating between ADHD and non-ADHD diagnostic classification.

**NR8-16**  
**MODERATORS OF EFFICACY AND ADVERSE EVENTS DURING ARIPIPRAZOLE TREATMENT OF PEDIATRIC BIPOLAR I DISORDER**

*Chair: Chang Kiki M.D.; Author(s): Joan Zhao, Eric Youngstrom, Benjamin Goldstein, Ron Marcus, Robert D. McQuade, Robert A. Forbes, Candace Andersson, Diane K. Ammerman, Elizabeth E. Bellocchio, Maia Miguelez, Raymond Mankoski*

**SUMMARY:**

**Objective:** In an effort to facilitate a personalized approach to treatment, we attempted to determine which patient or disease characteristics predict efficacy or adverse events (AEs) in pediatric patients (10-17 years) receiving aripiprazole (ARI) for an acute manic or mixed episode associated with bipolar I disorder. **Method:** This was a post-hoc analysis of subjects in

a 4-week trial of ARI (n = 197) vs. placebo (PBO, n=99). A random forests model screened 18 clinically plausible moderators. Interaction coefficients and p-values were derived from two-way interaction terms in the generalized linear model. Results: Random forests generated a short list of moderators to consider further, protecting against type I errors that would have been a problem in a direct examination of all potential moderators. Follow-up analyses identified several significant ( $p < 0.05$ ) interactions. Reductions in the Young Mania Rating Scale (YMRS) total score at endpoint were comparable in younger and older ARI-treated subjects (10–11 years =  $-14.9$  vs. 12–17 years =  $-15.9$ ); however, older subjects had a greater reduction on PBO ( $-10.0$ ) compared with younger subjects ( $-2.9$ ). Similar results held for subjects who were older at onset of illness ( $\leq 12$  or  $> 12$  years) for either YMRS total score reduction or percent meeting a pre-defined response criterion. Also, 67% of subjects with a decreased need for sleep who received ARI were responders, compared to 48% without; proportions of PBO responders were 23 and 31%, respectively. Race moderated PBO response when defined as a Clinical Global Impressions – Improvement of 1 or 2, with 34% of non-white subjects and 12% of white subjects meeting this criterion. Proportions in those receiving ARI were 57% and 59%, respectively. Two significant interactions were observed for AEs: proportions of subjects with an extrapyramidal event were higher in ARI-treated subjects without psychotic features in the current manic episode (40%) vs. those with (9%), and although all mean changes in HDL were small, decreases were greatest for non-rapid cyclers receiving PBO ( $-3.5$ ), followed by rapid cyclers receiving ARI ( $-0.3$ ). Conclusions: Although robust responses were seen for subjects receiving ARI vs. PBO, older subjects and those with a later onset of illness had a greater PBO response, perhaps reflective of a different underlying neuropathological subtype. Three times as many subjects with a decreased need for sleep responded to ARI vs. PBO, compared to one and a half times as many for those without a decreased need for sleep. Interestingly, clinicians rated non-white subjects nearly three times more likely than white subjects to be responding to PBO, which could be the result of a true moderator of illness or potential rater bias. Of the safety variables evaluated, only two potential predictors were identified, indicating that the AE profile of ARI is fairly consistent regardless of patient or disease characteristics.

#### NR8-17

#### TIME OF ONSET AND RESOLUTION OF COMMON ADVERSE EVENTS IN THE ARIPIRAZOLE TREATMENT OF PEDIATRIC

#### (10–17 YEARS) BIPOLAR I DISORDER

*Chair: Benjamin Goldstein M.D.; Author(s): Maia Miguez, Diane K. Ammerman, Joan Zhao, Kiki D. Chang, Eric Youngstrom, Ron Marcus, Robert D. McQuade, Robert A. Forbes, Candace Andersson, Elizabeth E. Bellocchio, Raymond Mankoski*

#### SUMMARY:

Objective: Evaluate the time course, severity, and time to resolution of adverse events (AEs) occurring during aripiprazole (ARI) treatment of manic or mixed episodes associated with bipolar I disorder in pediatric patients 10–17 years old. Methods: Post-hoc analysis of data (to 8 weeks) from a randomized double-blind placebo controlled trial of two fixed doses of ARI (10 and 30 mg/d) vs. placebo. AEs with an incidence of  $\geq 5\%$  were evaluated by incidence, time of first onset, severity, percent resolved, and median time to resolution. Results: 294 patients comprised the safety sample (97 PBO, 98 ARI 10 mg/d, 99 ARI 30 mg/d). Nineteen AEs occurred in  $\geq 5\%$  in either ARI arm. The five most common (10 mg/d, 30 mg/d, placebo) were somnolence (22%, 26%, 3%), extrapyramidal disorder (EPD) (12%, 27%, 3%), fatigue (14%, 10%, 4%), nausea (11%, 13%, 4%), and akathisia (8%, 13%, 2%). All AEs were classified as mild to moderate in severity except for three cases of somnolence (two in the 30 mg/d arm) and one case each of EPD, fatigue, nausea, and akathisia, all in the 10 mg/d arm. Some AEs (gastrointestinal AEs, dizziness, headache, nasal congestion, nasopharyngitis, and vision blurred) typically began during the first 2 weeks and usually resolved within 1 week while staying on the fixed dose schedule. Somnolence and fatigue had an onset during the first 2 weeks but resolved in fewer ARI cases ( $\sim 60\%$ , except for fatigue in the 10 mg/d arm, 79%), with a median time to resolution of 2–4 weeks. Akathisia, dystonia, EPD and salivary hypersecretion generally emerged shortly after steady-state was achieved ( $\sim 2$  weeks in the 10 mg/d arm and  $\sim 3$  weeks in the 30 mg/d arm). Dystonia and salivary hypersecretion resolved in all cases within 2 weeks at the lower dose and in most cases at the higher dose. Akathisia and EPD resolved in 54 – 63% of cases regardless of dose, with median times to resolution of about 4 weeks (although EPD at the higher dose resolved in a median of 19 days). Half the cases of increased appetite had an onset in the first week (because of the titration schedule, subjects in both arms were still receiving 10 mg/d at Day 6) and resolved in half of the cases; none of the eight cases of weight increase resolved. Decreased appetite was also observed to have an onset typically within the first 3 weeks and resolved in 71% of cases in the 10 mg/d arm and in half of the cases in the 30 mg/d arm. Conclusion:

Aripiprazole was generally well-tolerated in both dose groups, and many AEs resolved in the first 3–4 weeks of treatment. Some AEs had an onset soon after initiation but also had frequent and quick resolution. Others, such as those related to somnolence, EPD, or appetite tended to resolve more slowly and less frequently. However, it is important to note that the fixed-dose schedule of the study was more restrictive than clinical practice, in which dose adjustments or concomitant medication use can be used as potential mitigation strategies for AE

#### NR8-18

### USE OF THE TEST OF EMOTION COMPREHENSION IN CHILDREN WITH ATTENTION-DEFICIT HYPERACTIVITY DISORDER

*Chair: Alfredo Minervino M.D.; Author(s): Carla Alexandra da Silva Moita Minervino, Ph.D. Antonio Roazzi, Ph.D. Émille Burity Dias*

#### SUMMARY:

This study aimed to assess emotional competence through the use of the Test of Emotion Comprehension (versions: pencil / paper and computerized test) in children with Attention-Deficit Hyperactivity Disorder (ADHD). ADHD is a psychiatric disorder affecting 3-5% of school-age children in the world and Brazil. This developmental disorder is prevalent mainly characterized by impulsivity, inattention, and hyperactivity. Many studies have shown that children with ADHD perform worse than typically developing children on facial emotion recognition tasks. A study on the use of computerized tests for evaluation requires prior examination of the psychometric characteristics and comparative analysis of performance of individuals. Among the various instruments for the investigation of emotional competence, the Test of Emotion Comprehension (TEC) has contributed to the understanding of capacity development and recognition of expression of emotions. The study included 20 children with ADHD and 20 children without ADHD, aged between 7 and 11 years, girls and boys. Children with ADHD were treated at University Hospital. The instrument in the pencil-paper version (TEC) consists in an A4 book (male and female versions) presenting a series of cartoon scenarios placed on the top of each page; the bottom part of the same page shows four possible emotional outcomes depicted by facial expressions. While showing a cartoon scenario, the experimenter tells the child a story. After hearing the story, the child is asked to attribute an emotion (happy, sad, angry, scared or just alright) to the main character by pointing to one of the four depicted emotional

outcomes (non-verbal responses). Children get one point per component succeeded (min. = 0, max. = 9). (Pons & Harris, 2000) In the computerized version of the story is narrated while the answer choices appear, the figures move and the child has gained the field of mechanism, requiring little or no help for the procedure. The tests were administered individually to children, schools and hospital. We analyzed individual differences in emotion understanding. Data analysis shows that children have a clear improvement with age in their understanding of emotion. The overall score regularly increases with age. The analysis revealed statistically significant differences between the two groups (with and without ADHD), and differences from the version used the TEC.

#### NR8-19

### A NOVEL METHOD FOR IMPROVING DIAGNOSTIC AND EFFICACY ASSESSMENTS IN CHILD PSYCHIATRIC MULTINATIONAL CLINICAL TRIALS

*Chair: Joan Busner Ph.D.; Author(s): Dan DeBonis, Phillip B. Chappell, M.D., Mary Bachinsky, MSC, Gary Sachs, M.D.*

#### SUMMARY:

Introduction: Child psychiatric clinical trials present unique challenges. Rigorous diagnostic and efficacy assessment requires skilled weighting of often discrepant information from parents and children and requires a sophisticated understanding of the pathologic significance of symptoms that may differ dependent on developmental level. Child psychiatric research sites vary widely in experience and proficiency. When trials are multinational, the difficulties are compounded by differing languages, diagnostic practices, parental reporting norms, and culture-specific symptom expression. To assist in ensuring diagnostic and ratings accuracy in two multinational industry sponsored studies of bipolar I mania in 10-17 year olds a novel computer-based ratings diagnostic validation and efficacy assessment tool was designed to be used in tandem with site-clinician ratings. Method: A computer-based diagnostic validation and local-language prompted efficacy scale assessment system was developed. The system was designed to allow for a tandem rating approach wherein site clinicians and the computer prompted system would generate data that could be subjected to independent clinical evaluation and confirmation. The system was designed to be applicable to parents and children aged 10-17, with prompted customized scripts. Results: Site clinicians receive study-specific training in diagnostic scale and

efficacy scale administration and conventions. The site-based computer system provides local-language computer-prompted diagnostic and efficacy scale assessments for parents and children to complete at study visits. The computer-based assessment results and the site clinician assessment results are uploaded for review by an independent local-language clinician trained in the study-specific scale conventions. Agreement of the independent clinician and the site clinician on the diagnostic suitability of the patient is able to serve as a study entry criterion or a basis for a consensus discussion. Conclusion: A tandem ratings diagnostic validation and efficacy assessment program was designed to help ensure methodological rigor for two multinational child psychiatric clinical trials; the program is customizable to a variety of diagnostic and efficacy assessments.

**NR8-20**  
**ANXIETY AND DEPRESSION AMONG PARENTS OF CHILDREN WITH MENTAL RETARDATION**

*Chair: Muhammad Waqar Azeem M.D.; Author(s): Imtiaz Ahmad Dogar, MBBS, Snehal Shah, M.D., Mohsin Ali Cheema, MBBS, Alia Asmat, MSc, Madeeha Akbar, MSc, Sumira Kousar, MSc*

**SUMMARY:**

Background: Studies have shown an association between parental anxiety and depression, and caretaking of children with developmental cognitive delays. There is little data in developing countries, such as Pakistan, concerning the impact of raising children with Mental Retardation, upon the quality of parent functioning and risk for psychopathology. Objective: To evaluate for anxiety and depression among parents of children with Mental Retardation (MR). Methods: This was a prospective study conducted at a tertiary care hospital in Pakistan. Participants were 198 parents (99 fathers/99 mothers) of 100 children with the diagnosis of MR. The parents were assessed for anxiety and depression using DSM IV criteria. Informed consent was obtained. The study was approved by the Institutional Research Committee. Results: Mean age for mothers was 40.2 years and for fathers was 42.9 years. 19% of mothers and 10% of fathers were illiterate. The mean age of the children was 10.5 years (range: 2-25 years), with 30% females and 70% males. The degree of severity of Mental Retardation of this group was: 25 % mild MR, 42% moderate MR, 20% severe MR and 13% with profound MR. Comorbid diagnosis included: cerebral palsy 22%, epilepsy 34%, and autistic disorder 11%. 82% of the cases of MR were congenital. 79% of the

children have various behavioral difficulties, including aggression. Among mothers, 89% have anxiety, depression or both anxiety and depression as compared with fathers, 77% has anxiety, depression, or both. Among mothers, 35% met criteria for anxiety, 40% for depression and 13% for both anxiety and depression. Among fathers 42% had anxiety, 31% depression and 3% both anxiety and depression. There was association between mothers anxiety and depression and degree of mental retardation among children, with depression being highest in mothers of children with moderate MR (57%) and anxiety being highest (50%) among mothers of children with profound MR and both anxiety & depression together being highest among mothers of children with profound MR. There was no significant association among father's anxiety, depression or both and degree of MR in the children. Conclusions: 1. Parents of children with MR are at higher risk for anxiety, depression or both, needing mental health assessment. 2. There was correlation between mother's anxiety, depression or both and level of MR among children. 3. Limitations include lack of comparison group and small sample size.

**NR8-21**  
**CHILDREN'S PSYCHIATRIC HOSPITAL INITIATIVES IN REDUCING RESTRAINTS AND PROVIDING TRAUMA INFORMED CARE**

*Chair: Muhammad Waqar Azeem M.D.; Author(s): Debra Anderson, MS, Michelle Sarofin, LCSW, Linda Carabetta, RN, Treena Mazotta, MSW, Lisa Hayden, Ph.D, Jennifer Avenia, LCSW, JD, Akash Auja, M.D., Marianne Wudarsky, M.D., Ph.D, Mark Root, RN*

**SUMMARY:**

Background: Restraints are usually utilized in child and adolescent programs such as inpatient psychiatric units, residential programs, schools and juvenile justice settings as means of managing aggressive and self injurious behaviors. These procedures can be considered by patients as aversive and traumatizing, and in worse case scenarios deaths have been reported. There are limited studies looking at various programs in reducing restraints in inpatient child and adolescent settings. This study was conducted at 78 bed state run inpatient child and adolescent psychiatric hospital. Objective: To determine the effectiveness of Children's Psychiatric Hospital initiatives based on strategies developed by National Association of State Mental Health Program Directors (NASMHPD) in reducing restraints among youth during inpatient psychiatric hospitalization. These strategies are based on trauma informed and strength based care, and rooted in primary prevention

principles. Methods: This study was conducted between January 2005 and December 2010, over five years. Data was collected regarding youth involved in various types of restraints including mechanical and physical restraints, as well as admission data. Data was collected through an electronic database system and a quantitative analysis was completed. Empirical analysis was completed through observation and direct interviews. The strategies which were implemented at the facility to reduce restraints included 1) Leadership toward organizational change 2) Use of data to inform practice 3) Workforce development 4) Use of restraint reduction tools 5) Improve consumers role in inpatient setting 6) Vigorous debriefing techniques. Results: In 2005, the total number of admissions to the hospital were 178 (51% Males, 49% females) including 38% Caucasians, 34 % African Americans, 27 % Hispanics and 1 % others. In 2010, the total number of admissions to the hospital were 212 (59% Males, 41% females) including 34% Caucasians, 25 % African Americans, 35 % Hispanics and 4 % others. Mechanical restraints are probably the most traumatizing intervention among inpatient settings, with restraint reduction and trauma informed care initiatives, mechanical restraints decreased by more than 96 % from 485 in 2005 to 20 in 2010 and only 3 in last 6 months of 2010. Physical restraints were decreased by 71% from 3033 in 2005 to 878 in 2010. Decrease in restraints contributed to improved clinical outcomes, reduction in staff and patient injuries, and improved working environment. Conclusions: 1. This study shows downward trend in restraints among hospitalized youth after the implementation of the NASMHPD six core strategies based on trauma informed care. 2. Limitations of this study include data not available on restraints per one thousand patient bed days, and lack of control group.

**NR8-23**  
**SELECTIVE DISCHARGE OF MALE SUICIDE ATTEMPTERS FROM PSYCHIATRIC EMERGENCY ROOM**

*Chair: Evan Gilmer B.A.; Author(s): Kogan, Irina, Yaseen, Zimri., M.D., Galynker, Igor M.D., Ph.D.*

**SUMMARY:**

Objective: A female to male ratio of 3:1 for suicide attempts in the general population is consistently supported by literature. It would be of interest to examine whether this ratio is maintained upon admission to a psychiatric ER and to inpatient psychiatric unit. This study aims to investigate the gender differences for suicide attempters entering the psychiatric emergency room from attempters entering in-patient units in

a hospital in New York City. Methods: 183 subjects were interviewed in the course of a study of suicidal behavior. Of those, 131 subjects were interviewed in the psychiatric ER and 52 subjects were interviewed in the in-patient units at Beth Israel Medical Center in New York City. Participants were approached by trained research assistants who, after obtaining consents, collected demographic data and administered a battery of psychometric scales. The Columbia Suicide Severity Scale (CSSR-S) and the Beck Suicide Severity scale (BSS) were both administered to distinguish between suicide attempters and ideators. Statistical analyses included a Fisher's exact test. Results: Contradictory to previous gender ratio reports for suicide attempters in general population, our ER sample contained a 3:1 male to female ratio among suicide attempters examined and a 1:1 ratio for attempters hospitalized and admitted to the in-patient units was observed. The difference in gender ratio between the psychiatric ER group compared to the inpatient group approached significance ( $p=0.0999$ ). The consensus of the ER staff was that suicidal males were likely malingerers. Conclusions: Relative preponderance of female suicide attempters upon admission to the inpatient unit from the ER indicates preferential discharge of suicidal males. Future research needs to be conducted to fully comprehend the implications of preferential discharge of male suicide attempters from psychiatric ER.

**NR8-24**  
**A 3 YEARS SURVEY OF QUETIAPINE IN THE TREATMENT OF DEMENTIA PATIENTS WITH PSYCHOTIC SYMPTOMS IN TAIWAN**

*Chair: Hsinte Huang M.D.; Author(s): Wen-Kuei Lee M.D., Shu-Li Cheng Ph.D., Shang -Wen Chang M.D., Ruu-Fen Tzang M.D.*

**SUMMARY:**

Background: To survey the outcome of treatment with quetiapine with Behavioral and Psychological Symptoms of Dementia (BPSD) in a Taipei public institution. Method: We collected 108 subjects from Jan. 2001 to Dec. 2004, all dementia patients with psychotic symptoms, diagnosis was conformed DSM IV and lived in a chronic institution; each received quetiapine at the least 6 months for treatment. BPSD and Clinical Global Impressions (CGI) were used for evaluation by psychiatrists or staffs. EPSs and TD were also to assess. The data was analyzed using SPSS for Window 12.0 software to perform descriptive analysis. Result: The 108 subjects consist of 50 males (46.3%) and 58 females (53.7%), mean of age= 85.1± 5.9 years old, mean comorbidity with medical diseases= 4.0±1.8; the

most frequent systemic disease is hypertension (64.8%). The mean dose =  $25.3 \pm 15.2$  mg/day; 94.5% of subjects achieved moderate efficacy under stable vital signs; EPSs only noted in 3 patients (2.8%); TD was never found (0%). Conclusion: Low dose quetiapine is effective and safe in treating BPSD above 85 years old. Limitations of this study: 1. The subtypes of dementia cannot be confirmed due to insufficient information 2. Iatrogenic side effects may occur because different specialists prescribed drugs for patients' comorbid medical diseases.

#### NR8-25

### CORRELATION BETWEEN GRAY MATTER VOLUME OF TEMPORAL LOBE AND DEPRESSIVE SYMPTOMS IN PATIENTS WITH ALZHEIMER'S DISEASE

*Chair: Ji Hyun Son M.D.; Author(s): Doug Hyun Han, M.D., Ph.D. Baik Seok Kee, M.D., Ph.D. Woo Hyun Song, M.D. Se Hee Kim, M.D.*

#### SUMMARY:

Objective: Recent epidemiologic studies have declared that more than 20 percent of elderly people (age > 60 years) might be depressed. Moreover, some of depressed people were reported to have cognitive problem in the screening test at local community health center. Depressive symptoms would be associated with not only cognitive decline but also brain structure in patients with dementia. The aim of our study was to investigate the effect of depressive symptom on the change of clinical symptoms and brain change in individuals with minimal cognitive impairment and patients with Alzheimer's disease (AD). Methods: Forty-nine patients with AD, fifty seven subjects with mild cognitive impairment (MCI), and fifty healthy control subjects were recruited through Keum-Cheon center for dementia, Seoul South Korea. All subjects were screened with Mini Mental State Examination (MMSE). Cognitive functions in all subjects were assessed by psychologist using Korean version of the Consortium to Establish of a Registry for Alzheimer's disease (K-CERAD) test battery. Depressive symptoms in all subjects were evaluated using Geriatric Depression Scale (GDS). All Magnetic Resonance Imaging (MRI) was performed using Achieva 3.0 (Philips, Eindhoven, the Netherlands). Results: AD patients with depression showed decreased wordlist-immediate recall ( $8.7 \pm 1.1$  vs.  $10.1 \pm 1.5$ ,  $z = 3.6$ ,  $p < 0.01$ ) and constructional praxis sub-scale score ( $3.7 \pm 0.9$  vs.  $5.3 \pm 2.1$ ,  $z = 2.5$ ,  $p = 0.01$ ) of K-CERAD, relative to patients with dementia only. Additionally, compared to the patients with dementia only, AD patients with depression showed decreased gray matter volume in the left inferior temporal gyrus ( $-56, -19, -31,$

$BA34$ ) ( $?E = 578$  ( $>400$ ),  $t = 3.80$ , uncorrected  $p < 0.001$ ). However, there was no significant difference of gray matter volume between MCI with depression group and MCI only group. Conclusion: Current results suggested that depressive symptoms would be more associated with dementia, relative to MCI in the light of clinical symptom and brain change. We suggest that the more cognition declines, the more attention would be paid to depressed symptoms in elderly patients.

#### NR8-26

### JOINING EXTREMES-UNIENDO EXTREMOS EDUCATIONAL WORKSHOP IN ALZHEIMER DISEASE FOR PRE ADOLESCENT CHILDREN IN THE US MEXICO BORDER

*Chair: Bernardo Ng M.D.; Author(s): Elma Diana Garcia, SW Alvaro Camacho, M.D., M.P.H.*

#### SUMMARY:

Education and support to the caregivers of patients with Alzheimer's Disease (AD) is an essential component in the treatment of this disease. Caregivers are frequently relatives (i.e. spouse and adult children) however minors are not excluded and are also part of the family. This research study attempts to measure the possibility of educating and preparing minors regarding this illness. Addressing this population sector is immensely important in the development of current and future cultural perspectives about aging in general and AD in particular. This study included grade school (4th through 6th) children. They were exposed to a modified version of an educational workshop for adults; that is routinely given by Nuevo Atardecer Centro Geriatrico a nursing skilled facility. The study was approved by the Department of Human Sciences of the Universidad Autonoma de Baja California, and took place at their campus in in the city of Mexicali Mexico, right in the border with California. Besides the collection of sociodemographic data (age, gender, socioeconomic status, and number of seniors living at home) a pre and posttest was used to measure gain of knowledge. Teaching strategies to target critical thinking, memory, imagination, language and psychomotor skills were used. The total sample was of 50 children, 25 girls and 25 boys, ages 9 through 12. As to their perception of family income, there were 10 in low, 30 in middle, and 9 high economic status (1 did not answer). A total of 30 children did not have a senior living at home (19 girls and 11 boys) and 20 did have a senior living at home (6 girls and 14 boys). Out of the 50 children, less than 70% approved the pretest, and close 95% approved the post test, resulting in a gain of approximately 30%. We conclude that the adapted workshop was well accepted

based on the knowledge gained demonstrated by the increased rate of approved tests. This is an encouraging result and leads to believe that this type of intervention could and should be replicated in other communities especially in those where the senior population is expanding.

**NR8-27**  
**CORRELATION BETWEEN ATTITUDE TOWARD GAYS AND LESBIANS IN COLOMBIAN MEDICAL STUDENTS**

*Chair: Edwin Herazo M.D.; Author(s): Heidi C. Oviedo, M.D. Adalberto Campo-Arias, M.D., MSc*

**SUMMARY:**

Background: Some scientific theories postulate that attitude toward gay men (homophobia) and attitude toward lesbian women (lesbophobia) are actually distinct constructs. Nevertheless, there is not empirical evidence of that difference. Objective: To explore the correlation between homophobia and lesbophobia among medical students from a medical school in Bogota, Colombia. Method: A cross-sectional study was done with medical students over 18 years of a university. Homophobia and lesbophobia were measured with the Attitude Toward Gays and Lesbians (ATGL). The ATGL is compound of two ten-item scales: Attitude Toward Gay Men Scale (ATG) and Attitude Toward Lesbian Women Scale (ATL). Correlation between scales was computed with Pearson coefficient (r). It was hypothesized that homophobia and lesbophobia were different constructs if correlation between the scales were lower than 0.600. Results: A total of 359 medical students participated in the research. The mean of age was 20.2 years old (SD=1.9); and 59.1% were females. Correlation between ATG and ATL was  $r=0.641$  ( $p<0.001$ ). Cronbach alpha was 0,851 for ATG; and 0,735, for ATL. Conclusions: The ATG and ATL show high significantly correlation; it suggests that homophobia and lesbophobia are not different constructs. Other researches must corroborate the present finding.

**NR8-28**  
**RELIABILITY AND VALIDITY OF THE HOMOPHOBIA SCALE AMONG COLOMBIAN MEDICAL STUDENTS**

*Chair: Heidi Oviedo M.D.; Author(s): Edwin Herazo, M.D., MSc Adalberto Campo-Arias, M.D., MSc*

**SUMMARY:**

Background: The Homophobia Scale (HS) is a seven-item instrument for measuring attitude toward

homosexuality. Though, its reliability and validity has not been studied in Colombian medical students. Objective: To determine the reliability and validity of HS in a sample of Colombian medical students. Method: A total of 667 of medical students, between 18 and 30 years old (mean=20.9 years; SD=2.7), 59.1% women, completed the Attitude Toward Gay Men Scale (ATG), a five-item version of Zung's Rating Anxiety Scale (ZRAS), and HS. Cronbach alpha, McDonald omega, Pearson's correlations (r) and factor analysis were calculated. Results: The HS showed Cronbach alpha of 0.793; and McDonald omega, 0.796 (reliability). Pearson correlation with the ATG was 0.778 (convergent validity), and with ZRAS was -0.067 (divergent validity). Men reported higher scores than women [18.6 (SD=5.4) vs. 17.4 (SD=5.5)  $p=0.007$ ] (nomological validity). One salient factor was retained (Eigen value higher than 1.41). The factor explained 45.2% of the total variance (construct validity). Conclusions: The HS shows high reliability and good validity for measuring attitude toward homosexuality among Colombian medical students.

**NR8-29**  
**CRITICAL SUCCESS FACTORS IN IMPLEMENTING CASE MANAGEMENT IN TERTIARY PSYCHIATRIC CARE**

*Chair: Rathni Mahendran M.B.B.S Author(s): Margaret Hendricks BSc*

**SUMMARY:**

The Institute of medicine identified three fundamental quality of care issues: 1.use of unnecessary and inappropriate care 2. underuse of needed and appropriate care 3. shortcomings of technical and interpersonal aspects of care Psychiatric Case Management was introduced to IMH/WH to address these issues through a systematic collaborative approach to provide coordinated care for psychiatric patients. The aim was to decrease fragmentation and duplication of care and to enhance clinical outcomes. Several critical success factors led to the expansion of services from 3 (2007) to the present 24 (2011) in acute inpatient adult general psychiatry wards, geriatric psychiatry, forensic psychiatry and ambulatory care. 1.Organizational vision, support and acknowledgement for case management services through provision of funding for service expansion and staff training 2.Clinician support and acceptance of case managers 3.Dedicated Case Managers 9a) with passion for helping the mentally ill (b) who are open to learning new skills and practice behaviors to enhance delivery of care (c) creating and maintaining the focus of care delivery and

respect for patients (d) helping the hospital create a system of quality, affordable care that is accessible to all. 4. Evidence-based practice in Case Management 5. Close evaluation of service performance and outcome indicators. The case management Unit has set in place a rigorous care delivery system to provide continuity of care, coordination of services and importantly to keep our patients in contact with mental health services.

**NR8-30**

**ADHD IS A NOTABLE CHARACTERISTIC OF PATIENTS SUFFERING FROM CHRONIC LYME DISEASE: A SURVEY OF ADULTS AT THE MICHIGAN LYME DISEASE ASSOCIATION CONFERENCE**

*Chair: Joel Young M.D.*

**SUMMARY:**

**Objective:** To gain a greater understanding of the psychiatric implications associated with Lyme Disease. **Methods:** Participants in the study were drawn from the Michigan Lyme Disease Association Conference on August 21 and 22, 2009. The survey was open to individuals aged 18-80, and included 58 respondents with Lyme Disease and 26 control group participants. Survey packets included a demographic questionnaire and four behavioral rating scales. **Results:** In two assessments, Chronic Lyme Disease (CLD) subjects endorsed more ADHD symptoms than controls. The ADHD subscale of the Adult Self-Report Inventory (ASRI) scores showed significantly higher scores on the combined and inattentive scales. The AD/HD Self-Report Scale (ASRS) was significant for both inattentive and hyperactive subunits. Predictably, CLD subjects had statistically significantly higher scores on the Fatigue Severity Scale than their control group counterparts. The ASRI also revealed that the CLD group had dramatically higher rates of dysthymia, generalized anxiety, major depression and somatization. This study corroborates earlier findings that identified a relationship between CLD and anxiety and depression. This survey extends these findings to include a correlation between CLD and ADHD (inattentive and combined types). Although this is the first survey to identify the linkage of these two conditions, cognitive deficits associated with CLD have been demonstrated before. **Conclusions:** Two viable theories explain the link between CLD and ADHD. One consideration is that patients with CLD develop ADHD symptoms, inferring that chronic infection with *B. burgdorferi* taxes the central nervous system resulting in symptoms of fatigue and sometimes pain. An alternative model is that many CLD patients also have pre-existing, untreated

ADHD, and their cognitive and physical symptoms are manifestations of this condition. This presupposes that, as patients with ADHD age, their cognitive symptoms morph into complaints of fatigue and chronic pain. These concerns drive the patient into the medical marketplace in search of answers, where a portion of these patients learn about the overlapping somatic and psychiatric symptoms that characterize CLD and receive the diagnosis. The results of this survey give merit to this second argument.

**NR8-31**

**OUTCOME OF ADMISSION HYPONATREMIA AMONG PSYCHIATRIC INPATIENTS**

*Chair: Kevin Ray M.D.; Author(s): Peter Manu, M.D., Joshua L. Rein, B.S., John M. Kane, M.D., Christoph U. Correll, M.D.*

**SUMMARY:**

**Background:** Admission hyponatremia is associated with increased severity of illness and mortality in patients hospitalized for treatment of medical conditions, but this clinical outcome has not been studied in psychiatric inpatient populations. **Objective:** To determine the incidence, clinical characteristics and medical outcome of psychiatric inpatients with hyponatremia at time of admission. **Method:** Retrospective cohort study of 1,000 adults consecutively admitted to a single, free-standing psychiatric hospital in 2010. Hyponatremia was defined as a sodium level of less than 136 mEq/L (after correction for plasma glucose concentration) and emergency transfer to a general hospital was used as a proxy marker for poor medical outcome in 939 patients with usable data. **Results:** The incidence of hyponatremia at admission was 6.49 %. Compared with normonatremic patients, those with admission hyponatremia were older ( $p < 0.0001$ ), had increased rates of arterial hypertension ( $p < 0.0001$ ), dyslipidemia ( $p = 0.003$ ), coronary artery disease ( $p = 0.002$ ) and total number of somatic disorders ( $p = 0.018$ ), and lower levels of albumin ( $p = 0.009$ ) and hemoglobin ( $p = 0.003$ ). The groups were similar with regard to psychiatric diagnoses and psychotropic drug treatment. Significantly more patients with hyponatremia suffered a medical deterioration requiring emergency transfer to a general hospital (26.7% vs. 13.1%,  $p = 0.003$ ), but symptomatic hyponatremia was the reason for transfer in only one instance. **Conclusions:** Admission hyponatremia is relatively common among psychiatric inpatients and is associated with an increased rate of significant medical deteriorations. The presence of hyponatremia should trigger prompt medical evaluation and enhanced monitoring to prevent, identify and treat somatic

disorders.

### NR8-32

#### THE EVALUATION OF PRIMARY IDIOPATHIC FOCAL HYPERHIDROSIS PATIENTS IN TERMS OF ALEXITHYMIA AND TEMPERAMENT AND CHARACTER PROPERTIES

*Chair: Mehmet Ak M.D.; Author(s): Mehmet Ak M.D., Bikem Haciomeroglu, Didem Dincer M.D., Suleyman Akarsu M.D., Alper Cinar M.D., Ali Bozkurt M.D.*

#### SUMMARY:

Background: Primary Idiopathic Focal Hyperhidrosis is a disorder characterized by excessive sweating of mostly the axilla, hands, feet, and craniofacial areas. This study aimed to evaluate the temperament and character properties and the level of alexithymia of PIFH patients. Method: Ninety four participants (50 PIFH and 44 control subjects) ranging from 15 to 65 years old ( $M=25\pm 7.30$ ) participated in the study. Results: Among the PIFH subjects, 15.2% ( $n=7$ ) scored higher than 60 in TAS-20 and accepted as alexithymic. The percentage of subjects with middle alexithymia (TAS-20 scores between 52-60) and nonalexithymic (TAS-20 scores  $<51$ ) were respectively 30.4% ( $n=14$ ) and 54.3% ( $n=25$ ). Among the control group, only 1 subject (2.23%) was alexithymic, 7 subjects (15.9%) had middle alexithymia, and 36 (81.8%) subjects were nonalexithymic. PIFH group scored significantly higher compared to control group in Difficulty Identifying Feelings, Difficulty Describing Feelings subscales, and total score. In terms of temperament properties, PIFH group took significantly higher scores than control group in Fatigability and asthenia, Sentimentality, and significantly lower scores than control group in Attachment dimensions. In terms of character properties, PIFH group scored significantly lower than control group in Responsibility, Purposefulness, Resourcefulness, Self-acceptance, Self-Directedness, Acceptance, and scored significantly higher than control group in Self-forgetfulness, Transpersonal identification, Spiritual acceptance, and Self-Transcendence dimensions. Conclusion: PIFH patients differentiated from healthy controls in terms of their temperament and character properties and level of alexithymia. These properties might be affected from many factors including genetic, biological, environmental, and socio-cultural. Educational Objective: Participants should be able to define temperament and character properties and alexithymia levels of PIFH patients

### NR8-33

#### BENEFIT/RISK ANALYSIS OF OLANZAPINE LONG-ACTING INJECTION AT 1 AND 2 YEARS OF TREATMENT IN CLINICAL TRIALS OF SCHIZOPHRENIA

*Chair: John Lauriello M.D.; Author(s): Holland C. Detke, Ph.D., John Landry, M.Math., Susan B. Watson, Ph.D., David P. McDonnell, M.B., M.R.C.Psych.*

#### SUMMARY:

Objective: To evaluate the 1- and 2-year within-drug benefit/risk of olanzapine long-acting injection (LAI) using multiple methods. Method: Subjects were 1192 adults with schizophrenia or schizoaffective disorder in clinical trials with the opportunity for at least 2 years of continuous treatment with olanzapine LAI (45-405mg every 2-4 wks). First, frequencies of benefits and risks commonly observed with atypical antipsychotics were evaluated versus the average durations of those events. Patients with a baseline and  $\geq 1$  post-baseline assessment or, for injection-related events,  $\geq 1$  olanzapine LAI injection, were included. Rates and mean times with event reflect data for all patients rather than patients with the event unless otherwise specified. Second, the Transparent Uniform Risk/Benefit Overview (TURBO) method was employed, weighting a drug's 2 most potentially medically serious and/or frequent adverse events versus its primary benefit (treatment effectiveness) and an ancillary benefit. Each author independently applied the TURBO criteria; ratings were averaged across raters and placed on a t-score grid ranging from 1 (worst balance) to 7 (excellent balance). Results: The most frequent occurrence among all patients was remaining relapse-free (91.5% at 1 yr; 88.4% at 2 yrs). Mean cumulative number of relapse-free days was 308 (SD=113) at 1 yr and 549 (SD=261) at 2 yrs. The next most frequent occurrence was symptomatic remission (score of  $\geq 3$  on 8 key PANSS items) at any assessment point (82.1% at 1 yr; 84.2% at 2 yrs). Mean cumulative number of symptomatic remission days was 211 (SD=147) at 1 year and 410 (SD=288) at 2 years. Incidence of clinically significant weight gain ( $\geq 7\%$  of body weight) was 32.9% at 1 yr and 41.4% at 2 yrs; mean duration was 53 (SD=99) days at 1 yr and 121 (SD=208) days at 2 yrs. Per-patient incidence of post-injection delirium/sedation syndrome (PDSS) was 0.7% at 1 yr and 1.5% at 2 yrs. The vast majority of patients did not experience a PDSS event (mean duration was 0 days at 1 yr and 0 days at 2 yrs); for those who experienced an event (8 patients at 1 yr; 18 patients at 2 yrs), mean duration was 2 days at 1 yr and 2 days at 2 yrs. Data for other adverse events will also be presented. For the TURBO analysis, raters

unanimously selected PDSS and weight gain as key risks, although choice of ancillary benefit varied. Mean benefit rating was 5.0 out of 7. Mean risk rating was 2.8 out of 7, yielding a mean benefit/risk balance within the “acceptable” range (t-score=5), even when accounting for interrater differences in subjective weightings. Conclusions: Based on the TURBO method, olanzapine LAI’s benefit/risk balance was within the “acceptable” range. Based on a more quantitative evaluation, benefits such as remission days and relapse-free days outweighed lower-probability events such as PDSS, but higher-probability risks such as weight gain remain a significant clinical concern for many patients. Supported by Lilly.

**NR8-34**  
**COLLABORATIVE MODELS OF CARE FOR MEDICAL INPATIENTS WITH PSYCHIATRIC DISORDERS: A SYSTEMATIC REVIEW**

*Chair: Maria Hussain M.B.B.S Author(s): Dallas Seitz M.D., FRCPC*

**SUMMARY:**

**Purpose:** Psychiatric disorders are common among medical inpatients and psychiatric illness is associated with adverse medical outcomes. Collaborative models of care (CMC) involving mental health providers and other health care professionals have been demonstrated to improve medical and mental health outcomes in primary care settings. However, the effects of CMC on the outcomes of medical inpatients with psychiatric disorders (MIPD) are not known. The purpose of this project is to examine the evidence for CMC for MIPD. **Methods:** We searched MEDLINE, EMBASE and Google scholar for relevant articles using key words and medical subject headings. We included all English language publications that evaluated effects of CMC for MIPD when compared to usual care or another model of psychiatric care. We included both randomized controlled trials and other quasi-experimental studies. We defined CMC as models of care which integrated medical and psychiatric practitioners in the same care team. We excluded studies that only examined consultation or liaison models of psychiatric care. We extracted data on the effects of CMC on psychiatric outcomes, medical outcomes, and health service utilization where this information was reported. Included studies were described qualitatively and summarized in tables. **Results:** A total of 855 unique citations were identified and 38 articles retrieved and reviewed in detail for eligibility. After review, three studies met inclusion criteria. All studies had

methodological limitations placing them at potential risk of bias. The three studies were different in terms of study design, patient populations, and reported outcomes. In one study, the global improvement in psychiatric symptoms for the patients who received care in a CMC was significantly better than those admitted to an internal medicine ward. Two studies found that length of stay (LOS) was reduced with CMC while another study found the LOS was increased in the CMC when compared to usual care. One study reported an improvement in functional outcomes and decreased likelihood of placement at one year associated with CMC. There was limited information on the effects of CMC on medical outcomes or post-discharge health service utilization. Conclusions: Currently, there are few studies of the effects of CMC for MIPD. Based on the existing studies and evidence from other healthcare settings, CMC show some promise in improving psychiatric outcomes for this vulnerable population. There is a paucity of research on this topic and more studies examining health and economic outcomes are required.

**NR8-35**  
**ORIGINAL RESEARCH: TREATING SLEEP DISORDERS HAS POSITIVE OUTCOMES IN PSYCHIATRIC ILLNESSES**

*Chair: Umesh Vyas M.D.*

**SUMMARY:**

**Introduction:** Sleep is an essential physiological need; it is an active state that is critical for our physical, mental and emotional well-being. Sleep is also important for optimal cognitive functioning and sleep disruption results in functional impairment. Psychiatric and sleep disorders are common and often co-morbid. The disturbance in quality and quantity of sleep can exacerbate underlying psychological distress and psychiatric illnesses. Author hypothesized that treatment of sleep disorders improves outcomes in psychiatric illnesses. **Method:** Charts at the sleep disorders clinic, VAMC Milwaukee, from October to December 2007 were reviewed. Outcomes in patients with co-morbid psychiatric disorders were recorded at 6, 12 and 24 months after initiation of sleep disorder treatment. These patients received a baseline psychiatric status score of 0. Change in status at each subsequent time point was scored as: +2 (marked improvement), +1 (mild improvement), 0 (no change), -1 (mild worsening), or -2 (marked worsening). Change in average score for psychiatric disorders was compared individually at each time point to baseline using the signed rank test. Compliance was compared to sleep disorder treatment

between patients with and without psychiatric disorders using Fisher's exact test. Difference in score changes at each time point to baseline was compared for a specific psychiatric disorder using Wilcoxon test. Results: 127 charts reviewed, 10 were excluded as patients died within follow-up period. No death was due to suicide. Out of 117 patients 97.6% were men and 2.4% women. Age range: 21-40: 7.7%, 41-60: 42.7%, 61-80: 47.9%, >81: 1.7%. 54 patients (46.2%) had co-existing psychiatric and sleep disorder diagnoses. Psychiatric status progressively improved compared to baseline (Change in average score by +0.45, +0.56, and +0.79 at 6, 12, and 24 months, respectively,  $p < 0.0001$ ). There was no difference in provider documented compliance rate to sleep disorder treatment between patients with and without psychiatric disorders, (Fisher's  $p$  value 0.1031, 0.2290 and 0.2248 respectively). Wilcoxon test was used to find if there were significant differences in score change at each time point based on the presence of a specific psychiatric disorder. Author found this was not statistically significant. This may be due to small number (N) for a specific psychiatric disorder; since most subjects had various co-existing psychiatric disorders. All statistical analysis was performed in SAS (Cary, NC). Conclusions: 1) Treatment of co-morbid sleep disorders was associated with significant improvement in psychiatric disorders. 2) Psychiatric disorders did not affect compliance with sleep disorder treatment. 3) No significant improvement observed for specific psychiatric disorder. 4) There is a strong need for prospective studies with more subjects.

**NR8-36****AN ANALYSIS OF THE EFFICACY AND TOLERABILITY OF ARMODAFINIL IN HEALTHCARE WORKERS WITH EXCESSIVE SLEEPINESS ASSOCIATED WITH SHIFT WORK DISORDER**

*Chair: Richard Bogan M.D.; Author(s): Mary G. Umlauf, Ph.D., RN, Ronghua Yang, Ph.D.*

**SUMMARY:**

**Objective:** Healthcare workers who work permanent or rotating night shifts are vulnerable to developing excessive sleepiness and ultimately, shift work disorder (SWD). Excessive sleepiness in shift workers may lead to increased workplace accidents and mistakes. The wakefulness-promoting agent armodafinil has been shown to significantly improve clinical condition and wakefulness during the night shift and overall functioning in patients with SWD. Specifically, this study examined the late hours of the night shift. A post-hoc analysis examined efficacy and tolerability of

armodafinil in healthcare workers with SWD. **Methods:** Patients in this 6-week, randomized, double-blind study were clinically diagnosed with SWD (DSM-IV and ICSID-2 criteria), worked at least five 6-12 hour night shifts per month (between 2200 and 0800), with Global Assessment of Functioning (GAF) score  $< 70$ , and late-in-shift sleepiness (between 0400 and 0800) represented by a mean Karolinska Sleepiness Scale (KSS) score  $> 6$ . Following randomization, patients received 150 mg armodafinil or placebo 30-60 minutes before beginning their night shift. Efficacy assessments were change in Clinical Global Impression-Change (CGI-C) related to excessive sleepiness late in the shift (including the commute home), GAF, late-in-shift KSS, and modified Sheehan Disability Scale (SDS-M) from baseline to final visit. The SDS-M was modified to determine the effect of shift work on work, family, and social life. Final visit data included last observation carried forward. **Results:** Of the 383 patients enrolled in the original study, 56 (15%) were healthcare practitioners and 37 (10%) were healthcare support staff. After pooling both healthcare worker populations, 47 patients received armodafinil and 46 patients received placebo. In contrast to what was previously observed for the general study population, the proportion of patients in this analysis with an improvement in late-in-shift CGI-C from baseline was not significantly greater in the armodafinil group versus the placebo group at final visit (67% vs. 51%;  $p = 0.0978$ ). However, the proportion of patients with late-in-shift CGI-C improvement from baseline was significantly greater in armodafinil patients who completed the 6-week study (72% vs. 49%;  $p = 0.0350$ ). Significant improvements in the GAF, late-in-shift KSS, and SDS-M were observed at final visit and for Week 6 completers. Headache and nausea were the most common adverse events. **Conclusions:** These results show that armodafinil significantly improved late-in-shift clinical condition after 6 weeks of treatment. Armodafinil also significantly improved overall functioning and late-in-shift wakefulness and reduced patient disability score. Similar to the overall study population, headache and nausea were the most common adverse events. This study was funded by Cephalon, Inc.

**NR8-37****ZOLPIDEM TARTRATE SUBLINGUAL TABLET C-IV: PK/PD PROFILE SUPPORTS MIDDLE-OF-THE-NIGHT DOSING OF 1.75 MG IN WOMEN AND 3.5 MG IN MEN**

*Chair: David Greenblatt M.D.; Author(s): Thomas Roth, Ph.D.*

**SUMMARY:**

Introduction: Intermezzo sublingual tablet, formulated with carbonate-bicarbonate buffers to promote permeation across the oral mucosa, was recently approved by the FDA for as-needed treatment of insomnia characterized by MOTN awakening followed by difficulty returning to sleep. Intermezzo is the first drug approved specifically for this sleep disorder, and the first sleep drug where the dose for women is different than the dose in men. The maximum recommended dose in women is 1.75 mg and 3.5 mg in men. This analysis describes the PK/PD profile by gender subgroups. Methods: Data was obtained from a double-blind, placebo-controlled cross-over study which investigated the PK/PD of Intermezzo doses of 1.0, 1.75 and 3.5 mg in 11 non-elderly women (median age = 39 years, range 21-44) and 13 non-elderly men (32 yrs, range 21-44). Treatments were administered on 2 consecutive days, where PD response (based on digit symbol substitution (DSST) scores) was measured on Day 1 and PK was assessed on Day 2, to avoid learning effects on PD. The PK/PD in the combined group (n=24) has been previously published. (1) Results: The analysis demonstrated that the Intermezzo C<sub>max</sub> and AUC<sub>0-inf</sub> changed linearly and proportionally with dose in both women and men. At the same dose, the zolpidem plasma levels from Intermezzo in women were about 45% higher than those in men. In women, the average C<sub>max</sub>, AUC<sub>0-inf</sub>, and T<sub>max</sub> of the 1.75 mg Intermezzo dose were 37.47 ng/mL, 151.36 ng·h/ml, and 41.4 min, respectively. The C<sub>max</sub>, AUC<sub>0-inf</sub>, and T<sub>max</sub> of 3.5 mg in men were 53.15 ng/ml, 197.69 ng·h/ml, and 36.0 min. On average, the apparent clearance of Intermezzo in women at 1.75 mg was 2.66 ml/min/kg and that in men at 3.5 mg was 3.96 ml/min/kg. The plasma concentrations at 3, 4 and 5 hours also decreased linearly in both genders. Half-life did not differ substantially between genders. Plasma concentrations at these time points are important because Intermezzo is not indicated for treatment of MOTN insomnia when the patient has fewer than 4 hours of bedtime remaining before the planned time of waking. At the same dose, the PD response was greater in women than in men. In the aggregate, gender differences in PD response were partly explained by higher zolpidem plasma concentrations in women. DSST scores empirically correlated with the plasma concentration-time profiles of the drug in men and women at their therapeutic doses. Conclusion: The PK/PD profile of Intermezzo sublingual tablet supports MOTN dosing of 1.75 mg in women and 3.5 mg in men.

**NR8-38**
**SERIOUS OR UNDIAGNOSED MEDICAL CONDITIONS WITH BIPOLAR DISORDER PREVENTING CLINICAL TRIAL RANDOMIZATION: A CASE SERIES**

*Chair: Trisha Suppes M.D.; Author(s): Natalie S. Feldman, Iola S. Gwizdowski M.S. M.A., E. Grace Fischer B.S., Julia Hernandez M.S., Benjamin Raudabaugh B.A., Huaiyu Yang M.D.*

**SUMMARY:**

Objective: Studies have shown that patients with bipolar disorder have high rates of serious and/or untreated co-occurring general medical conditions. This case series examined reports on co-occurring medical conditions with bipolar disorder in potential clinical study participants, and in particular the percentage of participants in question who were previously unaware of their conditions. Method: Patients were potential participants in one of two medication trials who were excluded from those studies just prior to randomization from May, 2009 through July, 2011. Patients were compared to each other for a number of demographic criteria, including age, race, gender, reason for exclusion from the trial, and psychiatric diagnoses. Results: Of the patients excluded from the studies just prior to randomization, 30% (n = 10) were excluded because of medical conditions previously unreported by the patient. 70% of those excluded patients (n = 7) had no prior knowledge of their conditions. Conclusion: These results suggest that patients with bipolar disorder may not only have high rates of co-occurring medical conditions but also frequently remain unaware of those conditions. This indicates that co-occurring general medical conditions may be a more serious problem when treating bipolar disorder than previously appreciated, and that more stringent monitoring and guidelines are needed regardless of medication regimes. This case series asserts that, regardless of a patient's claim of having no medical conditions, more general medical screening may be needed in outpatient psychiatric settings. This research was supported by Pfizer Inc. and NIMH.

**NR8-39  
EVALUATION OF AFFECTIVE TEMPERAMENTS IN PATIENTS WITH VOCAL NODULES**

*Chair: Selcuk Aslan M.D.; Author(s): Emine Metin, Odiologist, Ph.D., Hale Yapici, M.D., Kemal Uygur, M.D., Turkey*

**SUMMARY:**

Patients with vocal nodules are the largest group in voice clinics and it is usually observed in females. The personality traits, reaction to stressful events and emotional states of individuals affects voice quality by changing physiologic conditions of phonation (1, 2). In this research we aimed to evaluate temperaments of individuals with vocal nodule and comparing to healthy controls. Method: 32 female voice disorder patients, admitted to Ear Nose Throat (ENT) Department of Gazi University Faculty of Medicine in Turkey were enrolled to the study. On physical and stroboscopic evaluation vocal nodule was demonstrated in all patients. The age matched control group consisted of 30 healthy female subjects who did not suffer from a voice disorder. The voice records were obtained from all subjects in voice laboratory. After completing voice evaluation form, aerodynamic evaluation (a, s, s/z time), voice handicap index, Rosenbaum's Learned Resourcefulness (LR), and Temperament and Character Inventory (TEMPS-A) (3) for evaluating personality traits were applied to all subjects. Acoustic analysis was done by using CSL program in M.D.VP and vocal assessment part from Dr. Speech. Results: There were significant decrease in Maximum Phonation Time scores in study group. There were statistically significant difference in Dr. Speech's vocal assessment analysis between two groups. Compared to control subjects, patients with vocal nodules had higher anxious temperament features, Anxious temperament features ( $8.0 \pm 6.5$ ) is significantly higher than control ( $4.6 \pm 5.2$ ) group ( $P < 0.05$ ). Trouble in resourcefulness with stressful situation ( $127.0 \pm 16.3$ ) is higher in vocal nodules group than control group ( $117.2 \pm 17.9$ ) ( $P < 0.05$ ) and patients with vocal nodules has poor solving strategies for the stressful situation. Our results suggest that evaluating patient's anxious temperament traits and unhealthy reaction to stress factors is important while evaluating the patients with vocal nodules. References 1. Aslihan S, Aslan S. (2005) Duygudurum The Relationship Between Mood Disorders and Temperament, Character and Personality," Turkish Journal of Psychiatry, 16 (4), 276-283. 2. Vahip S, Kesebir S, Alkan M ve ark. (2005) Affective temperaments in clinically – well subjects in Turkey: initial psychometric data on TEMPS – A. J Affect Disord, 85: 113-125. 3. Akiskal HS, Akiskal KK, Haykal RF ve ark. (2005) TEMPS-A: progress towards validation of a self-rated clinical version of the Temperament Evaluation of the Memphis, Pisa, Paris, and San Diego Autoquestionnaire. J Affect Disord 85: 3-16.

**NR8-40****CIGARETTE SMOKING, CHRONIC PAIN & DISABILITY IN HOSPITALIZED DEPRESSED****PATIENTS**

*Chair: Joseph Rieman D.O.*

**SUMMARY:**

**Introduction:** Major Depressive Disorder is estimated to occur in 2-6% of the general United States population, and some studies have shown that more than 40% of these patients suffer from chronic pain as well. It is believed that major depression and chronic pain are closely related, but the exact interaction of these debilitating conditions is not fully understood. Chronic pain significantly impacts quality of life and is a leading cause of disability in the United States. Identification of patterns in the behaviors and differing treatments for these patients could serve to enhance treatment, as well as improve the quality of life. **Objective:** The purpose of the present study was to examine the clinical correlates of depression with comorbid chronic pain. **Methods:** A cohort of patients who were admitted to the adult psychiatry unit at Sparrow-St. Lawrence Hospital in Lansing for treatment of depression, during calendar years 2010-2011, were provided with a survey to explore possible chronic pain, patterns of substance abuse and treatment outcome. Patients without chronic pain were compared to those with chronic pain to compare treatment strategies, length of stay, tobacco use and disability. **Results:** Forty-six patients participated in the study: 26 women and 18 men. The mean age was 42 (SD=13) years. The mean duration of depressive illness was 10 (SD=13) years. Twenty-two patients (48%) acknowledged chronic pain. Eleven (24%) were disabled from work. Nine of the 11 patients (82%), who were disabled, also reported concurrent chronic pain. There was no association between chronic pain, use of alcohol, drugs and length of stay or treatment variables. However, patients who were disabled were more likely to smoke (82% vs. 53%; Pearson chi-square  $t=63.85$ ,  $df=4$ ,  $p < 0.001$ ) and to have fewer supportive family members or friends: 5 (SD=4) vs. 3 (SD=4) than others. Patients who smoked were more likely to suffer from chronic pain than nonsmokers (62 vs 33%): Pearson chi-square  $t=4.5$ ,  $df=2$ ,  $p=0.113$ ). Twenty-one (46%) had been offered cognitive behavior therapy and 31 (67%) had practiced relaxation. All of the patients were maintained on antidepressant medications. Patients with chronic pain were less likely to have received cognitive therapy (39 vs 50%) but more likely to have received SNRI antidepressants (65 vs 9%; Pearson chi-square  $t=31.5$ ,  $df=2$ ,  $p < 0.001$ ) and practiced relaxation training than others. **Discussion:** Three findings emerge from this study. First, not surprisingly, patients with chronic pain and depression were more likely to be disabled from work compared to patients without chronic pain.

Second, only a minority of patients hospitalized for major depressive disorder have ever received cognitive behavior therapy, which is widely considered to be effective for the long term prevention of depressive relapse. Third, smokers were more likely to experience chronic pain and be disabled compared to non-smokers.

**NR8-41**

**DEEP BRAIN STIMULATION AND MOOD IN PARKINSON'S DISEASE: A PROSPECTIVE FOLLOW-UP STUDY CHOPRA A 1, SAMPSON S 1, KLASSEN B 2, LEE KH3, FIELDS J1**

*Chair: Amit Chopra*

**SUMMARY:**

**Introduction:** Deep brain stimulation (DBS) has been associated with anxiety, depression, mania, psychosis and suicide despite motoric improvement in advanced Parkinson's disease (PD). This prospective study evaluated the impact of mood symptoms and psychiatric history on DBS-associated mood outcomes in PD patients. **Methods:** Written informed consent was obtained to carefully evaluate mood in 54 PD patients (15F, 39 M) at baseline and follow-up visits after being approved by Mayo Clinic DBS Clinical Committee for surgery. Baseline and follow-up (2 weeks, 2, 3 and 6 months) assessments included: United Parkinson's Disease Rating Score (UPDRS) –both on and off, Levodopa equivalent daily dose (LEDD), Beck's Depression Inventory (BDI-II), Hamilton Depression Rating Scale (HDRS-17 item) Young Mania Rating Scale (YMRS) and Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form (Q-LES-Q-SF). All patients were evaluated by a board certified psychiatrist prior to surgery and were grouped into three categories: patients with no current or past psychiatric comorbidity, patients with depressive comorbidity, and patients with bipolar disorder / impulse control disorder comorbidity. Baseline to endpoint (6 month) change in mood outcomes between groups was assessed using paired t-tests and one-way ANOVA tests. **Results:** The mean age of patients (n=54), was 62±9 yrs. The mean UPDRS scores at baseline were 35.2±10 (off) and 16.4±8 (on) respectively. The mean LEDD was 1636 ± 1020 mg. 49/54 patients completed 6 months follow-up. The baseline psychiatric assessments were: BDI-II (9.0 ± 7.7), HDRS (8.7 ± 4.2), YMRS (2.0 ± 2.5), and Q-LES-Q-SF (3.4±0.9). Both mood symptoms and quality of life improved at study endpoint. No significant difference noted in LEDD reduction (p=0.5), or mood measures including BDI (p=0.53), HDRS (p=0.86), YMRS (p=0.26) and Q-LES-Q (p=0.95) amongst three groups at endpoint. One patient with no psychiatric

comorbidity developed psychotic mania requiring hospitalization and none of the patients attempted/completed suicide. **Conclusions:** The results of our prospective study underscore overall psychiatric safety of DBS in carefully selected PD patients including those with mood disorders comorbidity. Comprehensive psychiatric screening at baseline as part of DBS clinical evaluation and careful follow-up after DBS is recommended in developing DBS programs to prevent psychiatric complications in PD patients.

**NR8-42**

**EFFICACY AND SAFETY OF LU AA21004 IN A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED, ACTIVE-REFERENCED, FIXED-DOSE STUDY IN ELDERLY DEPRESSED PATIENTS**

*Chair: Christina Olsen, Ph.D.; Author(s): Cornelius Katona, M.D. FRCPsych Thomas Hansen, Ph.D.*

**SUMMARY:**

**Objective:** This multi-national study assessed the efficacy and tolerability of Lu AA21004 5mg/day in elderly patients with recurrent major depressive disorder (M.D.D). Lu AA21004 is a multimodal antidepressant that is thought to work through a combination of two pharmacological modes of action: reuptake inhibition and receptor activity. In vitro studies indicate that Lu AA21004 is a 5-HT<sub>3</sub> and 5-HT<sub>7</sub> receptor antagonist, 5-HT<sub>1B</sub> receptor partial agonist, 5-HT<sub>1A</sub> receptor agonist and inhibitor of the 5-HT transporter. In vivo nonclinical studies have demonstrated that Lu AA21004 enhances levels of the neurotransmitters serotonin, noradrenaline, dopamine, acetylcholine and histamine in specific areas of the brain. [1,2]. **Methods:** A total of 452 patients aged 65 years or older with a primary diagnosis of M.D.D (according to DSM-IV criteria), a current major depressive episode (M.D.E) of at least 4-week duration, at least one previous M.D.E before the age of 60 years, and a MADRS total score of 26 or more, were randomly assigned (1:1:1) to Lu AA21004 5mg/day, duloxetine 60mg/day (active reference), or placebo for 8 weeks in a double-blind study. The primary efficacy measure was the mean change from baseline in the 24-item Hamilton Depression Rating Scale (HAM-D24) total score using a hierarchical testing procedure. Cognitive performance was assessed using the DSST and RAVLT. **Results:** Patients had a mean age of 70.6 years (range=64-88), a mean baseline MADRS score of 30.5 and a mean baseline HAM-D24 score of 29.0. Lu AA21004 showed a significantly (p=0.0011) greater improvement on the primary efficacy endpoint versus placebo at Week 8 (mean difference to placebo of 3.3

HAM-D24 points). Duloxetine also showed superiority to placebo at Week 8 (mean difference to placebo of 5.5 HAM-D24 points). HAM-D24 response (53.2% versus 35.2%) and HAM-D17 remission (29.2% versus 19.3%) rates at endpoint were higher for Lu AA21004 than for placebo. Lu AA21004 showed superiority to placebo in cognition tests of speed of processing, verbal learning and memory. Withdrawals rates were 1.3% (Lu AA21004) and 4.8% (placebo) due to lack of efficacy, and 5.8% (Lu AA21004) and 2.8% (placebo) due to adverse events. Nausea was the only adverse event with a significantly higher incidence with Lu AA21004 (21.8%) versus placebo (8.3%). For duloxetine, discontinuation due to adverse events was 9.9%, and adverse events with significantly higher incidence than seen with placebo were: nausea (33.1%), constipation (13.9%), dry mouth (21.9%), hyperhidrosis (10.6%) and somnolence (10.6%). Conclusions: Lu AA21004 was efficacious and well tolerated in the treatment of elderly patients with recurrent major depressive disorder. Trial Registration: This study has the ClinicalTrials.gov identifier: NCT00839423 [1] Bang-Andersen B, Ruhland T, Jørgensen M, et al. *J Med Chem* 2011;54,3206-3221. [2] Mørk A, Montezinho LC, Hovelsø N, et al. *Eur Neuropsychopharmacol* 2011;21 (Suppl 3):S407-S408.

**NR8-43****THE ASSOCIATION BETWEEN CHILDHOOD ADVERSITY AND SUBCOMPONENTS OF METABOLIC SYNDROME IN ADULTS WITH MOOD DISORDERS**

*Chair: Danielle Cha None Author(s): McIntyre, Roger S., M.D., FRCPC Soczynska, Joanna Liaww, Samantha Wöldeyohannes, Hanna O. Brietzke, Elisa, M.D., FRCPC Nathanson, Jay Alsuwaidan, Mohammed, M.D., FRCPC Muzina, David J, M.D., FRCPC Kennedy, Sidney H, M.D., FRCPC*

**SUMMARY:**

**Objective:** We sought to determine whether a reported history of childhood adversity moderates the association between mood disorders and the National Cholesterol Education Program Adult Treatment Panel III (NCEP-ATP-III)-defined metabolic syndrome and its definitional components. **Method:** This was a post-hoc, cross-sectional analysis of adult outpatients (N=373; N=230 female, N=143 male; mean age [SD] = 42.9 [14.4]) from the International Mood Disorders Collaborative Project (University of Toronto and Cleveland Clinic) with DSM-IV-defined major depressive disorder and bipolar I/II disorder. Childhood adversity was measured with the Klein Trauma & Abuse-Neglect self-report scale (i.e., physical and sexual

abuse, parental loss and neglect under the age of 15). Logistic regression adjusted for age, sex and smoking was used to evaluate the association between childhood adversity and metabolic syndrome. **Results:** For the full sample, eighty-three subjects (22.3%) met criteria for NCEP-ATP-III-defined metabolic syndrome with no statistically significant between-group differences in overall rate. Individuals reporting a history of childhood adversity had higher systolic and diastolic blood pressure (systolic:  $p=0.039$ , diastolic:  $p=0.038$ ) and higher BMI ( $p=0.021$ ). There were no significant between-group differences in waist circumference, triglyceride, or HDL levels. Age at initial trauma, duration and severity were also not significantly correlated with metabolic syndrome or its definitional components. When evaluating the diagnostic groups separately, individuals with major depressive disorder reporting childhood sexual abuse were more likely to meet the waist circumference criterion while individuals with bipolar disorder reporting childhood physical abuse were more likely to meet the increased systolic blood pressure criterion. No association between major depressive disorder and bipolar disorder and other metabolic syndrome components were identified when adjusting for the effect of trauma. **Conclusion:** The results herein provide preliminary evidence suggesting that childhood adversity may moderate the association between mood disorders and components of the metabolic syndrome.

**NR8-44****ESCITALOPRAM FOR CHRONIC TENSION-TYPE HEADACHE IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER**

*Chair: Hyun Kim M.D.; Author(s): Kang Joon Lee, M.D., Ph.D.*

**SUMMARY:**

**Purpose of the study:** A wide variety of antidepressants have been used to treat tension headache in patients with major depressive episode. Tricyclic antidepressants (TCAs) are the only antidepressants that have demonstrated their effectiveness in treating chronic tension-type headache, amitriptyline being the drug of choice. However, the most frequently prescribed antidepressant group, selective serotonin reuptake inhibitors (SSRIs) and other families of antidepressants have not shown conclusive results up to date. Alterations in serotonergic neurotransmitter system have been implicated in the pathophysiology of major depressive disorder and chronic pain. So escitalopram, acting on serotonergic neurotransmitter system, can be effectively used in headache management in major depressive disorder. Although major depressive disorder and

headache are strongly associated, still there are few sufficient evidences. The purpose of this study was to investigate efficacy and tolerability of escitalopram treating tension-type headache in major depressive disorder patients. Methods used 52 patients diagnosed with major depressive disorder according to the Diagnostic and Statistical manual version IV (DSM-IV) diagnostic criteria, complaining of tension-type headache were included in this study. Exclusion criteria included recent head trauma history, severe cognitive impairment, substance abuse or dependence, bipolar or schizoaffective disorder, suicidal behavior, and other severe mental or medical illness. The dose was adjusted when required. The dose range was 10-20 mg/day. Visual analog scale for headache, Hamilton Depression Rating Scale (HDRS), Montgomery-Asberg Depression Rating Scale (MADRS), and Beck Depression Inventory (BDI) were administered at baseline and repeated after eight weeks of escitalopram trial. Summary of Results 52 patients had fulfilled this clinical trials. 31 patients were female and 21 subjects were male. Their mean age ( $\pm$  SD) of this group was  $40.35 \pm 12.45$ . Mean duration of their current depressive episode ( $\pm$  SD) at baseline was  $1.33 \pm 1.06$  months. After 8 weeks of trial, 39 patients (75.0%) reported that their daily headache was absent or improved and 30 patients (57.6%) remained free of analgesics. All patients who reported improvement in headache, also showed improvement in depressive symptoms. 8 patients (15.3%) reported no improvement in headache. However, half of them showed some improvement in mood states, both subjectively and objectively. The remaining 4 patients (7.6%) showed worsening of headaches and all of them showed no improvement in depressive symptoms. Conclusions These data suggest that escitalopram may be effective in reducing tension-type headache in patients with major depressive disorder.

#### NR8-45

#### GENDER DIFFERENCES IN BIPOLAR DISORDER: RETROSPECTIVE DATA ON ILLNESS SEVERITY AND TREATMENT STRATEGIES OF PATIENTS DIAGNOSED WITH A MANIC/MIXED EPISO

*Chair: Francisco Linares M.D.; Author(s): Barney Vaughan, M.D., Stephanie Stolberg, M.D., Igor Galynker, M.D., Ph.D., Lisa Cohen, Ph.D.*

#### SUMMARY:

**Objective:** To examine gender differences in episode severity and treatment strategies in a sample of patients with bipolar disorder, manic/mixed episode. **Introduction:** Previous research has demonstrated the

existence of gender differences in the presentation and course of bipolar disorder. The onset of the illness tends to occur later in women and they also experience higher rates of lifetime depressive/mixed episodes, rapid cycling and Bipolar II Disorder. Few studies, however, have attempted to examine the gender differences in symptom severity and treatment strategies, particularly on inpatient units. The goal of the present project was to fill this gap in knowledge using a retrospective chart review. **Method:** We conducted a retrospective chart review of a sample of patients discharged between 2005 and 2010 from an inpatient psychiatric hospital with a diagnosis of bipolar disorder, manic or mixed episode. Illness severity was measured with 2 clinical scales: the Clinician Administered Rating Scale for Mania (CARS-M) and the Clinical Global Severity and Improvement Scales (CGS and CGI). Charts were rated by 3 raters. Least difference criteria were used to achieve a consensus score for each item on the two scales. Data on sleep quantity (hours of sleep/night) were collected from nursing reports. In addition to illness severity, information on other clinical markers (e.g. prn requirements; seclusion and restraint requirement; medications prescribed) as well as demographic data was obtained. **Results:** Interim analysis of the ongoing study included thirty-four charts (16 males, 18 females). Charts were compared across gender groups on the CARS-M total, manic and psychotic symptom sub scores at day 1 and day of discharge; use of seclusion or restraints; and change in hours of sleep from day 1 to day of discharge by t-tests and Chi-square analyses. Males showed higher baseline mania scores and trended towards greater numbers of seclusion and restraints episodes. **Conclusions:** Retrospective chart review of a small sample of patients with bipolar mood disorder in an acute psychiatric unit showed gender differences in illness acuity at admission and in seclusion and restraints. Gender differences in illness severity and treatment strategies in bipolar mood disorder deserve further study.

#### NR8-46

#### INCORRECT DIAGNOSIS AND INEFFECTIVE TREATMENT OF ATTENTION DEFICIT HYPERACTIVITY (ADHD) MAY DECREASE CHILDREN'S IQ, THE EFFICACY OF QEEG AND NEUROFEED

*Chair: Tanju Surmeli M.D.; Author(s): Thomas Brod*

#### SUMMARY:

**Introduction:** Although stimulant medication has been proven as the most efficacious strategy in the treatment of ADHD some studies support the effect of stimulant

medication on academic achievement and some do not. There is a considerable need for effective treatment alternatives to help the sizeable number of children who do not respond to medication, suffer from intolerable side effects or whose parents are reluctant to administer stimulant medication to their children. One problem might be the incorrect diagnosis of ADHD using subjective measures and other might be the inefficacy of the treatment. If the problem is not addressed properly it may cause a decline in IQ scores as was seen in our population. We noticed that children in our study had their first IQ tests higher with the average of 15 points before coming to us than the baseline tests performed in our center. Method: The age range of 21 subjects was between 7 to 16 years-old with an IQ score of >80 were recruited from the outpatient service of the psychiatric clinic. All were previously diagnosed as ADHD before coming to the center. Measures: WISC-R, Attention Deficit Disorder Evaluation Scale, Learning Disability Evaluation Scale, TOVA, QEEG, Sleep EEG, Neurometric analysis. The objective of this study was to assess the children with attention and learning problems if they have ADHD, Learning Disorders (LD) or some other disorder such as Post Concussive Syndrome (PCS), epilepsy, or non-seizure epileptic activities with the use of quantitative EEG (qEEG) and Neurofeedback (NF) was chosen as a treatment modality since there is evidence that neurofeedback has shown to be effective in ADHD, LD, Epilepsy, and PCS and because parents decided on having a non-medication alternative. Results: 17 IQ point on Verbal, 14 IQ point on Performance and 15 point on Total IQ improvements were seen on WISC-R test scores after Neurofeedback Treatment. The improvement might indicate that long-lasting operant (voluntary) regulation of brain function can restore or even block some of the deterioration of brain plasticity in patients with treatment resistant ADHD or LDs or non seizure epileptic activities or PCS. Controlled study is warranted. Key words: ADHD, QEEG, Neurofeedback

*Ph.D.; Yue-Cune Chang, Ph.D.; Guochuan E. Tsai, M.D., Ph.D.; Hsien-Yuan Lane, M.D., Ph.D.*

#### SUMMARY:

The current study investigates whether social cognition varies with genetic variations of COMT and TPH2 which are related to two neurotransmissions thought to be involved in emotional regulation, dopamine and serotonin respectively, in healthy participants. Social cognition has been found to be affected by genetic variance in patients with schizophrenia. However, whether gene plays a role in social cognition in healthy participants is still unknown. To assess social cognition, the "Managing Emotions" branch of Mayer-Salovey-Caruso Emotional Intelligence Test (MSCEIT) was measured in one hundred and fifty Han Chinese healthy adults. Genetic polymorphisms of COMT Val158Met and TPH2 G703T were determined. Neurocognitive functions were also assessed. Subjects carrying the M allele (Met/Met and Met/Val) of COMT had better performance than carrying the V allele (Val/Val) in managing emotion branch ( $p = 0.032$ ) and emotional relation subtask ( $p = 0.037$ ). Subjects carrying the T group (T/T) of TPH2 performed better than carrying the G group (G/G, G/T) in emotional management subtask ( $p = 0.025$ ). COMT and TPH2 were further combined into four groups, M+T, M+G, V+T and V+G, for testing interaction of the two genes. Multiple linear regression showed that the subjects carrying M+T alleles had better performance than the other groups in managing emotion branch ( $p < 0.002$ ), emotional relation subtask ( $p = 0.023$ ) and emotional management subtask ( $p = 0.002$ ), even when neurocognitive functions is controlled. Furthermore, the effect sizes of the combined COMT-TPH2 genotype groups were larger than the sum of the effect sizes of COMT and TPH2 individually, suggesting a synergistic effect. The findings suggest that genetic variations of COMT and TPH2 have synergistic effects on social cognition in people without mental illness.

**TUESDAY MAY 08, 2012**

New Research Poster Session 9

**BIOLOGICAL PSYCHIATRY, NEUROSCIENCE, GENETICS AND OTHER**

#### NR9-01

**GENETIC VARIATIONS AND SYNERGISTIC EFFECTS OF COMT AND TPH2 ON SOCIAL COGNITION IN HEALTHY INDIVIDUALS**

*Chair: Chieh-Hsin Lin M.D.; Author(s): Kuo-Hao Huang,*

#### NR9-02

**GENETIC VARIABILITY AT IMPA-2, INPP-1 AND GSK-3B INCREASES THE RISK OF SUICIDAL BEHAVIOUR IN BIPOLAR PATIENTS**

*Chair: Ester Jimenez Other Author(s): Bárbara Arias, Ph.D.; Marina Mitjans, MSc; Jose M. Goikolea, M.D.; Pilar A. Sáiz, Ph.D.; M. Paz García-Portilla, Ph.D.; Julio Bobes, Ph.D.; Eduard Vieta, Ph.D. and Antoni Benabarre, Ph.D.*

#### SUMMARY:

Introduction: Suicidality rates in bipolar patients (BP)

are the highest among other psychiatric illnesses, including unipolar depression. Lithium, one of the most widely used treatments for the acute and long-term management of bipolar disorder, has also been suggested to present antisuicidal properties. However, molecular mechanisms underlying lithium's therapeutic action are still unclear, although there is increasing evidence supporting the involvement of both the Wnt/ $\beta$ -catenine pathway and the phosphoinositide second messenger system. Our aim was to investigate the association of the IMPA1, IMPA2, INPP1, GSK3 $\alpha$  and GSK3 $\beta$  genes with suicidal behaviour (SB) in BP. Considering that SB, as well as bipolar condition and response to lithium in bipolar patients, presents a strong genetic predisposition, we hypothesized that genetic variation of genes implicated in the above mentioned pathways would lead to an increased liability to SB in this group of patients. Methods: Our sample consisted of 199 unrelated Caucasian bipolar outpatients who were recruited from the Bipolar Disorder Unit of the Hospital Clinic of Barcelona and from primary care settings from Oviedo. Inclusion criteria were (a) bipolar I/II diagnosis and (b) age > 18 years. Exclusion criteria were the presence of (a) mental retardation and (b) severe organic disease. Genomic DNA was extracted from blood samples from each participant, according to standard protocols. Several polymorphisms at the IMPA1, IMPA2, INPP1, GSK3 $\alpha$  and GSK3 $\beta$  genes were genotyped. All patients were grouped and compared according to the presence or the lack of presence of history of SB. Categorical variables were compared using Chi-square or Fisher exact tests, as appropriate. Analyses were performed using PASW v18.0 and EpiInfo. All procedures were approved by the research ethics committees in each institution. Results: Our results showed that BP carrying T allele of the rs1732170-GSK3 $\beta$  gene (OR= 2.05; IC95% [1.02-4.16];  $\chi^2= 7.7$ ;  $p=0.029$ ) and A carriers of the rs11921360-GSK3 $\beta$  gene (OR= 3.2; IC95% [1.03-13.49];  $\chi^2= 4.7$ ;  $p=0.02$ ) presented a higher risk for attempting suicide. Moreover, significant associations were found when we compared allele frequencies distributions according to the presence of history of SB. Those BP who have attempted suicide at least once in their life presented significant higher frequencies of A allele of the rs669838-IMPA2 (OR= 2.92; IC95% [1.20-7.15];  $\chi^2= 7.015$ ;  $p=0.008$ ) and G allele of the rs4853694-INPP1 gene (OR= 3.69; IC95% [1.05-14.56];  $\chi^2=5.66$ ;  $p=0.02$ ) compared to nonattempters BP. Conclusions: Our results suggest that genetic variability at IMPA2, INPP1 and GSK3 $\beta$  genes is associated with the emergence of SB in BP. Hence, these findings would reinforce those studies that have suggested the potentially significant role of genetic variability at the Wnt / $\beta$ -catenine pathway and the phosphoinositide

second messenger system in both suicide and/or bipolar disorder.

**NR9-03**  
**OPERANT CONDITIONING OF**  
**FRONTAL-LIMBIC PATHWAYS IN RODENTS:**  
**FIRST STEPS TOWARDS A CLOSED-LOOP**  
**PSYCHIATRIC NEURAL PROSTHESIS**

*Chair: Alik Widge M.D.; Author(s): Chet Moritz, Ph.D.*

**SUMMARY:**

Increasing evidence suggests that a core feature of mental illnesses, particularly mood and anxiety disorders, is an insufficiency of descending regulatory control from frontal/prefrontal cortex over limbic brain structures. New neuromodulation therapies, especially deep brain stimulation, offer a way of altering limbic tone and thus relieving symptoms. However, these therapies operate in an "open loop" mode, where subcortical circuit tone is altered but the dysfunctional regulatory pathways remain in their diseased state. As a result, when stimulation ends or stimulator batteries fail, symptoms recur. Furthermore, the stimulation is continuously applied at constant pre-programmed parameters, which does not match the high intraday symptom variability seen in anxiety disorders. We therefore propose a new stimulation paradigm in which neuromodulation of midbrain/hindbrain structures involved in emotion is triggered on an as-needed basis by neural activity recorded from frontal cortex. In addition to matching stimulation to a patient's needs (thus extending battery life and perhaps reducing the burden of stimulator side effects), this model would help address ethical concerns surrounding psychiatric neuromodulation by placing control of stimulus delivery back into the patient's hands. This study represents the first steps towards constructing a proof-of-concept neuromodulation platform suitable for testing this hypothesis in animal models of psychiatric illness. Adult female rats were simultaneously implanted with recording electrodes targeting multiple areas of frontal cortex and stimulating electrodes targeting the medial forebrain bundle (MFB), a dopaminergic site where stimulation is associated with a strongly positive emotional/hedonic experience. The implanted animals were then offered an operant conditioning paradigm in which modulation of their cortical activity could trigger MFB stimulation at a level known to be reinforcing. We present here the first results from those conditioning experiments, along with suggestions for refining the paradigm and extending it into rodent behavioral models of mental illness.

**NR9-04**

### D-CYCLOSERINE IMPROVES SOCIABILITY AND SPONTANEOUS STEREOTYPIC BEHAVIORS IN 4-WEEK OLD MICE

*Chair: Stephen Deutsch M.D.; Author(s): Gerald J. Pepe, Ph.D., Jessica A. Burket, B.S., Erin E. Winebarger, B.A., Amy L. Herndon, B.S., Andrew D. Benson, B.S.*

#### SUMMARY:

Balb/c mice are a model of impaired sociability and social motivation relevant to autism spectrum disorders (ASDs). Impaired sociability of 8-week old Balb/c mice is attenuated by agonists of the glycineB site on the NM.D.A receptor, such as D-cycloserine. Although ASDs are often recognized in toddlerhood, there is interest in earlier identification (e.g., before 6 months) and disease-modifying interventions to improve functional outcomes. Thus, we wondered if D-cycloserine could improve sociability in 4-week old Balb/c mice, similar to its effects in 8-week old mice. D-Cycloserine improved measures of impaired sociability in 4-week old (i.e., one-week post-weanling) Balb/c mice. Moreover, because stereotypies can compete with the salience of social stimuli, we compared Balb/c and Swiss Webster mice on several spontaneous stereotypic behaviors emerging during social interaction with a social stimulus mouse. Interestingly, similar to 8-week old mice, spontaneous stereotypic behaviors during social interaction were more intense in the 4-week old Swiss Webster mice; furthermore, D-cycloserine reduced their intensity. Thus, D-cycloserine improves both sociability and stereotypic behaviors, but these effects may lack strain-selectivity. D-Cycloserine has the therapeutic properties of a desired medication for ASDs; specifically, a medication should not improve stereotypic behaviors at the expense of worsening sociability and vice versa. The data suggest that targeting the NM.D.A receptor can have promising therapeutic effects on two prominent domains of psychopathology in ASDs: impaired sociability and spontaneous stereotypic behaviors.

#### NR9-05

### LITHIUM-RESPONSE IN BIPOLAR DISORDER IS ASSOCIATED WITH GENETIC VARIABILITY AT IMPA2 AND INPP1 GENES

*Chair: Ester Jimenez Other Author(s): Bárbara Arias, Ph.D.; Marina Mitjans, MSc; Jose M. Goikolea, M.D.; Pilar A. Sáiz, Ph.D.; M. Paz García-Portilla, Ph.D.; Julio Bobes, Ph.D.; Eduard Vieta, Ph.D. and Antoni Benabarre, Ph.D.*

#### SUMMARY:

Introduction: Since the introduction of lithium in

psychiatry, it still considered as a first-line treatment in bipolar patients (BP) given its proven efficacy in both acute and maintenance phases. However, response to lithium is variable ranging from an excellent response in 24-45%, to a complete lack of response in 10-30% of patients. Bearing in mind that there is a growing consensus considering that good response to lithium is heritable and constitutes a differential phenotype, the search of a hypothetical genetic profile which could guide in mood stabilizer choice is a matter of concern. Despite molecular basis underlying lithium's therapeutic mechanism of action are still unclear, nowadays evidence supports that lithium inhibits enzymes associated to the inositol pathway. In this sense, our goal was to investigate the potential association of genetic variability at IMPA1, IMPA2 and INPP1 genes with response to lithium in BP. Methods: For this investigation 110 unrelated Caucasian bipolar outpatients were studied. All patients were recruited from the Bipolar Disorder Unit of the Hospital Clinic of Barcelona and from primary care settings from Oviedo. Inclusion criteria were (a) bipolar I/II diagnosis and (b) age>18 years. Exclusion criteria were the presence of (a) mental retardation and (b) severe organic disease. Genomic DNA was extracted from blood samples from each participant, according to standard protocols. Several polymorphisms at the IMPA1, IMPA2 and INPP1 genes were genotyped. All patients were grouped and compared according to their level of response to lithium. Patients were classified as excellent responders, partial responders and non-responders. For statistical purposes, excellent and partial responders were grouped. Patients showing no tolerability to lithium were not considered. Categorical variables were compared using Chi-square or Fisher exact tests, as appropriate. Analyses were performed using PASW v18.0 and EpiInfo. All procedures were approved by the research ethics committees in each institution. Results: Our results showed that those BP who were categorized as poor responders presented higher rates of GG genotype of the rs630110-IMPA2 gene (OR=2.9; 95% CI[1.05-8.19]; $\chi^2=4.9$ ; p=0.023). We also found that poor responders were more likely to present GG genotype of the rs909270-INPP1 gene (OR=3.19; 95% CI[1.08-9.52]; $\chi^2=5.66$ ; p=0.04) when compared to good responders to lithium. No association was found between any of the analyzed IMPA1 polymorphisms and response to lithium in our sample. Conclusions: Our findings suggest that lithium-responsive bipolar disorder's phenotype seems to be associated with genetic variability at IMPA2 and INPP1 genes. Therefore, these results not only would strengthen those studies that have suggested the potentially significant role of genetic variability at the inositol pathway in lithium prophylactic efficacy but

also reinforce its involvement in the pathophysiology of bipolar disorder.

**NR9-06**  
**INDICATORS OF NEURODEVELOPMENTAL, NEUROCOGNITIVE, NEUROMOTOR ABNORMALITIES AND STRESS SENSITIVITY RESPONSE IN SCHIZOPHRENIC OFFSPRING**

*Chair: Adel Elsbeshai M.D.; Author(s): George Simpson M.D., Adel Mostafa M.D., Maged Mikhail M.D., Maha El Tayebani M.D.*

**SUMMARY:**

During the past 50 years most models of etiology of schizophrenia have been guided by the diathesis-stress theory, which assumes that the interaction of congenital liabilities with postnatal factors leads to the expression of schizophrenia. Morphometric and cytoarchitectural abnormalities in various regions of the brain of schizophrenics implicate a developmental origin of the putative insult in schizophrenia. These, and reports of abnormal psychological development in preschizophrenic children add further support to the theory that schizophrenia has a neurodevelopmental origin. The aim of this work is to study the following: 1. Neuromotor abnormalities in children of schizophrenic patients through: a) Neuromotor rating scale. b) Minor physical abnormalities by Waldrop scale. c) Dermatoglyphic abnormalities. 2. Neurocognitive assessment by: a) Bender Visual Motor Gestalt test to assess perceptual motor maturation. b) Wechsler intelligence scale for children to assess mental encoding, immediate recall with ordering ability. 3. Stress response of children of schizophrenic parents assessed by estimating the cortisol in salivary sample. The study was done on 60 apparently healthy schizophrenic offspring (31 male and 29 female) from 50 schizophrenic families and on 21 apparently healthy children (12 male and 9 female) of 17 healthy families as a control group (with no psychiatric, neurological or chronic medical diseases). The study showed that: Schizophrenic offspring had significantly larger sum of atd angles of both hands than that of control group. Common finger-print pattern was studied for each finger separately, this revealed predominant ulnar loop pattern of both the right and left thumb of schizophrenic offspring, while whorls pattern were common of control children. Little finger showed opposite results. Schizophrenic offspring had more physical anomalies and less mean total IQ than controls. bender visual motor gestalt test was performed significantly worse by schizophrenic offspring. They also showed more neuromotor abnormalities than control. The overall mean salivary cortisol level was higher in

schizophrenic offspring.

**NR9-07**  
**ELECTROCONVULSIVE THERAPY-INDUCED LATE-APPEARING SEIZURE IN A PSYCHOTIC PATIENT WITH EPILEPSY**

*Chair: Hsinte Huang M.D.; Author(s): Wen-Kuei Lee M.D.*

**SUMMARY:**

Background: Late-appearing seizure, an additional seizures appearing after the electroconvulsive therapy (ECT), is a rare side effect of ECT. In our unique psychotic case with epilepsy, the ECT associated tardive seizure was noted and terminated by the injection of midazolam successfully. Case Report: A 41-year-old male diagnosed psychosis with epilepsy has been ever admitted our hospital 8 times since 1984. The psychotic symptoms and epilepsy were under well control with anticonvulsants and antipsychotics before first six admissions. During his 7th admission in 2002, there was little improvement despite of intensive treatment under clozapine 200 mg/day, phenytoin 900 mg/day and valproic acid 1500 mg/day. ECT was indicated after discussion with his family members. We tapered his anticonvulsants before ECT in compliance to the APA guideline, but recurrent seizure attacks made us decide to use anticonvulsants again. Our patient discharged after the full course of ECT despite of poorer seizure adequacy during each ECT. ECT with anticonvulsants was indicated in the 8th hospitalization. The pre-ECT general check-ups revealed unremarkable, and the first 3 ECTs were smoothly performed. Yet an additional seizures developed several hours after the 4th ECT, and were immediately terminated by the midazolam 2 mg intravenously. Then the ictal electroencephalogram (EEG) activities were terminated. Plus, ECT was discontinued and shift back on antipsychotic and anticonvulsants after discussion with neurologist. There was no significant abnormality on cognitive function and neurologic examination. Currently he regularly follows up under stable condition. in our outpatient clinic. Discussions: Late-appearing seizure may occur in case with preexisting seizure disorders. Rarely ECT precipitates the development of an epileptic disorder, and the rate of occurrence is extremely low. ECT was known has anti-kindling effect and increases the numbers of GABA receptors and increase seizure threshold like anticonvulsants. Though the exact mechanisms underlying ECT- induced late-appearing seizure seen in our case remain unclear, some studies suggest that ECT might increase permeability of BBB (blood-brain barrier) and cause instability of cell membrane. Further studies are warranted to clarify this

issue. Short-acting benzodiazepines can be pre-prepared in case that late-appearing seizure occurs.

**NR9-08****EFFECT OF ARIPIRAZOLE COMPARED WITH CAFFEINE ON PREATTENTIVE PROCESSING AS REFLECTED BY MISMATCH NEGATIVITY (MMN)**

*Chair: Youn Tak M.D.*

**SUMMARY:**

The effect of caffeine is on various cognitive and behavioral process such as attention, vigilance, arousal and information processing is well known, but electrophysiological property of caffeine effect in normal subjects is not studied well. Methods: we investigated the acute effect of multiple dosage of caffeine (0mg, 100mg, 200mg) on the mismatch negativity (MMN) event-related brain potential (ERP) using an equivalent current dipole (ECD) model of auditory MMN with high-density electroencephalography (EEG) in a double-blind randomized, placebo-controlled repeated measures design. The MMNs resulting from auditory stimuli with passive oddball paradigm in 21 normal subjects, were recorded by 64 channel EEG. The location and power of ECD sources at the peak point were calculated. Korean standard 3D brain magnetic resonance images (MRI) were used for realistic head modeling and for source localization. ERP is analysed by SCAN and Curry programs. Result: Caffeine enhance MMN amplitude and reaction time in a dose response manner. The findings are discussed in relation to attentional and neurobiological aspect of caffeine and of cognition in general.

**NR9-09****ONE YEAR HIGH REMISSION RATE WITH VAGUS NERVE STIMULATION FOR TREATMENT RESISTANT-DEPRESSION**

*Chair: Elise LaGarde R.N.; Author(s): Véronique Desbeaumes, B.Sc; Marie-Pierre Fournier-Gosselin, M.D.; Alain Bouthillier, M.D.; Simon Patry, M.D.; Valérie Tourjman, M.D., M.Sc and Paul Lespérance, M.D., M.Sc*

**SUMMARY:**

Objective: Since 2001, Vagus Nerve Stimulation (VNS) is used in treatment-resistant depression (TRD) in Europe and Canada and more recently in the USA. The European and American studies have shown a 50% response rate and 30% remission rate respectively after one year. Patients selection, driven both through biological correlates and resistance

criteria, might be the key to reach higher response and remission rates. Method: First, a review of the patient medical physical and mental health history is made in combination with the pharmacological, psychological and electroconvulsivotherapy history of treatment. A systematic psychiatric evaluation, including the Mini International Neuropsychiatric Interview details the current depressive episode, past episodes and co-morbidity. Borderline personality disorder is evaluated using the diagnostic interview for borderline revised questionnaire. A general consensus has to be reached to pursue with the clinical investigation in search of biological factors. These include a SPECT and a PET scan (dorsolateral-prefrontal cortex and cingulate cortex); an MRI for structural abnormalities; blood work (basic and inflammatory investigation); a dexamethasone suppression test (DST); a 24h urine collection (cortisol, catecholamine); a polysomnography; and a basic neuropsychological evaluation (executive functions and memory). If a doubt raises about the existence an «axe II resistance profile», we will treat the patient with VNS if at least one of the biological correlates is positive. However, the patient with a Cluster B personality will be excluded. Implanted patients will have various symptoms scales including the Hamilton Depression Rating Scale (HDRS 28-items) and 3 other scales to target depression, anxiety and mania, 3 self-reported scales; and memory and executive testing at 0,1,3,6,12 months and, yearly. Results: Since 2008, 16 patients have been implanted with VNS. 12 patients are now at 12 months of treatment. 58% of our patients responded to treatment, with a reduction of at least 50% of HDRS-28 score. 50% have reached remission rate (score <10 at HDRS-28) at one year. Of those, all are still in remission at the 24 months mark. Our clinical investigation enabled us to exclude patients of VNS treatment with findings such as hydrocephalus, severe sleep apneas, borderline personality disorders and inflammatory disease. The stability of the remission and the cognitive improvement is remarkable.

**NR9-10****RESIDUAL COGNITIVE IMPAIRMENT IN EUTHYMIC PATIENTS WITH BIPOLAR DISORDER: A STUDY WITH FUNCTIONAL MAGNETIC RESONANCE IMAGING (FMRI)**

*Chair: M. Carlotta Palazzo M.D.; Author(s): Bernardo Dell'Osso, M.D., Marta Cristoffanini, Psy.D., Cristina Dobra, M.D., Claudia Cinnante, M.D., Sabrina Avignone, M.D., Clara Sina, M.D., Laura Cremaschi, M.D., Beatrice Penzo, M.D., Alessandro Sillani M.D., Fabio M. Triulzi, M.D., A. Carlo Altamura, M.D.*

**SUMMARY:**

**Introduction.** Bipolar Disorder (BD) is a chronic mood disorder with a prevalence estimated around 1-2%. Bipolar patients may experience social and working residual impairment even during euthymic state. Furthermore, specific cognitive deficits, particularly involving working memory (WM), may persist during euthymia. The aim of the present study was to evaluate the possible presence of cognitive and functional differences between euthymic bipolar subjects and healthy controls by means of a WM task during functional Magnetic Resonance Imaging (fMRI) associated with neuropsychological evaluations. **Methods.** A sample of 39 subjects aged between 20 and 57 years (22 patients with BD and 17 healthy controls) underwent a 3 Tesla fMRI examination performing a task of WM (n-back: 0-back; 2-back and 3-back). All participants received a neuropsychological evaluation, including Stroop Color-Word Interference test, Tower of London, Trail Making test (TMT-A/B), Wisconsin Card Sorting Test (WCST) and Verbal Fluency Test. Comparison tests were performed using statistical software SPSS and SPM5. **Results.** The performance of the control group was significantly higher than BD patients, both at the 2-back and 3-back task ( $F=33.54$ ;  $p<0.00$ ) and at some neuropsychological tests (WCST  $F=6.469$ ,  $p>0.015$ ; TMT-B  $F=8.523$ ;  $p<0.006$ ). The full-factorial analysis of fMRI data showed at 0-back task that the visual cortex (Brodmann 19) was hyperactivated in BD subjects compared to controls ( $p<0.03$ ; cluster size=100). At 2-back task the somatosensitive associative cortex was more activated in controls vs BD ( $p<0.03$ ; cluster size=100), while prefrontal cortex and anterior cingulate cortex as well as caudate nuclei were more activated in BD patients ( $p<0.01$ ; cluster size=50). Considering 3-back task, the same cerebral areas involved in the 2-back task were more activated in BD patients ( $p<0.01$ ; cluster size=100). Controls, during 3-back task, hyperactivated some thalamic areas compared to BD patients ( $p<0.03$ ; cluster size=100). **Conclusions.** The results seem to confirm the existence of a residual dysfunction during euthymia in BD patients, suggesting two distinct patterns of activation in the two groups studied, both from a neuropsychological point of view and from a neuroimaging perspective.

**NR9-11****MAGNETIC RESONANCE SPECTROSCOPY IN ADULTS WITH BORDERLINE PERSONALITY DISORDER**

*Chair: Alaa Houry B.S.; Author(s): Caroline Schimunek, B.A., Kathryn Cullen, M.D., S. Charles Schulz, M.D.*

**SUMMARY:**

**Introduction:** Borderline Personality Disorder (BPD) is a chronic illness that affects social and psychological functioning, and includes symptoms such as unstable relationships and emotions, low self-esteem, or temporary feelings of suspiciousness or paranoia. The anterior cingulate cortex (ACC) is an area of the prefrontal cortex that has been implicated in key borderline features such as cognitive and affective processes (1). The authors examined metabolites acquired through Proton Magnetic Resonance Spectroscopy (1H-MRS) in adults with BPD. **Methods:** Seven adult BPD participants have been enrolled in this study thus far. Participants completed several diagnostic measures to confirm a BPD diagnosis, including the Zanarini Rating Scale for Borderline Personality Disorder Interview (ZAN-BPD) and the Zanarini Rating Scale for Borderline Personality Disorder: Self-report Version (ZAN-BPD: SRV). Each participant completed Proton Magnetic Resonance Spectroscopy (1H-MRS) scans which were acquired using a 3.0 Tesla Siemens scanner. A 1.5 x 1.5 x 1.5 cm<sup>3</sup> voxel was positioned in the central anterior cingulate cortex. Pearson correlations were calculated between the Zanarini rating scales and metabolites. **Results:** Participants with BPD demonstrated a significant negative correlation ( $r=-.785$ ,  $P=.036$ ) between the ZAN-BPD: SRV ratings of suspicion and total (NAA+NAAG)/Cr (tNAA) levels. This finding was only significant on the ZAN-BPD: SRV. **Conclusions:** This preliminary finding suggests a connection between neurochemicals and clinical features in BPD. In addition, the ACC, as a central region within the fronto-limbic network, has been implicated in adults with BPD (2). Previous studies have reported abnormalities in the ACC in participants with BPD (1). There is a paucity of research on BPD brain spectroscopy. This study aims to expand on the existing BPD brain imaging research. Further analysis will be completed to include rating scales and 1H-MRS data from healthy comparison participants. In addition, water-based metabolite processing will be conducted to provide a more stable reference to the metabolites than the currently used creatine reference. 1 Yucel, M., Harrison, B.J., Wood, S.J., Fornito, A., Clarke, K., Wellard, R.M., Cotton, S., Pantelis, C., 2007. State, trait, and biochemical influences on human anterior cingulate function. *NeuroImage* 34, 1766-1773. 2 Lis, E., Geenfield, B., Henry, M., Guile, J. M., & Dougherty, G., 2007. Neuroimaging and genetics of borderline personality disorder: a review. *Journal of Psychiatry and Neuroscience* 32, 162-173.

**NR9-12****OBSESSIVE-COMPULSIVE DISORDER (OCD):**

## INCREASE OF WHITE MATTER TISSUE WITHIN THE LEFT EXTERNAL CAPSULE – A VOXEL-BASED MORPHOMETRIC MRI STUDY

*Chair: Thomas Sobanski M.D.; Author(s): Gerd Wagner, Ph.D.; Gregor Peikert, Ph.D.; Uwe Grubn, M.D.; Heinrich Sauer, M.D.; Ralf G. Schlösser, M.D.*

### SUMMARY:

Objective: Several morphometric magnetic resonance imaging (MRI) studies have revealed structural brain abnormalities in obsessive-compulsive disorder (OCD), e.g. increase or decrease of total white matter (WM) volume, increased left frontal lobe WM, and reduced WM volume in prefrontal and right parietal areas. With regards to gray matter (GM) a reduction in parieto-frontal cortical regions as well as an increase in the basal ganglia have been reported. Considering the inconsistency of prior results we performed an MRI study employing a most recent VBM method. The main focus of the study was to investigate WM alterations in patients with OCD. Methods: Fourteen patients with obsessive-compulsive disorder (OCD) and fourteen healthy control subjects (HC) matched for age and gender were enrolled in the study. One patient had to be excluded due to imperfect segmentation. All patients (9 women, 4 men) were treated in our psychotherapy ward. MRI volumes were analyzed with the VBM toolbox using the unified tissue segmentation approach as implemented in SPM8. Voxel-by-voxel one-way ANOVA was performed to test for differences between controls (HC) and patients with OCD regarding regional WM and GM volume. All statistical images were thresholded at voxel-level  $p < 0.001$  (uncorrected for multiple comparisons). Results: Total WM volume was increased in patients with OCD ( $p < 0.021$ ). Additionally, we observed a significant increase of WM tissue volume within the left external capsule (EC) ( $x = -21, y = 17, z = 11, \text{cluster size} = 225, p < 0.001$ ). With regard to total and regional GM volumes there were no significant differences between groups. None of the results was correlated to age of onset or duration of the disease. Conclusions: Earlier results of increased total WM volume in patients with OCD are confirmed by our study and extended by the new finding of increased WM volume in the EC. Thus, the observed abnormalities of WM tissue provide further evidence for a disorganization of anatomical connectivity in OCD. References: Atmaca M, Onalan E, Yildirim H, Yuce H, Koc M, Korkmaz S: The association of myelin oligodendrocyte glycoprotein gene and white matter volume in obsessive-compulsive disorder. *J Affect Disord* 2010; 124:309-313 Yoo SY, Jang JH, Shin YW, Kim DJ, Park HJ, Moon WJ, Chung EC, Lee JM, Kim

SI, Kwon JS: White matter abnormalities in drug-naïve patients with obsessive-compulsive disorder: a diffusion tensor study before and after citalopram treatment. *Acta Psychiatr Scand* 2007; 116:211-219

### NR9-13

## ENLARGED THALAMIC VOLUME FOUND IN CHILDREN BUT NOT ADULTS WITH AUTISM SPECTRUM DISORDER

*Chair: Ish Bballa B.S.; Author(s): Suzanne Gob, M.D., MBA; Andrew Gerber, M.D., Ph.D.; Ravi Bansal, Ph.D.; Bradley Peterson, M.D.*

### SUMMARY:

Objective: Sensorimotor abnormalities in persons with ASD warrant study of the thalamus in ASD. Recent anatomical MRI, functional MRI and MRS studies have implicated the thalamus in the pathogenesis of ASD. The objective of this study is to determine the effect of an ASD diagnosis on thalamic volume. Methods: 64 persons with ASD ages 4.2 to 53.5 years (44 children, 20 adults) and 59 healthy controls matched for age and sex underwent anatomical MRI scanning on a 3 Tesla GE scanner to acquire high-resolution, FSPGR sequences. On each MR image, the thalamus was delineated manually and we computed the volume for left and right hemi-thalami. An ANCOVA was run testing thalamic volume using diagnosis, TBV, age and sex as covariants. Results: The total thalamic volume in children with ASD was significantly larger than those for healthy children ( $p = .05$ ); however, the thalamic volume did not differ significantly in either the adults ( $p = .98$ ) or the entire cohort ( $p = .07$ ). Similar findings were obtained for each hemi-thalamus. Morphometric analyses before GFR correction revealed differences in the posterior lateral region of the left hemi-thalamus in the child cohort. Conclusions: Because sensory abnormalities are commonly present in individuals with ASD, the thalamus has long been thought to have a potential role in the pathogenesis of ASD. The increased thalamic volume in children with ASD further implicates the thalamus in the pathogenesis of ASD. Morphometric analysis revealed diffusely enlarged hemi-thalami after GFR correction. Analysis to further increase the sample size is currently underway. These analyses advance our understanding of ASD, thereby improving the future diagnosis and treatment of patients with ASD.

### NR9-14

## COMPARISON OF RISPERIDONE AND QUETIAPINE IN ALZHEIMER'S DISEASE PATIENTS WITH BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS

*Chair: Kang Joon Lee M.D.; Author(s): Hyun Kim, M.D., Ph.D.*

**SUMMARY:**

**Objective :** Patients with behavioral and psychological symptoms of dementia (BPSD) can impose a high burden on their carers, who may experience high levels of psychological distress as symptoms of BPSD develop. Atypical antipsychotics have been attracting increasing attention in the management of BPSD, as they have fewer neuroleptic side effects than conventional antipsychotics. In this study we compared the effects and tolerability of risperidone and quetiapine in Alzheimer's disease with behavioral and psychological symptoms.

**Methods :** We conducted an 8-week, randomised study of 70 Alzheimer's disease patients with BPSD. For inclusion in the study, patients had to be aged 55-85 years; have a diagnosis of dementia of Alzheimer's to DSM-IV; suffer from behavioral disturbances, and an MMSE total score of 10-26. The patients received risperidone (0.5-2mg/day) or quetiapine (50-300mg/day). Assessments were made at each study visit: Baseline, Week 4, and Week 8. Primary efficacy measure is Neuropsychiatry Inventory (NPI). Secondary efficacy measures are Mini-Mental State Examination (MMSE), Clinical Global Impression (CGI). Safety evaluations included the incidence of extrapyramidal symptoms (EPS) and adverse events (AEs). Neurological side effects were measured by the Simpson-Angus scale (SAS).

**Results :** A total of 72 patients were enrolled in this 8-week study. 7 patients discontinued (1 lost to follow-up ; 3 due to AEs). 65 patients received risperidone (n=34; mean dose 1.0 0.4mg/day) or quetiapine (n=31; mean dose 75 35mg/day). There was no significant difference between treatments on NPI scores; within treatment group, NPI scores decreased significantly from base to Week 8 (p<.05). In the NPI, scores decreased from 58.0 to 45.1 with risperidone and from 60.3 to 48.7 with quetiapine. Most patients (risperidone 75%, quetiapine 68%) experienced clinical improvement (CGI-Improvement score). There was no cognitive impairment (MMSE). There were no significant differences between treatments in any safety measures, including EPS. There were no cerebrovascular AEs or deaths.

**Conclusion :** Risperidone or quetiapine were equally effective and generally well tolerated in the treatment of BPSD in Alzheimer's disease patients.

**References** 1) Rainer M, Haushofer M, Pfolz H et al. Quetiapine treatment for behavioural and psychological symptoms of dementia in Alzheimer's disease patient: a 6-week, double-blind, placebo-controlled study. *European Psychiatry* 2007;22:395-403. 2) Street JS, Clark WS, Gannon KS et al. Olanzapine treatment of

psychotic and behavioral symptoms in patients with Alzheimer disease in nursing care facilities. *Arch Gen Psychiatry* 2000;57:968-976.

**NR9-15**

**IGF-1, CRP AND TNF-A ROLE IN POST-OPERATIVE DELIRIUM**

*Chair: Mehmet Alper Cinar M.D.; Author(s): K. Nabit Özmenler M.D., Mehmet AK M.D., Ali Bozkurt M.D.*

**SUMMARY:**

**OBJECTIVE:** Delirium is common and life-threatening neuropsychiatric syndrome. Diagnosing delirium can be challenging, which increase mortality and mortality rates also health care costs. Biologic model of delirium is not definite yet but evidence supports cholinergic deficiency model. Delirium may be the result of processes and drugs, which trans passing compromised blood-brain barrier. We aim to evaluate possible diagnostic utilization and the role of certain biomarkers as CRP, TNF-a and IGF-1 in delirium etiology.

**METHODS:** A total of 93 inpatients that planned to undergo cardiovascular surgery were informed to participate and 35 of them completed the study. Medical history and current cognitive status were evaluated pre-operatively. Mini Mental State Examination and Clock Drawing Test were performed to assess cognitive status. Blood samples were collected for cytokine analysis before and after cardiac surgery. Participants were assessed for delirium symptoms with Turkish version of DRS-R98.

**RESULTS:** Delirium was developed more in participants who had worse pre-operative cognitive status. MMSE scores of delirium group was  $25.6 \pm 2.87$  and non-delirium group was  $28.3 \pm 2.1$  (p=0.002). Also, low pre-operative IGF-1 levels were detected in delirium group (p=0.048). Pre-operative CRP and TNF-a levels were not found different between delirium and non-delirium groups.

**CONCLUSION:** Pre-operative IGF-1 screening may help to predict post-operative delirium. However, complex nature of cytokines and delirium itself makes it difficult to utilize cytokines to predict delirium. Preoperative IGF-1 levels may contribute post-operative delirium prediction models.

**Educational Objectives:** 1. The participant should be able to define how preoperative IGF-1 levels may help to predict post-operative delirium.

**NR9-16**

**DTNBP1, HSPS AND TAAR6 VARIATIONS INFLUENCE SCHIZOPHRENIC PHENOTYPE AND TREATMENT RESPONSE**

*Chair: Tae-Youn Jun M.D.; Author(s): Tae-Youn Jun (First*

and Corresponding author), Chi Un Pae, Hee Ryung Wang, Hoo Rim Song, Young Sup Woo, Won-Myong Bahk

#### SUMMARY:

Objectives : A pharmacogenetic approach is used to challenge the hypothesis that DTNBP1, HSP-70 and TAAR6 mutations may impact the clinical presentation or treatment outcome in a sample of 240 Schizophrenic in patients Design and Methods : A sample of 240 Schizophrenic Korean in patients was enrolled in the study. Patients were administered the PANSS test at the moment of admission and at the moment of discharge, 45 days after on average. Patients were treated with typical and atypical antipsychotics with low benzodiazepine doses as the only other treatment allowed. Sociodemographic, clinical and treatment related variables entered the analysis as covariates. For power analysis on average, we had a power of 0.8 to detect a minimum difference of about 2% in the PANSS scores. Results : DTNBP1 haplotype A-A (rs3213207, rs1011313) haplotype was associated with lower PANSS total and positive scores at baseline ( $p=0.01$ ;  $p=0.005$ ) and at discharge ( $p=0.008$ ;  $p=0.005$ ). HSPs haplotypes A-C-G-G and G-C-C-C (rs2075799, rs1043618, rs562047, rs539689) were found to be associated with worse baseline PANSS negative scores ( $p=0.0001$ ) and clinical improvement ( $p=0.04$  and  $p=0.03$  respectively). TAAR6 rs8192625 G/G genotype was found to be associated with worse clinical presentation ( $p=0.01$ ), whilst no significant associations were found after haplotype analyses. Conclusions : Variations within the DTNBP1, HSPs and TAAR6 genes seem to be associated with the psychotic symptoms' severity at the beginning of treatment. DTNBP1, HSPs variations seem to impact the antipsychotic treatment response too.

#### NR9-17

### DIFFERENCES OF SELECTIVE DNA METHYLATION OF BDNF GENE BETWEEN BIPOLAR PATIENTS AND CONTROLS AND POTENTIAL INFLUENCE OF PHARMACOLOGICAL TREATMENTS

Chair: Bernardo Dell'Osso M.D.; Author(s): Claudio D'Addario, Ph.D., Maria Carlotta Palazzo, M.D., Beatrice Benatti, M.D., Licia Lietti, M.D., Daniela Galimberti, Ph.D., Chiara Fenoglio, Ph.D., Francesca Cortini, Ph.D., Elio Scarpini, M.D., Beatrice Arosio, Ph.D., Manuela Di Benedetto, Ph.D., Patrizia Romualdi, Ph.D., Daniela Mari, M.D., Mauro Maccarrone, Ph.D and A. Carlo Altamura, M.D.

#### SUMMARY:

Introduction: The etiology of bipolar disorder (BD) is only partially understood, involving genetic, epigenetic mechanisms as well as environmental contributions. In particular, brain-derived neurotrophic factor (BDNF) promoter altered methylation levels were associated in literature with risk of psychosis and cognitive impairment. The present study was therefore aimed to investigate the degree of DNA methylation at BDNF gene promoter in peripheral blood mononuclear cells (PBMCs) isolated from patients with BD. Methods: DNA was isolated from the blood of 94 BD patients (49 BD I and 45 BD II) and 52 healthy controls and converted with sodium bisulfite. Real Time Methylation Specific PCR was performed to quantify promoter methylation. Peripheral blood was considered a proper material to evaluate epigenetic modifications as peripheral markers reflect brain damage with a good approximation. Results: A significant BDNF gene expression down-regulation was observed in BD II  $0.53 \pm 0.11\%$ ;  $p<0.05$ ), but not in BD I ( $1.13 \pm 0.19\%$ ) patients compared with controls (CONT:  $1 \pm 0.2\%$ ). Consistently, an hypermethylation of the BDNF promoter region was specifically found in BD II patients (CONT:  $24.0 \pm 2.1\%$ ; BDI:  $20.4 \pm 1.7\%$ ; BDII:  $33.3 \pm 3.5\%$ ,  $p<0.05$ ). Of note, higher levels of DNA methylation were observed in BD subjects on pharmacological treatment with mood stabilizers plus antidepressants ( $34.6 \pm 4.2\%$ , predominantly BD II) compared with those exclusively on mood stabilizing agents ( $21.7 \pm 1.8\%$ ;  $p<0.01$ , predominantly BD I). Moreover, among the different pharmacological therapies, lithium ( $20.1 \pm 3.8\%$ ,  $p<0.05$ ) and valproate ( $23.6 \pm 2.9\%$ ,  $p<0.05$ ) were associated with a significant reduction of DNA methylation compared to other drugs ( $35.6 \pm 4.6\%$ ). Conclusions: Present findings suggest selective changes in DNA methylation of BDNF promoter in subjects with BD type II and highlight the importance of epigenetic factors in mediating the pathophysiology treatment response of BD.

#### NR9-18

### INVESTIGATING TELOMERE LENGTH AND PSYCHOLOGICAL STRESS IN SOUTH AFRICAN RAPE VICTIMS

Chair: Sian Hemmings Ph.D.; Author(s): Stefanie Malan, M.Sc Martin Kidd, Ph.D Lindi Martin, M.A Soraya Seedat, M.B.Ch.B., F.C.Psych., M.Med.Psych., Ph.D

#### SUMMARY:

Introduction: Women are at an increased risk of depression and other mental health problems following rape. Various etiological factors for depression, including predisposing genetic factors, have been

identified. Telomeres are repetitive nucleoprotein structures located at chromosomal ends that protect them from premature degradation. Telomeres reduce in length with each cell division, resulting in cellular senescence and apoptosis. Additional factors, such as oxidative and psychological stress, can further induce telomere shortening. **Methods:** This study performed relative quantification of telomeric repeats with the use of real-time PCR methods to investigate whether shorter relative leukocyte telomere length (LTL) in a cohort of rape victims was associated with resilience, the development of trauma-related major depressive disorder (M.D.D), as well as the development of PTSD after three months. **Results:** No significant associations were observed between relative LTL and resilience or the development of M.D.D at either baseline or after three months in this cohort. However, a significant association was evident between relative LTL and PTSD status. **Conclusion:** The significant association between relative LTL and PTSD suggests that shorter relative LTL might have acted as a predisposing factor to the development of PTSD after a severely traumatic event. Telomere shortening may be an important marker of PTSD risk, which has implications for early intervention and timely treatment.

#### NR9-19

#### CHARACTERISTICS OF PATIENTS SELECTED TO RECEIVE GENETIC TESTING TO INFORM PSYCHIATRIC TREATMENT

*Chair: Rachel Dicker Phar M.D.; Author(s): Bryce Kasuba, MA, MBA Lauren Novasitis, BS Herb Harris, M.D., Ph.D. Jay Lombard, DO*

#### SUMMARY:

**Background:** Response to psychotropic therapy is highly variable and can be attributed, in part, to heritable traits. Therapies targeted, at least in part, to a patient's genetic data have the potential to produce optimal outcomes. Collecting outcomes data from subjects in actual practice settings poses challenges not normally presented in typical research studies. This research study offers unique designs to overcome these challenges, including electronic consent and secure online capture of study assessments. Aims include characterization of the population of patients selected for pharmacogenetic testing by their clinicians and demonstration of the impact of genetic testing on clinician treatment decisions and patient outcomes as measured by change in severity of depression. **Methods:** This is an open label, prospective analysis of clinicians who order the Genecept Assay and patients for whom the test is ordered. The study will consent and collect responses

from clinician study participants and subjects and analyze genetic data from these subjects. Genes tested include the serotonin transporter protein (SLC6A4), gated calcium channel (CACNA1C), dopamine receptor subtype two (DRD2), catechol-O-methyl transferase (COMT) and methylenetetrahydrofolate reductase (MTHFR) as well as cytochromes P450 2D6 (CYP2D6) and 2C19 (CYP2C19). Analytic results reports will be provided to clinician study participants, who will be asked to complete a baseline survey which asks about the assay's influence on treatment, subject's psychiatric history and severity of illness using CGI-S. A follow up assessment occurs at 3 months which includes an assessment of improvement of illness severity using CGI-I. Subjects will be asked to complete at baseline and 3 months an assessment of depression symptoms, and quality of life. All analyses will be performed in SAS and PROC MIXED will be used for the primary hypothesis. **Results:** This study begins recruitment in December 2011 and 200 Subjects are expected to be recruited by March 2012. **Conclusion:** It can be difficult to choose from the multitude of treatment options available for patients with depression, but targeted medication therapy, guided by genetic data may ease this burden and improve patient outcomes. This prospective research will provide outcomes data to establish utility of this genetic assay in clinical practice.

#### NR9-20

#### APOLIPOPROTEIN E E4-E2 ALLELES REDUCE THE AGE OF ONSET AND INCREASE THE RISK OF DEVELOPING SCHIZOPHRENIA IN MEDELLIN, COLOMBIA: A CASE-COHORT STUDY

*Chair: Juan Arango M.D.; Author(s): Jenny Garcia-Valencia M.D. MSc Ph.D., Ana V Valencia-Duarte Ph.D., Ana L Paez-Vila Biol.Manuel J Castilla Biol*

#### SUMMARY:

**Background:** The e4 allele of Apolipoprotein E (APOE), has been associated with Alzheimer's disease and other neurologic and psychiatric disorders. This has led to investigate the role of the APOE genotypes in schizophrenia; although with contradictory results. Discrepancies could be explained either by the fact that the association between APOE genotypes and schizophrenia could differ between different populations or perhaps, methodological issues such as the reduced sample size may underline the conflicting findings. **Objective:** To evaluate the association of APOE alleles and genotypes with schizophrenia and its age of onset in Medellin, Colombia. **Methods:** We used a case-cohort design instead of a case/control, because the former

is more efficient in dealing with the age of onset of any condition. In this model, traditionally, all the events or cases are taken from a cohort and compared with a random sample of the same cohort, known as sub-cohort, which may or may not include events. Cases were 319 adults with schizophrenia drawn from the less affluent areas of Medellin (Colombia). A sub-cohort of 845 subjects from the same areas of the city was used as comparison group. This was accomplished by a multistage random sampling in which the first stage was stratified by economical level; the second was a cluster sampling taking the blocks as conglomerates and in the third stage people were selected randomly and these were the final analysis unit. Hazard Ratio (HR) and 95% CI for alleles and genotypes by means of an unweighted Cox regression model were estimated. Results: When taking the age of onset of schizophrenia as event time, the e2/e4 genotype was associated with schizophrenia (HR = 2.64, 95% CI: 1.08 – 6.45) when compared with the e3/e3 genotype. In addition, individuals with e2/e4 and e4/e4 genotypes (e4 carriers) showed an increased risk to develop schizophrenia when compared with individuals with different APOE genotypes (HR = 2.25, 95% CI: 1.16 – 4.38,  $p = 0.02$ ). Conclusion: Our data supports an association between APOE genotype and schizophrenia, the APOE e3 allele seems to be protective while the e2/e4 and e4/e4 genotypes are significantly associated with the risk of schizophrenia.

**NR9-21****THE DIFFERENCES IN CHARACTERISTICS OF BIPOLAR AND SCHIZOPHRENIC PATIENTS PREMATURELY DYING FROM CIRCULATORY DISEASES**

*Chair: Shang-Ying Tsai M.D.; Author(s): Chian-Jue Kuo, M.D.Ph.D.; Shou-Hung Huang, M.D.; Kuo-Hsuan Chung, M.D.; Ying-Fung Wang, B.S.*

**SUMMARY:**

**Background:** Both bipolar and schizophrenic patients are at high risk to prematurely die from circulatory diseases [1, 2]. However, the useful characteristics to early identify the high risk subgroup to prematurely die from circulatory diseases in each diagnostic group may vary and remain unclear. **Objective:** We attempted to find out the difference in clinical and demographic features between schizophrenic and bipolar patients dying from circulatory causes before reaching geriatric age. **Methods:** Patients with bipolar I disorder (DSM-IV) and schizophrenics disorder (DSM-IV) admitting to a 300-acute-bed psychiatric teaching hospital after 1987 were retrospectively followed for cause of death until 2010 through record linkage to

the Death Certification System in Taiwan. Circulatory diseases include cardiovascular diseases [ICD 390-429] and cerebrovascular diseases [ICD 430-438]. Patients dying from circulatory morbidity before 65 years old were recruited. All clinical data including the results of physical examination and laboratory tests of the most recent hospitalization were obtained by reviewing medical records. The Framingham Risk Score was utilized to estimate the 10-year cardiovascular risk of an individual. Results: There were 36 bipolar patients who died at the mean  $49.9 \pm 8.7$  years old and 69 schizophrenic ones dying at mean age of  $47.2 \pm 10.3$  years in our study. Compared with schizophrenic patients, bipolar subjects had significantly higher proportion (60.6% vs 30.4%,  $p < 0.005$ ) with abnormal electrocardiography in the last acute hospitalization and higher mean heart beat in the first three days after the last acute hospitalization (92.8 bpm vs 85.9 bpm,  $p < 0.025$ ). There was no difference in rates of smoker and alcohol abuser and mean value of Framingham Risk Score, number of previous hospitalization, age of illness onset along with the last acute admission, interval from last hospitalization to death, levels of blood sugar and lipid between two groups. Conclusion: Bipolar and schizophrenic patients may have similar risk factors for circulatory mortality. However, elevated heart rate and more EKG abnormality in acute phase could characterize bipolar patients prematurely dying from circulatory causes. The state-dependent cardiac pathophysiology of bipolar disorder may vary from that of schizophrenia. 1. Tsai SY, Lee CH, Kuo CJ, et al. A retrospective analysis of risk and protective factors for natural death in bipolar disorder. *J Clin Psychiatry* 2005; 66: 1586-1591. 2. Ösby U, Brandt L, Correia N, et al. Excess mortality in bipolar and unipolar disorder in Sweden. *Arch Gen Psychiatry* 2001; 58: 844-850.

**NR9-22****NEUROPSYCHIATRIC MANIFESTATIONS OF AUTOIMMUNE LIMBIC ENCEPHALITIS**

*Chair: Robini Ravindran M.D.*

**SUMMARY:**

Limbic Encephalitis was originally characterized as a paraneoplastic syndrome typically seen in patients with lung or testicular cancer. Recently, a new non-paraneoplastic form has been recognized which is associated with Voltage-Gated Potassium Channel antibodies in the CSF. It falls under the category of Autoimmune dementia. This poster discusses a case of a 77 year old retired surgeon who presented with rapidly progressing dementia, florid psychosis, and insomnia. The patient did not fit the picture for Alzheimer's

disease because of the rapid onset of his symptoms. He was ruled out for various syndromes including Herpes Encephalitis and CJD. To date there are only 15 documented cases of this disease but this number is growing. The likely explanation for the limited number of cases is the lack of recognition by clinicians. This review's main goal is to educate psychiatrists about Autoimmune Dementia and when to initiate the workup. The importance of recognizing these syndromes is they are in fact highly treatable with immunosuppressive therapy.

### NR9-23

#### MUSICAL HALLUCINATIONS AND COCHLEAR NUCLEUS INFARCTS

*Chair: Michael Serby M.D.; Author(s): Anil Lakwani, M.D.*

#### SUMMARY:

**Introduction:** Musical hallucinations (MH) are a disturbing phenomenon that occurs in 2% of individuals with significant hearing loss. There is generally no psychotic elaboration of the origin or meaning of MH. The impact on the stricken individual can be benign or quite disturbing. Clinical characteristics, such as onset of MH, can vary. The nature of the underlying pathophysiology and neuroanatomy is unknown, although there are some studies that have shed light. For example, a PET study demonstrated that the neural networks involved in MH are the same as those that are activated by real music. We now report three cases of elderly patients who had sudden onsets of MH that seem to be related to pontine microinfarcts in the area of the cochlear nucleus. **Methods:** Three geriatric patients presented for psychiatric treatment of MH. All 3 patients were evaluated by a geriatric psychiatrist (MS) and an otolaryngologist (AL). The 3 patients also received MRI scanning of the brain; all scans were reviewed by a neuroradiologist. **Results:** One patient had had pontine-cochlear nucleus lacunar infarcts demonstrated on MRI scan done after the sudden onset of her MH; these infarcts were not seen on an MRI just before the MH began. The 2 other patients had similar changes in their MRI scans. **Conclusions:** Sudden onset of MH may be due to cerebrovascular accidents that affect portions of the auditory system, including the cochlear nucleus. Information regarding the impact of cochlear nucleus damage on the possible release of MH will be presented.

### NR9-24

#### ASSOCIATION BETWEEN DOMAINS OF DEPRESSIVE SYMPTOMS AND EXECUTIVE DYSFUNCTION THREE MONTHS POST

#### STROKE: THE INFLUENCE OF THE MAJOR DEPRESSIVE EPISODE

*Chair: Matldes Sobreiro Psy.D.; Author(s): Luisa Terroni M.D.Ph.D, Eliane Miotto Psy.Ph.D, Valeri G. Delgado Psy., Mara C.De Lucia Psy.Ph.D, Dan V.Iosifescu M.D. Gisela Tinone M.D.Ph.D, Milberto Scaff M.D.Ph.D, Renério Fráguas M.D.Ph.D.*

#### SUMMARY:

**Background:** We have previously reported an association between the retardation domain of depressive symptoms and executive dysfunction one month after stroke. **Objective:** To investigate the association between domains of depressive symptoms and executive function (EF) 3 months post stroke. In addition, we investigated the influence of major depressive episodes (M.D.E) on this association. **Methods:** We assessed 72 patients (34,7% females, 65,3%) with diagnosis of first ischemic supratentorial stroke admitted to a neurology clinic at a university hospital. All patients were 18 years or older and had no previous history of M.D.E. They were evaluated three months after stroke (mean=91.6; SD±5.4 days). A psychiatrist diagnosed M.D.E according to DSM-IV criteria and assessed seven domains of depressive symptoms (cognitive symptoms, accessory symptoms, retardation, fatigue and interest, eating and weight, insomnia, and anxiety) using the HAM-D-31. A neuropsychologist assessed executive function using the Digit Span (WAIS-R), the Verbal Fluency words/min (FAS) and the Stroop Test. We analyzed separately patients with (n=22) and without (n=50) current post-stroke M.D.E. **Results:** In subjects with M.D.E we found a correlation between the retardation domain and Stroop 2 (words,  $t=.799$ ;  $p=.003$ ) and with Stroop-1 (dots,  $t=.722$ ;  $p=.012$ ) and a correlation between fatigue/interest and Digit Span backward ( $t=-.557$ ;  $p=.007$ ). Patients without poststroke M.D.E had a correlation between Fatigue/Interest and Digit Span backward ( $t=-.293$ ;  $p=.039$ ) and between the anxiety domain and Stroop-1 (dots,  $t=-.362$ ;  $p=.049$ ). **Conclusion:** The association between retardation and executive dysfunction persists three months post stroke; this association is moderated by the presence of current M.D.E.

### NR9-25

#### EFFECTS OF ANTIDEPRESSANTS ON NEUROPSYCHOLOGICAL FUNCTION RELATED TO COMBAT PERFORMANCE

*Chair: Ralph Tuttle D.O.; Author(s): Heather M. Kurera D.O.; Robert McLay, M.D./Ph.D.; Massoud Nikkboy, M.P.H.*

**SUMMARY:**

Objectives: Psychiatrists are sometimes asked to make recommendations as to if a patient should be allowed to carry a firearm. Unfortunately, there are no established criteria for how such a determination is to be made. The objective of this study was to establish what factors predict aspects of firearms performance, and lay the groundwork for more evidence-based methods of screening. Methods: Subjects between the ages of 18 and 65 were recruited from military bases and clinics in San Diego. Both psychiatric patients and controls were included. Participants were excluded if they were suicidal, homicidal, psychotic, bipolar, or owned the video game being used. Participants who gave informed consent were asked about demographics, psychiatric symptoms, psychiatric medication and treatment. They were then given a traditional, computerized assessment (the Automated Neuropsychological Assessment Metrics) and asked to engage in simulated target shooting and firefights using a video game and a light gun (Lethal Enforcers). Performance in the video game was measured with overall "score," and by recording target accuracy, number of times a person reacted too slowly and got shot, and the number of times that an incorrect (civilian) target was hit. Correlations were examined among firearms performance, psychiatric symptom scores, and traditional measures of neuropsychological function. T-tests were used to examine firearms score between patients and controls, as well as those who were, and were not, taking psychiatric medication. Finally, stepwise linear regression models were constructed to best predict firearms score, and safety (civilian targets hit), based on available information. Results: Eighty participants, including 65 patients and 15 controls, enrolled in the study. Firearms score was significantly correlated with reaction time ( $R=0.41$ ,  $p<0.01$ ), and tendency to shoot an incorrect target was correlated with go/no-go testing ( $R=.31$ ,  $p<0.01$ ). Psychiatric patients, as a whole, did not score worse with firearms performance than controls, and depression, anxiety and PTSD symptom severity did not correlate significantly with firearms performance (all  $p>0.05$ ). In linear regression modeling, gender and simple reaction time were the best predictors of firearms score. Go/no-go testing, hand steadiness, and procedural reaction time predicted safety. Conclusions: Being identified as a mental health patient, or self-report of symptoms for depression, anxiety or PTSD did not predict performance in a simulated firearms exercise. Gender and reaction time were the best predictors of simulated combat firearms performance, and go/no-go testing was the best predictor of firearms safety. Psychiatrists may be better served to use

neuropsychological testing rather than symptom severity in determining who should carry weapons. Further work is needed to establish norms, and examine real world performance.

**NR9-26****EFFECTS OF LOW-DOSE QUINIDINE ON THE STEADY-STATE PHARMACOKINETICS OF DEXTROMETHORPHAN**

*Chair: Laura Pope Ph.D.; Author(s): Andrea E. Formella, Ph.D., Benjamin Rix Brooks, M.D.*

**SUMMARY:**

Objectives: 1) Describe quantitatively the pharmacokinetic impact of quinidine (Q) on dextromethorphan (DM) concentrations 2) State the role of this interaction in treating pseudobulbar affect (PBA) and potential implications for exploring future CNS applications. Background: Dextromethorphan/quinidine (DMQ) is a therapeutic combination of DM and low-dose Q. DM is an uncompetitive NM.D.A receptor antagonist and sigma-1 receptor agonist; it also binds to SERT. Q is a potent CYP2D6 inhibitor that blocks first-pass DM metabolism. DMQ significantly reduced PBA symptoms in well-controlled trials, and DMQ 20/10mg twice daily is now indicated to treat PBA. Methods: Pharmacokinetic data from 3 trials were evaluated: a phase I study in healthy subjects taking 0, 2.5, 10, 25, 50 or 75mg Q with DM 30mg twice daily; an initial phase III study in PBA patients with ALS randomized to DM 30mg, Q 30mg, or DMQ 30/30mg twice daily; and a third phase III study of PBA patients with ALS or MS randomized to DMQ 20/10, 30/10 or placebo twice daily. Plasma concentrations were obtained at 7 days in the phase I trial and at 29 days in the phase III trials. Results: In healthy subjects ( $n=7$  to 8 per dose), inhibition of DM metabolism was seen at Q doses as low as 2.5mg;  $C_{max}$  increased in an asymptotic fashion, plateauing at Q doses  $>25$ mg/day. A total of 0, 14%, 86% and 100% of subjects were converted to poor metabolizer phenotypes by Day 7 at Q doses of 0, 2.5, 10, and  $\approx 25$ mg, respectively, with corresponding  $C_{max}$  for DM 30mg of 2.9, 35.3, 63.7, 98.9, 110.12, and 115.71 ng/mL. In the initial phase III trial mean DM concentrations measured within 8 hrs post-dose were  $5.2\pm 5.0$  ng/mL in PBA patients taking DM 30mg alone ( $n=23$ ) compared to  $96.4\pm 46.7$  ng/mL with DMQ 30/30 ( $n=35$ ). Enhanced DM bioavailability was associated with a significant decrease in PBA symptoms [CNS-LS  $-7.4\pm 0.6$  for DMQ 30/30 vs.  $-4.1\pm 0.9$  for DM 30mg (LS mean $\pm$ SE;  $P=0.001$ )]. In the third phase III trial, DM concentrations (1-3 hrs post-dose) were  $80.4\pm 42.8$  ng/mL for DMQ 30/10 ( $n=91$ ) and  $47.8\pm 27.6$

ng/mL for DMQ 20/10 (n=76). PBA episodes were significantly lower for both DMQ doses than placebo [46.9% lower than placebo for DMQ 30/10, and 49.0% lower for DMQ 20/10 by longitudinal negative binomial regression;  $P < 0.001$  for both]. Conclusions: An evaluation of data across studies demonstrates that inhibition of DM metabolism by Q is not linear; a 67% reduction in Q dose (from 30 to 10mg) would be expected to result in a decrease in DM concentration of about 35%. Data from DMQ trials in PBA highlight the therapeutic benefit of a carefully selected drug combination that substantially increases DM bioavailability and consequently its pharmacodynamic profile. The findings encourage reexamination of previous research exploring therapeutic utility of DM across multiple clinical applications, including those where prior findings were inconclusive possibly due to poor or inconsistent bioavailability.

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*Chair: Laura Pope Ph.D.; Author(s): Andrea E. Formella, Phar M.D., Benjamin Rix Brooks, M.D.*

**SUMMARY:**

**Objectives:** 1) Describe quantitatively the pharmacokinetic impact of quinidine (Q) on dextromethorphan (DM) concentrations 2) State the role of this interaction in treating pseudobulbar affect (PBA) and potential implications for exploring future CNS applications. **Background:** Dextromethorphan/quinidine (DMQ) is a therapeutic combination of DM and low-dose Q. DM is an uncompetitive NM.D.A receptor antagonist and sigma-1 receptor agonist; it also binds to SERT. Q is a potent CYP2D6 inhibitor that blocks first-pass DM metabolism. DMQ significantly reduced PBA symptoms in well-controlled trials, and DMQ 20/10mg twice daily is now indicated to treat PBA. **Methods:** Pharmacokinetic data from 3 trials were evaluated: a phase I study in healthy subjects taking 0, 2.5, 10, 25, 50 or 75mg Q with DM 30mg twice daily; an initial phase III study in PBA patients with ALS randomized to DM 30mg, Q 30mg, or DMQ 30/30mg twice daily; and a third phase III study of PBA patients with ALS or MS randomized to DMQ 20/10, 30/10 or placebo twice daily. Plasma concentrations were obtained at 7 days in the phase I trial and at 29 days in the phase III trials. **Results:** In healthy subjects (n=7 to 8 per dose), inhibition of DM metabolism was seen at Q doses as low as 2.5mg;  $C_{max}$  increased in an asymptotic fashion, plateauing at Q doses  $>25$ mg/day. A total of

0, 14%, 86% and 100% of subjects were converted to poor metabolizer phenotypes by Day 7 at Q doses of 0, 2.5, 10, and  $\geq 25$ mg, respectively, with corresponding  $C_{max}$  for DM 30mg of 2.9, 35.3, 63.7, 98.9, 110.12, and 115.71 ng/mL. In the initial phase III trial mean DM concentrations measured within 8 hrs post-dose were  $5.2 \pm 5.0$  ng/mL in PBA patients taking DM 30mg alone (n=23) compared to  $96.4 \pm 46.7$  ng/mL with DMQ 30/30 (n=35). Enhanced DM bioavailability was associated with a significant decrease in PBA symptoms [CNS-LS  $-7.4 \pm 0.6$  for DMQ 30/30 vs.  $-4.1 \pm 0.9$  for DM 30mg (LS mean  $\pm$  SE;  $P = 0.001$ )]. In the third phase III trial, DM concentrations (1-3 hrs post-dose) were  $80.4 \pm 42.8$  ng/mL for DMQ 30/10 (n=91) and  $47.8 \pm 27.6$  ng/mL for DMQ 20/10 (n=76). PBA episodes were significantly lower for both DMQ doses than placebo [46.9% lower than placebo for DMQ 30/10, and 49.0% lower for DMQ 20/10 by longitudinal negative binomial regression;  $P < 0.001$  for both]. Conclusions: An evaluation of data across studies demonstrates that inhibition of DM metabolism by Q is not linear; a 67% reduction in Q dose (from 30 to 10mg) would be expected to result in a decrease in DM concentration of about 35%. Data from DMQ trials in PBA highlight the therapeutic benefit of a carefully selected drug combination that substantially increases DM bioavailability and consequently its pharmacodynamic profile. The findings encourage reexamination of previous research exploring therapeutic utility of DM across multiple clinical applications, including those where prior findings were inconclusive possibly due to poor or inconsistent bioavailability.

**NR9-27**  
**COGNITIVE FUNCTIONS OF THE DEPRESSIVE PATIENTS COMPARED WITH HEALTHY CONTROLS THROUGH META-ANALYSIS**

*Chair: Cheolmin Shin M.D.; Author(s): Changsu Han, M.D., PH.D., MHS*

**SUMMARY:**

**Introduction:** Major depression is a mood disorder often accompanied by the impairment of cognitive functions. However, conflicting patterns of cognitive impairment have been reported across studies. We therefore conducted a meta-analysis in order to determine which neuropsychological domains and tasks were most sensitive to discriminating patients with major depressive disorder from healthy controls. **Methods:** A meta-analysis was conducted to examine the differences in cognitive function between Major Depressive Disorder patients and the healthy controls, using the

mean of neuropsychological test performance. Individual meta-analyses were conducted for composite measures of cognitive functional domains (attention: Digit Span, CPT, processing speed: TMT A, Digit Symbol, Finger Tapping Task, executive function: Stroop test, TMT B, WCST, Verbal Fluency, memory: Verbal-RAVLT, Luria Verbal Learning Test, WMS/Visual-WMS). Results: Significant differences between M.D.D patients and the healthy controls were found in the tasks of Digit Span, CPT, TMT A, Digit Symbol, Stroop test, WCST, verbal fluency, verbal memory immediate, but not for Finger Tapping Task, Visual memory (immediate/delayed). Conclusions: These results provide neuropsychological evidence for compose the cognitive test battery for the cognitive evaluation of depressive disorder.

**NR9-28**  
**MEMANTINE FOR COGNITIVE DEFICITS IN BIPOLAR DISORDER**

*Chair: Dan Iosifescu M.D.; Author(s): William S. Gilmer, M.D., Alexander Fan, M.D., Christopher Randolph, Ph.D., Mark H. Rapaport, M.D., Amy Peters, B.A., Thilo Deckersbach, Ph.D., Andrew A. Nierenberg, M.D.*

**SUMMARY:**

Background: Subjects with bipolar disorder experience significant cognitive dysfunction, even when euthymic, but few studies have evaluated potential treatments for such deficits. Objective: We completed a three-site, 12-week, randomized, placebo-controlled study to evaluate the efficacy of memantine, a glutamatergic modulator, for the treatment of cognitive deficits in bipolar disorder. Method: N=72 euthymic subjects with bipolar disorder, who reported subjective cognitive deficits, were randomized 2:1 to memantine or placebo for a 12-week treatment study with flexible doses (5-20 mg/day). At baseline and endpoint all subjects were administered neuropsychological tests, including tests of attention (the Rapid Visual Information Processing Task, RVIP of CANTAB), short-term/working memory (the Spatial Working Memory, SWM of the CANTAB), verbal and episodic memory (the California Verbal Learning Test, CVLT-II and the Delayed Matching to Sample, DMS of the CANTAB). We also administered the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), which includes five subscales (attention, immediate memory, visuospatial construction skills, delayed memory and language). Mood scales and subjective cognitive questionnaires were administered monthly. Study completers were offered open label treatment with memantine for additional 12 weeks; neuropsychological tests were again administered at the end of the follow-up. Results:

Bipolar subjects experienced significant improvement in subjective cognitive symptoms over the 12 week treatment, with no significant difference between memantine and placebo groups. Memantine treated patients had no significant improvement on any RVIP measure (attention) compared to placebo, but experienced significant improvement over placebo in spatial and working memory (SWM subscales Between errors, Strategy, Total Errors) and in verbal and episodic memory (DMS subscales Percent correct and Total correct; CVLT subscales Trial 2; Trial 4; Recognition hits; Recognition of false positives). The total RBANS score was significantly improved in the memantine group compared to placebo; of the 5 RBANS indexes statistical significance was achieved on 3: attention, language and delayed memory. The improvements in neuropsychological tests achieved during the randomized treatment were maintained over the 12 weeks of open follow-up treatment. Conclusion: Twelve weeks of treatment with memantine was associated with acute improvements on several cognitive domains in euthymic subjects with bipolar disorder and these improvements persisted over an additional three months with ongoing treatment.

**NR9-29**  
**EFFECT OF THE MULTIMODAL ANTIDEPRESSANT LU AA21004 ON RECOGNITION MEMORY AND HIPPOCAMPAL PLASTICITY IN RATS**

*Chair: Nasser Haddjeri Ph.D.; Author(s): Adeline Etievant M.Sc., Alan Pebrson Ph.D., Connie Sánchez Ph.D. and Cécile Bétry M.Sc.*

**SUMMARY:**

Objective: Many patients with depression have cognitive disturbances [1]. Antidepressant treatments often leave patients with residual cognitive symptoms, and there is thus a need for new antidepressants more effectively targeting cognitive symptoms. Lu AA21004 is a multimodal antidepressant that functions as a 5-HT<sub>3</sub> and 5-HT<sub>7</sub> receptor antagonist, 5-HT<sub>1B</sub> receptor partial agonist, 5-HT<sub>1A</sub> receptor agonist and inhibitor of the 5-HT transporter in vitro. In vivo nonclinical studies have demonstrated that Lu AA21004 enhances levels of the neurotransmitters serotonin, noradrenaline, dopamine, acetylcholine and histamine in specific areas of the brain [2]. Here we report the preclinical effects of Lu AA21004 on several parameters involved in cognitive processing. Methods: We evaluated the effect of Lu AA21004 (10 mg/kg i.p.) on hippocampal synaptic plasticity. Field excitatory postsynaptic potentials were recorded in the CA1 area

of dorsal hippocampus before and after high frequency stimulation (HFS) of the Schaffer's collaterals in control and stressed rats placed on an elevated platform for 30 min before anesthesia and recordings. The novel object recognition (NOR) test in a Y-maze was used to evaluate episodic memory. Lu AA21004 (10 mg/kg i.p.) was administered 60 min before the acquisition trial, in which rats explored two identical objects. After a 24 h delay, one familiar object was reintroduced together with a novel object and the time spent exploring the objects was measured. The effect of LuAA21004 for 1, 3, 7 and 14 days on hippocampal cell proliferation was measured by immunohistochemistry. Results: In control rats, HFS provoked a stable long term potentiation (LTP) of ~30%. Lu AA21004 reduced LTP to ~10%. Interestingly, whereas acute stress suppressed LTP, Lu AA21004 pre-treatment completely prevented this suppressant effect. In the NOR test, Lu AA21004 administered 60 min before training significantly increased the time spent exploring the novel object during the retention test (index of recognition of ~40% versus ~10% for control rats) and this effect was partly prevented by the selective 5-HT<sub>3</sub> receptor agonist SR57227. Finally, LuAA21004 induced an increase of cell proliferation in the dentate gyrus after 1, 3 and 14 days of treatment. Conclusion: Lu AA21004 produced an effect on LTP similar to that of serotonergic antidepressants, but was able to prevent the LTP suppressant effect of acute stress. Lu AA21004 also enhanced episodic memory, an effect that seems to be at least partly mediated by its 5-HT<sub>3</sub> receptor antagonism. Finally, Lu AA21004 induced a surprisingly rapid increase of hippocampal cell proliferation. Taken together, these preclinical data suggest that the antidepressant, Lu AA21004, may have a beneficial effect on cognitive processes. 1. Gotlib IH, Joormann J. *Annu Rev Clin Psychol*; 2010;6;285-312. 2. Mørk A, Montezinho LC, et al. *Eur Neuropsychopharmacol*; 2011; 21; 3, S407-S408

### NR9-30

#### LISDEXAMFETAMINE DIMESYLATE IN THE TREATMENT OF COGNITIVE DYSFUNCTION IN PATIENTS WITH PARTIALLY OR FULLY REMITTED MAJOR DEPRESSIVE DISORDER

*Chair: Richard Keefe Ph.D.; Author(s): Alan Boyd, Ph.D., M.D., Manisha Madhoo, M.D., Robert M. Roth, Ph.D., Angelo Sambunaris, M.D., James Wu, Ph.D., Madbukar Trivedi, M.D., Colleen Anderson, MEd, Robert Lasser, M.D.*

#### SUMMARY:

Objective: A placebo (PBO)-controlled double-blind study in participants with mild major depressive

disorder (M.D.D) on selective serotonin reuptake inhibitor (SSRI) monotherapy examined the effects of lisdexamfetamine dimesylate (LDX) augmentation on executive dysfunction based on subjective ratings from the Behavior Rating Inventory of Executive Function-Adult Version (BRIEF-A). Here, we report the effects of LDX on objective performance-based neurocognitive measures (secondary outcomes) from the same study. Methods: This study enrolled men and women (18–55 y) with mild M.D.D (Montgomery-Åsberg Depression Rating Scale total score  $\leq 18$ ) and executive dysfunction (BRIEF-A Global Executive Composite T-score [GEC]  $\geq 60$ ) on stable SSRI monotherapy for  $\geq 8$  weeks. After a 2-week screening period, participants were randomized to 9 weeks of double-blind LDX (wk 1: 20 mg/d; wks 2–6: maintain or increase LDX in 10-mg increments weekly to 70 mg/d; wks 7–9: maintain optimized LDX dose) or PBO augmentation. Performance-based neurocognitive assessments were based on 3 indices derived from CNS Vital Signs test battery domains: complex information speed processing index (processing speed, working memory, and executive function), executive functioning index (executive function and reaction time), and neurocognitive index (memory [verbal, visual, working, composite], sustained and complex attention, cognitive flexibility, executive function, processing speed, and reaction time). Secondary outcomes were assessed all randomized participants who took  $\geq 1$  study drug dose and had  $\geq 1$  postbaseline BRIEF-A assessment. The study was not powered for statistical comparisons of secondary outcomes. Results: Of 143 randomized participants (LDX, 71; PBO, 72), 119 completed double-blind treatment (LDX, 60; PBO, 59). Least-squares mean reductions from baseline to study endpoint in BRIEF-A GEC T-scores (primary endpoint) were  $-21.2$  with LDX and  $-13.2$  with PBO (difference:  $-8.0$ ;  $P=0.0009$ ). Mean  $\pm$  SD complex information speed processing index baseline scores were  $97.4 \pm 14.87$  and  $98.9 \pm 13.12$  with LDX and PBO, respectively, and increased by  $8.7 \pm 10.13$  with LDX and  $3.7 \pm 9.02$  with PBO at endpoint. Mean  $\pm$  SD executive function index baseline scores were  $93.4 \pm 17.97$  and  $94.8 \pm 17.47$  with LDX and PBO, respectively, and increased by  $11.0 \pm 14.80$  with LDX and  $6.0 \pm 14.43$  with PBO at endpoint. Mean  $\pm$  SD neurocognitive index scores at baseline were  $92.7 \pm 15.46$  and  $96.5 \pm 12.81$  with LDX and PBO, respectively, and increased by  $11.5 \pm 17.14$  with LDX and  $2.5 \pm 13.74$  with PBO at endpoint. For these outcomes, there were no statistically significant treatment differences in median scores at endpoint; however, findings from the computerized performance-based test battery complemented the subjective findings of the BRIEF-A. Conclusions: These

objective secondary endpoints further support subjective reports of improved executive function with LDX and serve as a signal for future research. Supported by Shire Development

**NR9-31**

**QUALITY OF LIFE AND FUNCTIONAL STATUS OUTCOMES WITH TMS IN ROUTINE PRACTICE: A PRAGMATIC CLINICAL TRIAL IN THE TREATMENT OF MAJOR DEPRESSION**

*Chair: Mark Demitrack M.D.; Author(s): Scott Aaronson, M.D., Terrence Boyadjis, M.D., David G. Brock, M.D., Linda Carpenter, M.D., Ian Cook, M.D., David L. Dunner, M.D., Philip G. Janicak, M.D., Karl Lanocha, M.D., H. Brent Solvason, M.D., Ph.D.*

**SUMMARY:**

Background: Transcranial magnetic stimulation (TMS) is a safe and effective antidepressant for patients who have failed to benefit from initial medication treatment for major depression in controlled trials. This study was designed to assess the patient-reported quality of life and functional status outcomes of TMS in clinical practice. Patient perception of clinical benefit on such measures is an important accompaniment of symptomatic benefit and may indicate patient acceptance of treatment, and therefore longer term adherence. Methods: Three hundred and seven patients with a primary diagnosis of unipolar, non-psychotic major depressive disorder, who had failed to receive benefit from prior antidepressant treatment, received TMS treatment with TMS in clinical practice. Forty three clinical practices contributed to this study. TMS treatment was provided as clinically determined by the evaluating physician, initiated consistent with labeled use. Patient reported quality of life was obtained using the Euro-QOL 5D. Functional status was measured using the Medical Outcomes Study Short Form, 36-Item (v2) questionnaire. Assessments were performed prior to initiation of the first TMS treatment, and again at the point at which the clinician determined that maximal acute treatment was reached. Results: The study population included 205/307 females. The average age of the population was 48.6 years. The most common primary diagnosis was recurrent, non-psychotic unipolar major depressive disorder (92.8% of the sample). 82.7% of patients completed acute treatment. 44.4% had two or more adequate antidepressant medication treatments in current episode. Self-reported quality of life was statistically significantly improved ( $P < 0.0001$ ) compared to baseline on all measures within the EQ-5D (Mobility, Self-Care, Usual Activities, Pain/Discomfort and Mood/

Anxiety). Similarly, all functional status factors (Mental Health, Role-Emotional, Social Functioning, Vitality, General Health, Bodily Pain, Role-Physical, Physical Functioning) reported on the SF-36 were statistically significantly improved compared to baseline ( $P < 0.0001$ ). Conclusion: In clinical practice TMS shows statistically significant benefits on patient-reported outcomes of quality of life and functional status. These data validate the results of prior controlled studies and support the use of TMS as an effective treatment in patients who have failed to benefit from initial antidepressant treatment.

**NR9-32**

**A POOLED ANALYSIS OF VILAZODONE IN THE TREATMENT OF MAJOR DEPRESSIVE DISORDER: EFFICACY ACROSS SYMPTOMS**

*Chair: Arif Khan M.D.; Author(s): Wenjie Song, Ph.D., John Edwards, M.D., Adam Ruth, Ph.D.*

**SUMMARY:**

Objective: Vilazodone, a serotonin reuptake inhibitor and 5-HT<sub>1A</sub> receptor partial agonist, is approved by the US Food and Drug Administration for the treatment of M.D.D in adults. Efficacy and safety were established in two 8-week, double-blind, randomized, placebo-controlled pivotal trials (RCT-1: NCT00285376; RCT-2: NCT00683592). Methods: Data from RCT-1 and -2 were pooled to analyze the effects of vilazodone versus placebo. Patients 18-70 years of age with DSM-IV-TR-defined M.D.D and a minimum score  $\geq 22$  on the 17-item Hamilton Depression Rating Scale (HAM.D.17) participated. Study design was similar in both trials (a 1-week screening period followed by 8-week double-blind treatment). Patients randomized to vilazodone were titrated to a target dose of 40 mg, taken once daily (QD) with food, over a 2-week period (10 mg QD for 7 days, 20 mg QD for the next 7 days, and 40 mg QD thereafter). The primary efficacy parameter (change from baseline to Week 8 in Montgomery-Asberg Depression Rating Scale [MADRS] total score) was analyzed using an analysis of covariance (ANCOVA) model based on the intent-to-treat (ITT) population and the last observation carried forward (LOCF) approach. Secondary efficacy endpoints included HAM.D.17, Clinical Global Impressions-Improvement (CGI-I) and -Severity (CGI-S), Hamilton Anxiety Rating Scale (HAM.A), response (MADRS  $\geq 50\%$  improvement from baseline; HAM.D.17  $\geq 50\%$  improvement from baseline; CGI-I score  $\leq 2$ ) and remission (MADRS  $\leq 10$ ). Change from baseline on MADRS single items and remission MADRS  $\leq 12$

were also evaluated. Results: The ITT population comprised 432 vilazodone- and 431 placebo-treated patients. Vilazodone significantly improved MADRS scores relative to placebo; the least squares mean difference (LSM.D. [95% CI]) was -2.79 (-4.14, -1.44) ( $P < .0001$ ). Significant improvement on all secondary measures in favor of vilazodone was also seen ( $P < .01$ ). Response for vilazodone vs placebo based on MADRS and HAM.D.17  $\geq 50\%$  improvement was 42% vs 29% ( $P = .0002$ ) and 44% vs 33% ( $P = .0007$ ), respectively; CGI-I response was 49% vs 35% ( $P < .0001$ ). Remission for vilazodone vs placebo using MADRS  $\leq 10$  and  $\leq 12$  criteria was 29% vs 20% ( $P = .0041$ ) and 35% vs 22% ( $P < .0001$ ), respectively. Significant improvement in favor of vilazodone versus placebo was seen on change from baseline in every MADRS single item (LSM.D.): apparent sadness, -0.24; reported sadness, -0.29; inner tension, -0.31; reduced sleep, -0.30; reduced appetite, -0.20; concentration difficulties, -0.24; lassitude, -0.27; inability to feel, -0.25; pessimistic thoughts, -0.35; suicidal thoughts, -0.29 ( $P < .01$  for all). Conclusion: Pooled data from 2 pivotal trials demonstrated significantly higher rates of response and remission for vilazodone treatment relative to placebo. Vilazodone was significantly superior to placebo on all depression rating scales tested and showed efficacy on all MADRS single items. This study was funded by Forest Laboratories, Inc.

### NR9-33

#### LEVOMILNACIPRAN IN THE TREATMENT OF MAJOR DEPRESSIVE DISORDER: AN ANALYSIS OF EFFICACY DATA FROM 2 PHASE III STUDIES

*Chair: Anjana Bose Ph.D.; Author(s): Carl Gommoll, MS, Hua Li, Ph.D., Adam Rut, Ph.D.*

#### SUMMARY:

Objective: Levomilnacipran (1S, 2R-milnacipran) is a potent and selective serotonin and norepinephrine reuptake inhibitor (SNRI) with preference for the norepinephrine transporter. Efficacy of levomilnacipran SR in major depressive disorder (M.D.D) was evaluated using data from recently completed Phase III fixed-dose (Study 1, NCT00969709) and flexible-dose (Study 2, NCT00969150) studies. Statistical superiority on the primary efficacy measure was seen for levomilnacipran SR versus placebo in Study 1 only; other trials are ongoing. Methods: Studies were 11-week, double-blind, multicenter, randomized, placebo-controlled; they comprised a 1-week single-blind, placebo lead-in, 8-week double-blind treatment, and 2-week double-blind down-taper.

Patients had MADRS-Clinician Rated (MADRS-CR) scores  $\geq 30$  with a current major depressive episode  $\geq 8$  weeks (Study 1) or  $\geq 4$  weeks (Study 2). Patients were randomized to levomilnacipran SR 40, 80, or 120 mg QD or placebo in Study 1 or to levomilnacipran SR 40-120 mg/day QD or placebo in Study 2. Analyses were conducted using pooled data from the 2 studies. Primary efficacy: change from baseline to end of Week 8 in MADRS-CR total score; secondary efficacy: change from baseline to Week 8 in SDS total score; additional efficacy: HAM.D.-17, CGI-S, and CGI-I. Potential factors leading to variable response pattern in sites common to both studies were explored. Continuous variables were analyzed using a mixed-effects model for repeated measures. Results: Pooled baseline characteristics were similar for placebo (n=358) and levomilnacipran SR (n=712) patients. Significant improvement was seen in the levomilnacipran SR group versus placebo at study endpoint on the MADRS-CR (LSM.D.=-2.73;  $P = .0009$ ) and SDS (LSM.D.=-1.44;  $P = .0190$ ). Significant differences at endpoint in favor of levomilnacipran SR were also seen on change in HAM.D.17 (LSM.D.=-1.35,  $P = .0175$ ) and CGI-S (LSM.D.=-0.28,  $P = .0032$ ), and on CGI-I score at Week 8 ( $P = .0040$ ). Significant MADRS-CR improvement was noted in levomilnacipran-treated patients with severe depression defined as MADRS-CR baseline  $\geq 35$  (LSM.D.=-3.31,  $P = .0045$ ) or CGI-S  $\geq 5$  (LSM.D.=-4.22,  $P < .0001$ ). For sites that participated in both studies, similar improvements were seen on MADRS-CR total score for levomilnacipran SR; however, placebo response was higher in Study 2 versus Study 1. Conclusion: Pooled analyses of completed studies showed that levomilnacipran SR- versus placebo-treated patients achieved statistically significant and clinically meaningful improvement in depressive symptoms and functional impairment. Higher placebo response in Study 2 relative to Study 1 may explain the different outcomes in the individual studies. This study was funded by Forest Laboratories, Inc.

### NR9-34

#### VILAZODONE IN THE TREATMENT OF MAJOR DEPRESSIVE DISORDER: EFFECTS ON WEIGHT AND LABORATORY VALUES

*Chair: Michael Thase M.D.; Author(s): Wenjie Song, Ph.D., John Edwards, M.D., Adam Ruth, Ph.D.*

#### SUMMARY:

Objective: Vilazodone, a serotonin reuptake inhibitor and 5-HT<sub>1A</sub> receptor partial agonist, is approved by the US Food and Drug Administration for the treatment of M.D.D in adults. Efficacy and safety

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were established in two 8-week clinical trials (RCT-1: NCT00285376; RCT-2: NCT00683592); safety was supported by results from a 52-week open-label trial (OL: NCT00644358). The effects of vilazodone on body weight, body mass index (BMI), and laboratory values were evaluated in post hoc analyses. Methods: Post hoc analyses were conducted on pooled safety data from two 8-week, double-blind, randomized, controlled trials (RCT-1 and RCT-2) of vilazodone (n=436) versus placebo (n=433); additional analyses were performed on 52-week, OL data (N=599). Patients were 18-70 years of age with DSM-IV-TR-defined M.D.D and a minimum score  $\geq 22$  (RCT-1 and -2) or  $\geq 18$  (OL) on the 17-item Hamilton Depression Rating Scale (HAM.D.17). Study designs were similar in the 8-week trials; patients randomized to vilazodone or receiving OL treatment were titrated to a 40-mg target dose, taken once daily with food, over 2 weeks. Post hoc analyses of double-blind and open-label data evaluated body weight changes stratified by baseline BMI (kg/m<sup>2</sup>) categories (underweight,  $<18.5$ ; normal,  $18.5 \leq$  to  $<25.0$ ; overweight,  $25.0 \leq$  to  $<30.0$ ; obese,  $\geq 30.0$ ). Potentially clinically significant (PCS) weight gain ( $>7\%$  increase from baseline) and laboratory values associated with liver enzymes and blood glucose were also investigated. Results: Mean baseline body weight (kg) was 86.0 and 86.5 for vilazodone and placebo patients, respectively, in the pooled studies, and 89.6 in the OL study. Mean baseline BMI was 30.2 for vilazodone and 30.1 for placebo patients in the pooled studies ( $\geq 70\%$  were overweight or obese) and 31.6 in the OL study. In the pooled studies, mean change in body weight (kg) from baseline to end of treatment (EOT) for vilazodone and placebo patients, respectively, was 0.16 and 0.18 overall, 0.0 and 0.32 for patients with normal BMI, 0.08 and 0.57 for overweight patients, and -0.39 and 0.18 for obese patients. PCS weight gain occurred in 1 vilazodone and 1 placebo patient with normal BMI; in overweight patients, PCS weight gain occurred in 1 vilazodone and 1 placebo patient. In the OL study, mean change in body weight (kg) from baseline to EOT was 1.20 overall, and 1.13, 1.21, 1.50, and 1.06 for underweight, normal, overweight, and obese patients, respectively; PCS weight gain occurred in 2%, 3%, and 5% of normal, overweight, and obese patients, respectively. In the pooled 8-week studies, changes in liver enzymes and blood glucose were small and similar between vilazodone and placebo. Conclusions: In acute and long-term treatment, change in body weight suggested a weight neutral profile for vilazodone across BMI categories; changes in clinical laboratory measures for vilazodone were small and similar to placebo. This study was funded by Forest Laboratories, Inc.

**NR9-35****PREDICTORS OF RELAPSE IN A FIXED-DOSE, RANDOMIZED, DOUBLE-BLIND, 52-WEEK RELAPSE PREVENTION TRIAL OF SELEGILINE TRANSDERMAL SYSTEM (STS)**

*Chair: Saebeon Jang M.D.; Author(s): Sungwon Jung M.D., Ph.D., Chiun Pae M.D., Ph.D., Youngmyo Jae M.D., Ph.D., Kimberly Blanchard Portland Ph.D., Paul Mastoridis, Pharm. D., Ashwin A Patkar M.D., M.R.C.Psych*

**SUMMARY:**

**Objective:** The variability in treatment relapse in major depressive disorder (M.D.D) has led to investigations of the relevance of patient characteristics. We investigated clinical characteristics predictive of relapse in a 52-week controlled trial of selegiline transdermal system (STS). **Method:** After 10 weeks of open-label stabilization with STS, 322 remitted patients with M.D.D were randomized to 52-weeks of double-blind treatment with STS (6mg/24hrs) or placebo. Relapse was defined as Hamilton Depression Rating Scale (HAM.D.-17) score of  $\geq 14$  and a CGI-S score of  $\geq 3$  with at least 2-point increase from the beginning of double blind phase on 2 consecutive visits. Pretreatment demographics, illness course, treatment resistance and symptom domains were studied to identify predictors of relapse. **Results:** Significantly fewer STS patients (16.8%) relapsed compared to placebo (30.7%) ( $p < 0.005$ ) and had a significantly longer time to relapse than did placebo ( $p < 0.005$ ). Baseline total HAM.D.-28 score, somatic anxiety, recurrent M.D.D, atypical depression, and analgesic use (celecoxib, naproxen) predicted relapse. Significant predictors of differential outcome were identified: 1) high baseline HAM.D.-28 score ( $p < 0.001$ ), high somatic anxiety ( $p < 0.05$ ) and celecoxib use ( $p < 0.05$ ) predicted relapse with STS; 2) atypical symptoms ( $p < 0.05$ ), recurrent episodes ( $p < 0.05$ ) and naproxen use ( $p < 0.01$ ) predicted relapse with placebo. **Conclusions:** For patients on STS, higher baseline depression severity, somatic anxiety or receiving celecoxib predicted relapse, while predictors of relapse with placebo were atypical or recurrent depression or naproxen use. The results provide indirect evidence of treatment specificity by identifying characteristics which may be of value in selection of patients for STS treatment.

**NR9-36****LEVOMILNACIPRAN IN THE TREATMENT OF MAJOR DEPRESSIVE DISORDER: AN ANALYSIS OF SAFETY AND TOLERABILITY DATA FROM 2 RANDOMIZED PLACEBO-CONTROLLED TRIALS**

*Chair: William Greenberg M.D.; Author(s): Hua Li, Ph.D., Carl Gommoll, MS, Adam Ruth, Ph.D.*

### SUMMARY:

**Objective:** Levomilnacipran (1S, 2R-milnacipran) is a potent and selective serotonin and norepinephrine reuptake inhibitor (SNRI) with preference for the norepinephrine transporter. Safety and tolerability of levomilnacipran SR in major depressive disorder (M.D.D) were evaluated using data from recently completed Phase III fixed-dose (Study 1, NCT00969709) and flexible-dose (Study 2, NCT00969150) studies. Statistical superiority on the primary efficacy measure was seen for levomilnacipran SR versus placebo in Study 1 only; other trials are ongoing. **Methods:** Studies were 11-week, double-blind, multicenter, randomized, placebo-controlled; they comprised a 1-week single-blind, placebo lead-in, 8-week double-blind treatment, and 2-week double-blind down-taper. Patients had MADRS-Clinician Rated (MADRS-CR) scores  $\geq 30$  with a current major depressive episode  $\geq 8$  weeks (Study 1) or  $\geq 4$  weeks (Study 2). Patients were randomized to levomilnacipran SR 40, 80, or 120 mg QD or placebo in Study 1 or to levomilnacipran SR 40-120 mg/day QD or placebo in Study 2. Analyses were conducted using pooled data from the 2 studies. Safety and tolerability evaluations included adverse events (AEs), laboratory measures/vital signs, and the Columbia-Suicide Severity Rating Scale (C-SSRS). **Results:** Baseline characteristics were similar for placebo (n=358) and levomilnacipran SR (n=712) groups. Overall, 80.2% of placebo and 70.6% of levomilnacipran SR patients completed the study; 84.1% of placebo and 73.5% of levomilnacipran SR patients were exposed to study drug for  $\geq 6$  weeks. During 8-week double-blind treatment, 1 placebo (0.3%) and 3 levomilnacipran SR patients (0.4%) had serious AEs (SAEs); 1 SAE (aggression) in a levomilnacipran SR patient was considered related to drug. Discontinuation due to AEs occurred in 2.0% of placebo and 9.1% of levomilnacipran SR patients. During double-blind treatment, 63.1% of placebo and 78.8% of levomilnacipran SR patients reported a treatment-emergent AE (TEAE). The majority of TEAEs were transient and mild to moderate in intensity. The most common ( $\geq 10\%$ ) TEAEs (levomilnacipran vs placebo) were headache (12% vs 17%), nausea (3% vs 16%), and dry mouth (8% vs 10%); median time to onset and mean duration of these AEs were similar between placebo and levomilnacipran SR. Potentially clinically significant (PCS) changes in blood pressure/pulse were seen in 0.3%/0.8% of placebo and 0.1%/0.1% of levomilnacipran SR patients. PCS

weight changes ( $\geq 7\%$  increase/decrease) occurred in 1.1%/0.6% placebo and 0.7%/1.8% of levomilnacipran SR patients. C-SSRS-rated suicidal ideation was reported in 27% of placebo and levomilnacipran SR patients; suicidal behavior was reported in 0.3% of placebo and 0.6% of levomilnacipran SR patients. **Conclusion:** Safety data from 2 double-blind trials suggests that levomilnacipran SR was generally well tolerated. Most TEAEs were transient and mild-moderate intensity. This study was funded by Forest Laboratories, Inc.

### NR9-37

#### EXTERNAL TRIGEMINAL NERVE STIMULATION: NONINVASIVE NEUROMODULATION IN MAJOR DEPRESSION

*Chair: Ian Cook M.D.; Author(s): Christopher M. DeGiorgio M.D., Patrick R. Miller, Eve R. Maremont M.D., Lara M. Schrader M.D.*

### SUMMARY:

**Background:** Modulation of brain activity via stimulation of the Trigeminal Nerve (TNS) is an emerging therapy for epilepsy, with an excellent safety profile and significant reductions in seizures in pilot studies in subjects with medically refractory epilepsy [cf 1]. The Trigeminal nerve has reciprocal projections to the nucleus tractus solitarius, the locus coeruleus, and the reticular formation, suggesting TNS may be able to alter activity in structures implicated in mood regulation [1]. In this proof-of-concept project, the effects of TNS on depressive symptoms were examined in Major Depressive Disorder (M.D.D) as an adjunct to pharmacotherapy. Initial findings on the first five subjects were positive [2]; we now present findings on the full set of eleven subjects. **Methods:** Eleven adults (age 31-59, mean 48.9 (8.3 s.d.)) with non-psychotic unipolar M.D.D were studied in an 8-week open label outpatient trial at an academic medical center. Current episodes were required to be of  $>4$  mo. duration, with non-response to at least 1 antidepressant trial over at least 6 weeks during the current episode (ATHF =1), and concomitant use of at least 1 antidepressant. All had prominent residual symptoms, with mean 28-item Hamilton Depression Rating Scale (HDRS-28) scores at study entry of 28.0 (6.9 s.d.), range 19 to 41. Subjects placed stimulating electrodes over the supraorbital branches of the trigeminal nerve for at least 8 hours per day (primarily while asleep), with current adjusted to maximal comfortable levels. Primary outcome was change in HDRS-28 at 8 weeks, with secondary outcomes of 17-item HDRS-17, the Quick Inventory

of Depressive Symptomatology (QIDS), and Beck Depression Inventory (BDI). Results: TNS was well tolerated, no serious adverse events occurred during the 8-week treatment period. Decreases in HDRS-28 scores were significant, from 28.0 (6.9) at entry to 15.8 (6.8) at week 8 (2-tail t-test  $p=0.0001$ ). Responses on the HDRS-17 were also significant, decreasing from 19.3 (5.1) to 9.6 (4.6) ( $p=0.0002$ ). BDI scores similarly declined, from 27.9 (8.3) to 11.7 (7.5) ( $p=0.0003$ ), as did scores on the QIDS, decreasing from 12.4 (4.9) to 6.1 (4.1) ( $p=0.007$ ). Conclusions: Significant decreases in depression severity were achieved in the 8 weeks of acute TNS treatment. This novel approach to brain stimulation may have use as an adjunct to pharmacotherapy in depression. Additional examinations will be needed to delineate efficacy and tolerability with greater reliability, and to examine the range of therapeutic parameters (“dose finding”).

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**NR9-40**  
**EFFICACY AND TOLERABILITY OF VILAZODONE IN PATIENTS WITH MODERATE, MODERATELY SEVERE, AND SEVERE DEPRESSION – POOLED ANALYSES FROM 2 PHASE III TRIALS**

*Chair: Donald Robinson M.D.; Author(s): Wenjie Song, Ph.D., John Edwards, M.D., Adam Ruth, Ph.D.*

**SUMMARY:**

Background: Vilazodone, a serotonin reuptake inhibitor and 5-HT<sub>1A</sub> receptor partial agonist, is approved by the US Food and Drug Administration for treatment of M.D.D in adults. The efficacy and tolerability of vilazodone were evaluated across a spectrum of baseline depression severity in post hoc analyses of data from 2 positive, placebo-controlled trials. Methods: Data from the Phase III, 8-week, double-blind, randomized, placebo-controlled trials (NCT00285376, NCT00683592) were pooled to assess the efficacy of vilazodone across a range of depression severity. The trials included patients 18-70 years of age with DSM-IV-TR-defined M.D.D and a 17-item Hamilton Depression Rating Scale score  $\geq 22$ . Both trials were of similar design, comprising a 1-week screening period followed by an 8-week double-blind treatment period.

Patients randomized to vilazodone were titrated to a target dose of 40 mg, once daily taken with food, over a 2-week period according to a fixed-titration schedule. The primary efficacy outcome (mean change from baseline to Week 8 in Montgomery-Asberg Depression Rating Scale [MADRS] total score) was assessed using an analysis of covariance (ANCOVA) model based on the intent-to-treat (ITT) population with missing values imputed by the last observation carried forward approach. Subgroup analyses stratified patients by baseline depression severity defined by MADRS threshold scores: moderate depression (MADRS $<30$ ), moderately severe depression ( $30 \leq \text{MADRS} < 35$ ), and severe depression (MADRS $\geq 35$ ). Results Of 869 patients (Safety Population), 31% (placebo=143; vilazodone=130) had moderate depression, 49% (placebo=205; vilazodone=220) had moderately severe depression, and 20% (placebo=85; vilazodone=86) had severe depression. In the ITT population, least squares mean difference (LSM.D.) for change from baseline in MADRS was significantly better for vilazodone relative to placebo in each depression subgroup, with no obvious trend across severity of illness: moderate (LSM.D.=-2.9;  $P=.0056$ ), moderately severe (LSM.D.=-2.3;  $P=.0314$ ), and severe (LSM.D.=-4.1;  $P=.017$ ). The percentages of responders ( $\geq 50\%$  MADRS improvement) for vilazodone vs placebo were 41% vs 31% in the moderate ( $P=.0810$ ), 41% vs 29% in the moderately severe ( $P=.0130$ ) and 44% vs 26% in the severely depressed ( $P=.0124$ ) subgroups. Adverse event profiles were similar across severity subgroups. Discussion: Vilazodone treatment compared with placebo showed significantly greater improvement in MADRS in patients with moderate, moderately severe, and severe depression. Mean differences in MADRS change from baseline versus placebo exceeded 2.0 in all 3 groups, treatment effects of clinical significance. The efficacy and tolerability of vilazodone was similar among different depression severity subgroups. This study was funded by Forest Laboratories, Inc.

**NR9-41**  
**MANIA AND ANTISOCIAL PERSONALITY DISORDER TRENDS IN UPPER MIDDLE CLASS CAUCASIAN ADULTS**

*Chair: Sally Blanco-Lutzen B.A.; Author(s): Jena Bobish B.A., Igor Galynker M.D. Ph.D.*

**SUMMARY:**

Introduction: In bipolar mood disorder (BM.D.), symptoms of mania have been shown to correlate with features of narcissistic personality disorder features (NPD). However, less is known about the

relationship between symptoms of mania and features of antisocial personality disorder (ASPD). To this end, we investigated the relationship between the presence of cluster B personality disorder traits and manic symptoms in a group of patients diagnosed with bipolar spectrum disorder. **Methods:** As part of the routine intake for a treatment program, twenty-eight patients, diagnosed with a bipolar spectrum disorder, were administered a diagnostic battery, which included the Self-Report Mania Inventory (SRMI) and Millon Clinical Multiaxial Inventory (MCMI). Using data from these assessments, we ran T-tests to compare patients exhibiting euthymic versus manic symptoms and correlation analyses were conducted to determine what, if any, relationship exists between manic symptoms and traits of cluster B personality disorders. **Results:** Of the twenty-eight subjects, 93% were Caucasian and 60% were female. Their mean age was 39.74 and 60% reported income greater than \$100,000. The mean SRMI score was 10; 9 subjects met the cut off for hypomania and 3 met the cut off for mania, resulting in a total of 12 subjects exhibiting manic symptoms. Further, 2 subjects met the cut off for ASPD and 9 met the cut off for NPD. Of the 12 subjects with SRMI scores greater than 10, two met the cut off for ASPD and 5 met the cut off for NPD. Correcting for multiple comparisons, significant correlations were found between symptoms of mania and scores for ASPD ( $R=.590$ ) and between symptoms of mania and scores for NPD ( $R=.548$ ). **Conclusion:** Similar to the association between narcissistic personality traits and manic symptoms, there exists a strong association between antisocial personality features and manic symptoms. Further research is needed to establish if symptoms of mania should be selectively evaluated and targeted for treatment in patients with antisocial and narcissistic personality traits.

#### NR9-42

### CARIPRAZINE IN THE TREATMENT OF ACUTE MANIA IN BIPOLAR DISORDER: A DOUBLE-BLIND, PLACEBO-CONTROLLED, PHASE III TRIAL

*Chair: Anju Starace B.S.C.; Author(s): Anjana Bose, Ph.D., Qing Wang, Ph.D., Elizabeth Diaz, M.D., Jennifer Goodman, BS, Adam Ruth, Ph.D., György Németh, M.D., István Laszlovszky, M.D.*

#### SUMMARY:

**Objective:** Cariprazine, a D3-preferring dopamine D3/D2 receptor partial agonist, is a novel antipsychotic in development for the treatment of schizophrenia and bipolar mania. Higher affinity for and greater receptor antagonism at D3 versus D2 receptors,

may be associated with antipsychotic efficacy, better tolerability, and beneficial effects on mood. A Phase III clinical trial (NCT01058096) evaluated the efficacy, safety, and tolerability of cariprazine in patients with acute mania associated with bipolar I disorder. **Methods:** In a 6-week, multicenter, placebo-controlled, parallel-group, flexible-dose study, patients (age, 18-65 years) with acute mania associated with DSM-IV-TR-defined bipolar I disorder and a Young Mania Rating Scale (YMRS) score  $\geq 20$  were randomized to cariprazine 3-12 mg/day or placebo for 3 weeks of double-blind treatment. Patients were hospitalized for a 4-7 day wash-out screening and at least 14 days of treatment. There was a subsequent 2-week safety follow-up period. Primary efficacy endpoint: YMRS total score change from baseline to the end of Week 3 analyzed using a mixed-effects model of repeated measures (MMRM) approach on the intent-to-treat (ITT) population; secondary efficacy: Clinical Global Impressions-Severity (CGI-S). Safety was evaluated by adverse events (AEs), clinical laboratory values, vital signs, electrocardiograms (ECGs), and extrapyramidal symptom (EPS) scales. **Results:** A total of 312 patients were randomized and received at least 1 dose of double-blind treatment (placebo, 154; cariprazine, 158); 69% and 68% of placebo and cariprazine patients, respectively, completed the study. Baseline YMRS scores were similar between groups (placebo, 32.0; cariprazine, 32.8). Statistically significant improvement was demonstrated in cariprazine 3-12 mg/day patients relative to placebo on YMRS (LSM.D., -4.3;  $P<.001$ ; MMRM) and CGI-S (LSM.D., -0.4;  $P<.01$ ; MMRM) change from baseline to Week 3. Overall premature discontinuation rates were similar for cariprazine and placebo patients (32% and 31%). Treatment-emergent AEs (TEAEs) occurred in 80% and 63% of cariprazine and placebo patients, respectively; the most common AEs ( $\geq 10\%$  and twice the rate of placebo) were akathisia, extrapyramidal disorder, tremor, dyspepsia, and vomiting. Cariprazine was generally well tolerated; 10% of cariprazine- and 7% of placebo-treated patients discontinued due to AEs. EPS-related AEs occurred in 46% and 12% of cariprazine and placebo patients, respectively. **Conclusions:** Results from this Phase III study demonstrated that cariprazine was effective in the treatment of acute mania associated with bipolar I disorder. Cariprazine was safe and generally well tolerated in this group of patients. This study was funded by Forest Laboratories, Inc. and Gedeon Richter Plc.

#### NR9-43

### A RANDOMIZED CONTROLLED TRIAL OF ESCITALOPRAM AND

**TELEPHONE-ADMINISTERED  
PSYCHOTHERAPY IN MAJOR DEPRESSIVE  
DISORDER: FOCUS ON WORK  
PRODUCTIVITY**

*Chair: Raymond Lam M.D.; Author(s): Sagar V. Parikh, M.D.; Rajamannar Ramasubbu, M.D., M.Sc.; Erin E. Michalak, Ph.D.; C.V. Manjunath, M.D.*

**SUMMARY:**

Objectives: There is still little information about gains in work productivity with effective treatment of major depressive disorder (M.D.D), in part because the intensive nature of randomized controlled trials (RCTs) makes it difficult for working patients to participate. In this study, we used a novel clinical trials methodology to examine work productivity outcomes in treatment of M.D.D. Methods: The WORKER Study was a 12-week RCT of escitalopram plus cognitive-behaviour therapy (CBT) in employed patients with M.D.D. Eligible patients were treated with 10-20 mg of escitalopram and then randomized to 8 sessions of a validated brief CBT program administered by trained therapists over the telephone, or to adherence reminder telephone calls. Outcome measures included the Montgomery Asberg Depression Rating Scale (MADRS) administered by blind raters over the telephone, and work productivity questionnaires (e.g., Lam Employment Absence and Productivity Scale [LEAPS], Sheehan Disability Scale [SDS]) were completed on-line over a secure web site. Analysis was conducted using repeated measures multivariate analysis of variance in a modified intent-to-treat sample (patients who had at least one post-baseline assessment). Results: A total of 105 patients were randomized, with 98 evaluable patients in the modified intent-to-treat sample. At the primary 12-week endpoint, there were no significant differences between conditions in change in MADRS score or in response or remission rates. However, the escitalopram + Tel-CBT condition showed significantly greater improvement than the escitalopram + reminders condition on measures of work productivity (LEAPS) and psychosocial functioning (SDS). Conclusions: Compared to escitalopram alone, the addition of telephone-administered CBT did not improve symptom-based depression rating scale scores or response/remission rates in patients with M.D.D, but did significantly improve functional outcomes, including work productivity. These results also confirm other studies showing differences between symptom-based and functioning outcomes, suggesting that these outcomes should be assessed independently in clinical trials of M.D.D.

**NR9-44**

**THE RELATIONSHIP BETWEEN  
PERSONALITY TRAITS AND COPING  
STYLES IN BIPOLAR PATIENTS AND  
THEIR CAREGIVERS PRESENTING FOR  
FAMILY-INCLUSIVE TREATMENT**

*Chair: Allison Lee M.D.; Author(s): Jena Bobish, B.A., Deimante McClure, B.S., Stan Kats, B.S., Igor Galynker, M.D., Ph.D.*

**SUMMARY:**

Introduction: Patients' coping styles are known to affect the course and treatment outcome of Bipolar Disorder. While personality characteristics in bipolar patients have been well-studied, little is known about personality characteristics in caregivers of bipolar patients and how these characteristics may relate to coping styles in patients and caregivers. In this study, we assessed personality dimensions and coping styles in bipolar patients and their caregivers compared with healthy controls. Methods: Patients diagnosed with Bipolar Disorder by the Structured Clinical Interview for DSM-IV, Patient Edition (SCID-IP) were recruited from the Family Center for Bipolar in New York City as part of a larger study of Family-Inclusive Bipolar Treatment. Healthy controls were recruited by internet advertisement. At study intake, participants were administered the NEO-Five Factor Inventory (NEO-FFI) to assess personality characteristics and the Brief COPE to measure coping styles. Results: Eighteen patients, nineteen caregivers, and nineteen healthy controls were recruited. Caregivers and controls did not differ significantly in personality dimensions. However, patients scored significantly higher on neuroticism ( $p = .000$ ) and lower on extraversion ( $p = .004$ ) and conscientiousness (trend,  $p = .06$ ) than controls. Patients and caregivers differed significantly, with higher neuroticism ( $p = .000$ ) and lower agreeableness ( $p = .00$ ) and conscientiousness ( $p = .001$ ) than caregivers. In patients, neuroticism appeared to have the strongest relationship with coping styles, being negatively correlated with active coping ( $t = -.576, p = .01$ ) and positively correlated with substance use ( $p = .03$ ), use of emotional support ( $p = .01$ ), behavioral disengagement ( $p = .03$ ), and self-blame ( $p = 0.16$ ). In caregivers, openness was the personality characteristic most related to style of coping, being positively correlated with self-distraction ( $p = .012$ ), active coping ( $p = .015$ ), use of instrumental support ( $p = .003$ ), and venting ( $p = .008$ ). Discussion: In our sample of bipolar family treatment participants, we found that patients and caregivers differed substantially in their personality characteristics and in the relationship of those characteristics with

coping strategies. These differences may be due to role differences or to differences in the stressors with which each group is coping. These results may have implications for family therapy which could help improve clinical outcome for these dyads.

#### NR9-45

### A PILOT STUDY OF FUNCTIONAL OUTCOME IN POSTPARTUM DEPRESSION IN WOMEN TREATED WITH DESVENLAFAXINE

*Chair: Shaila Misri M.D.; Author(s): Jasmin Abizadeh, B.A.; Deirdre Ryan, M.D.; Diana Carter, M.D.*

#### SUMMARY:

**Objective:** This prospective, open-label study examined the functional outcome, impact of change in depression and anxiety symptoms and tolerability of Desvenlafaxine in the treatment of postpartum depression. Impact of treatment on restoring women to full functionality, and not simply remission of symptoms, was assessed. **Methods:** Thus far, 17 postpartum, non-nursing women have enrolled in this study with a diagnosis of Major Depressive Disorder, postpartum onset and often with a comorbid anxiety disorder. This is a 12 week study, with bi-weekly assessments of mood, anxiety, panic, obsessions/compulsions and quality of life. Blood pressure, weight and side effects were recorded regularly. The dose ranged from 50mg-100mg/day of Desvenlafaxine. **Results:** Recruitment for this pilot study is ongoing. So far, dropout rate has been 35.29%, completion rate is 52.94% and in progress rate is 11.76%. At study entry, the mean level of depression was of severe levels and the mean level of anxiety was at moderate levels. Functionality was markedly impaired in all three areas of work/school, home responsibilities and social life. 88.9% reached remission of depressive symptoms by week 12 (MADRS,  $p=.05$ ) and 77.8% reached remission of anxiety symptoms by the same time point (HAM-A,  $p=.05$ ). Functionality was only mildly to moderately impaired for work/school (50%) ( $p=.05$ ), home responsibilities (77.8%) ( $p=.005$ ) and social life (77.8%) ( $p=.005$ ), with about half of all women only experiencing mild impairments. The average dose of response was 100 mg/day of Desvenlafaxine for 88.88% of the participants. No significant change in weight or blood pressure was observed from baseline to week 12. Symptoms associated with generalized anxiety disorder, panic disorder and obsessive compulsive disorder decreased over the course of 12 weeks, but not everyone experienced complete remission. Nausea and hot and cold flashes were the most commonly reported side effects. Nausea was a transient side effect, along with headaches, compared to hot flashes, which were

more persistent and did not cease by week 12. Dropout reasons included side effects (anxiety, rash, lethargy, headache) (33.33%), conception on the medication (16.67%) and noncompliance with the medication/study regime (e.g. inconsistent use, willingness to start/attend appointments, etc.) (50%). **Conclusion:** Majority of patients reached remission of depressive and anxiety symptoms on 100mg of Desvenlafaxine. Functionality improved for all participants, but only 50% reached mild levels of impairment, with the others still experiencing moderate impairments in work, family and social areas. Particularly, those patients with comorbid anxiety disorders continued to show clinically significant levels of anxiety or impaired functionality. Nausea was a minimal and transient side effect, where as hot flashes were persistent. Blood pressure and weight remained unchanged.

#### NR9-46

### USE OF ADJUNCTIVE L-METHYLFOLATE AS PERSONALIZED THERAPY IN SSRI-RESISTANT MAJOR DEPRESSIVE DISORDER

*Chair: George Papakostas M.D.; Author(s): John M. Zajecka, M.D.; Richard C. Shelton, M.D.; Alisabet Clain, Ph.D.; Lee Baer, Ph.D.; Michael Pencina, Ph.D.; Allison Meisner, Ph.D.; Maurizio Fava, M.D.*

#### SUMMARY:

**Objectives:** L-methylfolate modulates the synthesis of monoamines, including serotonin, norepinephrine, and dopamine. As a consequence, L-methylfolate is a trimonoamine modulator (TMM) and indirect regulator of trimonoamine neurotransmitter synthesis and monoamine concentrations. Various surrogate markers have been identified that predict the response to treatment in major depressive disorder (M.D.D). For instance, obesity (body mass index [BMI] =30 kg/m<sup>2</sup>) is known to increase the risk of M.D.D (Luppino et al, 2010; Simon et al, 2008) and a decreased response to antidepressants (Kloiber et al, 2007). The objectives of this analysis were to evaluate the presence of specific biomarkers (L-methylfolate serum level, BMI, methylenetetrahydrofolate reductase C677T genotype) on the efficacy and tolerability of adjunctive L-methylfolate 15 mg in a multi-center, double-blind, placebo-controlled trial of L-methylfolate used as an adjunct to selective serotonin reuptake inhibitors (SSRIs). **Methods:** 75 outpatients with SSRI-resistant M.D.D were enrolled in a 60-day, multi-center, double-blind, placebo-controlled trial divided into two 30-day phases. Patients were randomized to receive L-methylfolate 15 mg/day for 60 days, placebo for

30 days followed by L-methylfolate 15 mg/day for 30 days or placebo for 60 days. Secondary genomic and biomarker endpoints were evaluated for their association with treatment effect. Results: Increased efficacy was observed with adjunctive L-methylfolate 15 mg/day vs. SSRI therapy plus placebo [pooled difference in response rates on the HDRS-17 (17.7%,  $p=0.04$ )]. Pooled differences in mean change on HDRS-17 and HDRS-28 were significantly different ( $p=0.05$  and  $p=0.02$ , respectively). Treatment effects were similar in patients with baseline L-methylfolate levels below vs. above the median. A numerically greater treatment effect was observed in patients with an allelic variant in the MTHFR (methylentetrahydrofolate reductase) C677T genotype (difference in mean change in HDRS-28 of -3.75 for 't' allele (homozygotes and heterozygotes combined) vs. -1.99 for 'cc' allele). Patients with a BMI =30 kg/m<sup>2</sup> experienced a significantly greater reduction in depressive symptoms with L-methylfolate (difference in mean change in HDRS-28 of -4.66;  $p=0.001$ ). Conclusion: L-methylfolate 15 mg/day added to SSRIs can be an effective and well-tolerated adjunctive treatment strategy for M.D.D patients who are partial- or non-responders to antidepressant therapy. Adjunctive L-methylfolate may be particularly effective in patients with a BMI =30 kg/m<sup>2</sup>, or in patients with a MTHFR C677T 'T' allele.

**NR9-47**  
**RESULTS OF TRANSCRANIAL MAGNETIC STIMULATION (TMS) IN A NATURALISTIC CLINICAL SETTING: A BIOPSYCHOSOCIAL INTEGRATED CLINICAL CARE APPROACH**

*Chair: James Halper M.D.; Author(s): Alan Manevitz, M.D. Yoko Kanamori John Keilp, Ph.D.*

**SUMMARY:**

As the first clinical providers of TMS in New York City, we are presenting results with a large number of patients treated in the naturalistic setting of a private care office. Patients requesting TMS in the 'real world' do not present 'cleanly' with only a major depressive disorder (as were the cases included in both the pivotal FDA Approval studies and the NIH double-blind study that appeared in the May, 2010 Archives of General Psychiatry). Patients referred to us in the first three years of TMS were some of the most 'treatment-resistant' cases seen by our colleagues. They presented with a range of medication trial failures (4-20) and multiple psychotherapy failures (including CBT, DBT, group and multiple dual diagnoses (for example, Depression and Anxiety, Depression and Borderline Disorders) and a broad age range (17-92). Our patients all had treatment

resistant depression and additional diagnoses. We report on our clinical 'biopsychosocial' approach that yielded remission and response rates exceeding those reported in the 2 pivotal studies alluded to above despite failures to respond to multiple medications

**NR9-48**  
**THE EFFICACY OF LEVOMILNACIPRAN IN THE TREATMENT OF MAJOR DEPRESSIVE DISORDER: RESULTS FROM A PHASE III CLINICAL TRIAL**

*Chair: Carl Gommoll M.S.; Author(s): Anjana Bose, Ph.D., Changzheng Chen, Adam Ruth, Ph.D.*

**SUMMARY:**

Objective: Levomilnacipran (1S, 2R-milnacipran) is a potent and selective serotonin and norepinephrine reuptake inhibitor (SNRI) with preference for the norepinephrine transporter. To determine the efficacy of levomilnacipran sustained released (SR) across symptom domains in major depressive disorder (M.D.D), prospective and post hoc analyses were conducted on a positive fixed-dose Phase III trial (NCT00969709). Methods: An 11-week, double-blind, multicenter, parallel-group, placebo-controlled, fixed-dose study in patients aged 18-65 years who met DSM-IV-TR criteria for M.D.D. Patients had a current major depressive episode  $\geq 8$  weeks and a score  $\geq 30$  on the Montgomery-Asberg Depression Rating Scale-Clinician Rated (MADRS-CR). The study comprised a 1-week single-blind, placebo lead-in, 8-week double-blind treatment, and 2-week double-blind down-taper. Patients were randomized to placebo or once-daily levomilnacipran SR 40 mg, 80 mg, or 120 mg, initiated at 20-mg and titrated to target dose over 7 days. Primary efficacy: MADRS-CR total score change from baseline to end of Week 8 analyzed using a mixed-effects model for repeated measures (MMRM) approach on the intent-to-treat (ITT) population. Secondary efficacy: Sheehan Disability Scale (SDS) total score change from baseline to Week 8 analyzed using a similar approach. Additional efficacy: HAM.D.17, SF-36, CGI-S, and CGI. Safety and tolerability were evaluated. Post hoc analyses evaluated change from baseline to Week 8 on MADRS-CR single items (MMRM, ITT). Results: The least squares mean difference (LSM.D.) for MADRS-CR total score change from baseline showed all dose groups were significantly superior to placebo: levomilnacipran SR 40 mg (-3.23,  $P=.0186$ ), 80 mg (-3.99,  $P=.0038$ ), and 120 mg (-4.86,  $P=.0005$ ). On the SDS, significantly greater improvement versus placebo was seen for levomilnacipran SR 80 mg (LSM.D., -2.51;  $P<.05$ ) and 120 mg (LSM.D., -2.57;  $P<.05$ ). For levomilnacipran SR

80- and 120-mg dose groups, significant improvement relative to placebo was also seen on the HAM.D.17, SF-36, CGI-S, and CGI-I assessments. Improvement across symptom domains was demonstrated by significantly greater decrease in most MADRS-CR single item scores for levomilnacipran SR 80 mg and 120 mg versus placebo ( $P < .05$ ). Levomilnacipran SR was generally well tolerated; however, significantly more patients in the levomilnacipran SR groups discontinued due to AEs (1.7% for placebo and 7.3%, 14.5%, and 6.7%, for levomilnacipran SR 40 mg, 80 mg, and 120 mg, respectively). Conclusions: Levomilnacipran SR 40 mg, 80 mg, and 120 mg demonstrated significant, dose-proportional improvement in depressive symptoms relative to placebo. Post hoc analysis demonstrated superiority for the levomilnacipran 80- and 120-mg doses across symptom domains. Levomilnacipran SR was generally well tolerated; however, significantly more levomilnacipran SR patients discontinued due to AEs. This study was funded by Forest Laboratories, Inc.

#### NR9-49

### THE CLINICAL RELEVANCE OF RESULTS ACHIEVED WITH VILAZODONE IN THE TREATMENT OF MAJOR DEPRESSIVE DISORDER

*Chair: John Edwards M.D.; Author(s): Arif Khan, M.D., Wenjie Song, Ph.D., Adam Ruth, Ph.D.*

#### SUMMARY:

**Objective:** Vilazodone, a serotonin reuptake inhibitor and 5-HT<sub>1A</sub> receptor partial agonist, is approved by the US Food and Drug Administration for the treatment of major depressive disorder (M.D.D) in adults. Efficacy and safety were established in two 8-week clinical trials (RCT-1: NCT00285376; RCT-2: NCT00683592). To evaluate the clinical relevance of vilazodone, efficacy and safety outcomes from these trials were used to estimate the number needed to treat (NNT) for response and remission, and the number needed to harm (NNH) for adverse events (AEs) and discontinuation. **Methods:** Post hoc analyses of pooled data from two 8-week, double-blind, randomized, controlled trials (RCT-1 and RCT-2) of vilazodone (n=436) versus placebo (n=433) were conducted. Patients were 18-70 years of age with DSM-IV-TR-defined M.D.D and a minimum score  $\geq 22$  on the 17-item Hamilton Depression Rating Scale (HAM.D.17). Study design was similar in both trials; patients randomized to vilazodone were titrated to a 40-mg target dose, taken once daily with food, over 2 weeks. Mean change from baseline to Week 8 in Montgomery-Asberg Depression Rating Scale (MADRS) and safety variables were assessed in

both studies; secondary efficacy endpoints included HAM.D.17, Clinical Impressions-Improvement (CGI-I) and -Severity (CGI-S). Post hoc analyses estimated the effect of vilazodone relative to placebo on NNT for response (MADRS  $\geq 50\%$  improvement, CGI-I  $\leq 2$ ) and remission (MADRS  $\leq 10$ , MADRS  $\leq 12$ ); NNH for time to discontinuation due to AEs and common AEs were also estimated. For efficacy endpoints, the last observation carried forward (LOCF) approach was used. Results: Pooled baseline demographic and disease characteristics were similar between groups. Pooled MADRS change from baseline was significantly superior for vilazodone versus placebo (LSM.D. [95% CI] -2.79 [-4.14, -1.44];  $P < .0001$ ); significant improvement on secondary measures in favor of vilazodone was also seen ( $P < .01$  for all 3). The NNT (95% CI) for response was 8 (5, 17) for MADRS  $\geq 50\%$  improvement and 7 (5, 14) for CGI-I  $\leq 2$ . The NNT (95% CI) for remission was 12 (7, 37) for MADRS  $\leq 10$  and 8 (5, 15) for MADRS  $\leq 12$ . AEs tended to occur early in the course of treatment; 7% of vilazodone- and 3% of placebo-treated patients discontinued due to AEs. The NNH (95% CI) for discontinuation due to AEs was 26 (15, 106). Conclusion: Vilazodone treatment compared with placebo was associated with significant improvement in symptoms of M.D.D. An NNT for response  $\leq 10$  is generally regarded as evidence for clinical relevance in depression treatment; NNT values for remission reported here are well within the range observed for other antidepressants. This NNT and NNH analysis suggested a lower risk of discontinuation due to AEs relative to clinically meaningful improvement for vilazodone. This study was funded by Forest Laboratories, Inc.

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#### NR9-50

### 12-MONTH, OPEN-LABEL, RELAPSE-PREVENTION STUDY OF L-METHYLFOLATE 15 MG AS ADJUNCTIVE THERAPY WITH SSRIS FOLLOWING ACUTE REMISSION OF M.D.D

*Chair: John Zajecka M.D.; Author(s): George I. Papakostas, M.D.; Richard C. Shelton, M.D.; Maurizio Fava*

#### SUMMARY:

**Objective:** The optimal goal of therapy in major depressive disorder (M.D.D) is long-term remission of signs and symptoms. However, maintenance of remission during long-term therapy in M.D.D patients can still result in high rates of relapse and recurrence (Paykel et al, 1995). In two short-term, randomized, placebo-controlled trials, the efficacy and tolerability of L-methylfolate 15 mg/day added to SSRI therapy were

demonstrated in patients with M.D.D not responding to monotherapy. The objective of this analysis was to determine the efficacy of adjunctive L-methylfolate in preventing relapse and maintaining remission in a 12 month of open-label treatment in double-blind phase remitters. Methods: All subjects completing one of two double-blind, placebo-controlled studies of L-methylfolate 7.5-15 mg as adjunctive therapy with SSRIs were offered participation in a 12-month continuation/maintenance phase of open-label treatment with SSRI + L-methylfolate. Subjects were assessed over a 12 month period for relapse/recurrence (HDRS-17 >15), sustained response (=50% decrease in HDRS-17), sustained remission (HDRS-17 =7), and adverse events. Results: 165 subjects completed the double-blind study phases and also participated in the open-label phase for up to 12 months. 13 subjects who achieved remission during the double-blind study phase entered the open-label maintenance phase. No subject experienced relapse/recurrence (HDRS-17 >15) at any time point. Twelve (92%) of 13 remitted subjects on L-methylfolate + SSRI completed the 12-month open-label phase. At the end of 12 months, 7 of 13 (53.8%) subjects had sustained full remission (HDRS-17 =7). The incidence of adverse events during the open-label phase was lower than during double-blind treatment, and none of the 165 subjects discontinued due to adverse events. Conclusion: L-methylfolate as an adjunct to SSRIs in partial or non-responders was associated with prevention of relapse/recurrence of M.D.D in subjects receiving open-label treatment for 12 months following acute remission. High retention rates, lack of relapse/recurrence, and high rates of sustained remission suggest that L-methylfolate is a valuable additional to standard monotherapy for treating M.D.D. L-methylfolate was well tolerated during long-term, open-label treatment. Conclusions are limited by the open-label design; however, the majority of subjects maintained remission achieved during the double-blind, placebo-controlled trial for an additional 12 months and none relapsed. Additional research is needed to clarify the role of L-methylfolate for enhancing the likelihood of achieving a sustained remission in M.D.D.

**NR9-51**  
**PREDICTORS OF RESPONSE AND REMISSION**  
**DURING AN OPEN-LABEL 10-WEEK TRIAL**  
**WITH SELEGILINE TRANSDERMAL SYSTEM**  
**(STS)**

*Chair: Sungwon Jung M.D.; Author(s): Saebeon Jung M.D., Chiun Pae M.D., Ph.D., Prakash S Masand, M.D., Kimberly Blanchard Portland Ph.D., Paul Mastoridis, Pharm. D., Ashwin A Patkar M.D., M.R.C.Psyc*

**SUMMARY:**

Objective: Patient and treatment characteristics that influence treatment response and remission in major depressive disorder (M.D.D) are of clinical interest. This post hoc analysis investigated clinical characteristics predictive of response and remission in a 10-week open-label trial of selegiline transdermal system (STS). Method: The data analyzed included 10 weeks of open-label treatment with 6 mg/24 hrs of STS in patients with M.D.D. This was the stabilization phase of a 52-week, placebo-controlled double-blind relapse prevention trial with STS. Response was defined as = 50% reduction in Hamilton Depression Rating Scale (HAM.D.-17) score and remission was defined as HAM.D.-17 score of = 10. Pretreatment demographics, illness course, treatment resistance and symptom domains were studied to identify predictors of response. Results: 675 patients entered the trial. The response rate was 53.3% by the end of 10 weeks and remission rate was 47.1%. Dropout rate was 15.4%. Early response (within first 2 weeks of treatment) ( $p < 0.005$ ), retardation ( $p < 0.05$ ), sexual difficulties ( $p < 0.005$ ) and hypnotic use ( $p < 0.05$ ) were significant predictors of response. The same factors also significantly predicted remission. Subjects with atypical, melancholic or anxious features had comparable response and remission rates on STS to those without those features. Conclusions: Early response was a strong predictor of end of treatment response and remission with STS. Retardation and sexual difficulties also predicted outcome with STS. Patients with atypical or melancholic features responded equally well. The results demonstrate patient characteristics that may be helpful for clinicians while treating patients with STS. Key words: selegiline transdermal system, major depressive disorder, predictors, relapse

References 1. Amsterdam JD, Bodkin JA. Selegiline transdermal system in the prevention of relapse of major depressive disorder: a 52-week, double-blind, placebo-substitution, parallel-group clinical trial. *J Clin Psychopharmacol.* 2006 Dec;26(6):579-86 2. Patkar AA, Pae CU, Masand PS. Transdermal selegiline: the new generation of monoamine oxidase inhibitors. *CNS Spectr.* 2006 May;11(5):363-75. EDUCATIONAL OBJECTIVE At the conclusion of this session, the participant can understand clinical characteristics that may predict response/remission with short term (10 week) treatment with selegiline transdermal system in patients with major depressive disorder.

**TUESDAY MAY 08, 2012**

**NEW RESEARCH OTHER****NR10-01****INTERNET ADDICTION: A REVIEW OF AVAILABLE MEASURES**

*Chair: Jayce Fryman None Author(s): Delaney Smith, M.D.*

**SUMMARY:**

**Objectives:** At the conclusion of this session, the participant should be able to appreciate the different tests available to screen for and diagnose internet addiction. **Methods:** A literature review was performed in pub med using terms “Internet Addiction and Criteria,” “Internet Addiction and Measure,” “Internet Addiction and Test” and “Internet Addiction and Diagnosis” These articles were then reviewed for references to additional studies. **Results:** Ten scales were identified which purported to evaluate for internet addiction or maladaptive internet use. There was significant overlap in the items assessed by the test; including preoccupation with internet use, increasing amount of time spent on line, and social, educational, and financial impacts of internet use. The selection of participants to study the tests varied but was frequently college students. Several tests used existing DSM-IV diagnoses including pathological gambling and substance dependence as a basis for their diagnostic criteria. **Conclusions:** While there are many measures available to help clinician assess for problematic internet use, the diagnosis remains controversial.

**NR10-02****SELEGILINE TRANSDERMAL SYSTEM (STS) FOR MAJOR DEPRESSIVE DISORDER (M.D.D): USE PATTERN, ADHERENCE, AND EFFECT ON HEALTH SERVICE EXPENDITURES**

*Chair: David Sclar Ph.D.; Author(s): Lawrence J. Cohen, M.D. Kimberly Blanchard Portland, Ph.D.*

**SUMMARY:**

**Objective:** There is renewed interest in the use of MAOIs for the treatment of M.D.D, specifically M.D.D with atypical features, anxious features, and treatment-resistant depression (TRD). The American Psychiatric Association and the British Association for Psychopharmacology guidelines for depression list use of MAOIs as an option for TRD. Selegiline is an irreversible inhibitor of MAO enzymes. The selegiline transdermal system (STS) bypasses first pass metabolism, and thereby inhibits MAO in the brain without

significantly inhibiting MAO in the gut. The present study was designed to discern: (i) the pattern (sequence) of use of STS in M.D.D; (ii) level of adherence to STS as compared to alternative antidepressant pharmacotherapy; and (iii) health service expenditures. **Methods:** This research employed patient-level data abstracted from domestic (U.S.) longitudinal archives (Medicaid; Medicare; managed care), cross-sectional surveys (U.S. National Center for Health Statistics), and the published literature. M.D.D was defined as ICD-9-CM codes 296.2, 296.3, 300.4 or 311. Treatment failure (TF) was defined as receipt of <90 days of antidepressant pharmacotherapy. For longitudinal analyses primary criterion were: (1) ambulatory patients aged 18 through 75 years; (2) continuous enrollment of 18 months (six months prior to an ICD-9-CM code for M.D.D (index date); 12 months post index date); (3) no ICD-9-CM code(s) for co-morbid mental illness; (4) initial antidepressant pharmacotherapy: SSRI, SNRI, or STS. Chi-square, multivariate logistic regression, and log-transformed multivariate linear regression were used to assess sequential use of antidepressant pharmacotherapy, predictors of level of adherence, and health service expenditures (intent-to-treat (ITT) and propensity-score basis), respectively. For longitudinal data, cross sectional data, and published literature, Monte-Carlo simulation (10,000 iterations) was used to further discern and compare 12 month fiscal-risk profiles for the observed use pattern. **Results:** For the majority of patients (94%), STS was prescribed as a second or third treatment option for M.D.D. Specifically, post TF with one SSRI or SNRI (22%); post TF with a second SSRI or SNRI (67%); or post TF with an SSRI or SNRI and augmentation with an atypical antipsychotic (11%). Adjusted for use pattern sequence, STS was associated with a greater probability of receipt of 90 or 180 days of pharmacotherapy ( $p<0.05$ ). On an ITT or propensity-score basis, use of STS as the last medication prescribed resulted in comparable ( $p=NS$ ) or reduced ( $p<0.05$ ) health services expenditures, and greater probability of receipt of 90, or 180 days of pharmacotherapy ( $p<0.05$ ). **Conclusion:** Treatment failure is associated with increased health service expenditures. Use of STS post TF (ITT or propensity-score basis) resulted in increased adherence and comparable or reduced health service expenditures. After an antidepressant TF, early use of STS may be warranted.

**NR10-03****A COMPARISON OF DIAGNOSTIC CLARITY USING THE MINI AND SCID IN A COMMUNITY MENTAL HEALTH SETTING**

*Chair: Raymond Kotwicki M.D.; Author(s): Philip D. Harvey, Ph.D., Kimberly D. Farris, Ph.D., MSW*

**SUMMARY:**

Background: Psychiatric diagnoses are important for treatment planning, particularly of pharmacological interventions. Some data indicate that clinician diagnoses early in the course of psychiatric illnesses or of certain conditions, such as bipolar disorder, are likely to be changed after reconsideration or after reassessment with structured diagnostic assessments. The length of psychiatric interviews varies markedly, with brief assessments such as the MINI taking much less time than traditional measures. In a previous study we found that applying the Structured Clinical Interview for the DSM (SCID) led to very low rates (5%) of modification of diagnosis over the course of an outpatient rehabilitation treatment. Methods: In this study, we implemented an abbreviated structured psychiatric interview procedure for all new admissions to a private outpatient rehabilitation facility, using the MINI International Neuropsychiatric Interview. Diagnostic interviews were conducted by clinicians at the time of admission. We examined the likelihood of changes in MINI-derived diagnoses from admission to discharge (averaging 13 weeks) for one year of consecutive admissions. We compared those rates of change to other indices: the proportion of cases where the MINI diagnosis differed from Clinical diagnoses provided by referring clinicians and our previous one year study with the SCID. Results: Two hundred and two cases received a MINI at admission and discharge diagnoses were available for 137 of those cases. The MINI assessment found disagreement with referring clinician diagnoses in 64% of cases. When the MINI diagnoses were examined for their rates of being changed by clinicians prior to discharge, we found that 89% of the diagnoses generated at admission with the MINI were listed as the primary discharge diagnosis for the patients. Thus, when compared to historical SCID data from the previous year, the stability of MINI diagnoses compared quite favorably (89% vs 95% stability) and suggested considerable improvements on unstructured clinical diagnoses. Discussion: In this community rehabilitation setting, there appears to be a reasonable trade-off between brevity and accuracy through the use of the MINI compared to the SCID. Clinical diagnoses were minimally overlapping with the results of structured diagnoses and suggest that structured assessment, particularly early in the course of illness, may lead to more accurate treatment planning. Implications: These results suggest that structured interviews lead to admission diagnoses that are more consistent with the longer-term impressions of patient's clinical condition.

It is likely that patients whose diagnosis is decided early in the case of long-term treatment will receive treatments that are more consistent and, in the case of pharmacological interventions, more consistent with approved therapies for their illness.

**NR10-04**

**ADOLESCENTS AT RISK OF DEPRESSIVE DISORDERS: PREVALENCE AND ASSOCIATED FACTOR IN COLOMBIAN STUDENTS**

*Chair: Zuleima Cogollo R.N.; Author(s): Edna M. Gómez-Bustamente, Nurs, MSc, Ph.D. (c) Edwin Herazo, M.D., MSc Adalberto Campo-Arias, M.D., MSc*

**SUMMARY:**

Background: Around the world, it is increases adolescents at risk of depressive disorders. However, few Colombian studies have explored the prevalence and associated factors with risk of depression among adolescent students in Colombia. Objective: To establish the prevalence and associated variables with risk of depressive disorders in a probabilistic sample of adolescent students from private and State school in Cartagena, Colombia. Method: A cross-sectional research was carried out. A cluster sample of middle- and high-school students completed the Well-Being Index (WHO-5); scores under six were taken as at risk of depressive disorders. Logistic regression was computed to adjust associated variables. Results: A total of 2,625 adolescents participated in the research. The mean of age was 13.8 years old (SD=2.0); and 54.3% were females. WHO-5 showed high reliability (Cronbach alpha 0.745 and McDonald omega 0.752). It was found that 189 students (7.2%) were at risk of depressive disorders. Family dysfunction (OR=3.9; 95% CI 2.7-5.6), poor health perception (OR=2.1; 95% CI 1.5-2.9) and female gender (OR=1.4; 95% CI 1.1-2.0) were associated with risk of depressive disorders. Conclusions: Near one out thirteen Colombian adolescent students is at risk of depressive disorders. Family dysfunction is the main associated variable. It is important to identify adolescents at risk of depressive disorders and modify related factors.

**NR10-05**

**MOOD DISORDER QUESTIONNAIRE FOR SCREENING BIPOLAR DISORDERS IN EMERGENCY DEPARTMENT PATIENTS IN LATIN-AMERICAN COUNTRIES**

*Chair: Ruby Castilla-Puentes M.D.; Author(s): Ricardo Secin M.D.; Roxana Galeno M.D.; Arturo Grau M.D.; Jorge Ospina M.D.; Alvaro Camacho M.D.; Alfredo Cia M.D.;*

*Jose Luis Ayuso M.D.; Castulo Cisneros M.D.; Jorge Tellez M.D.*

#### **SUMMARY:**

This study examines how effectively the Mood Disorder Questionnaire (M.D.Q), a self-administered screening instrument, recognizes bipolar disorders (BPD) in Emergency Department (ED) patients from hospitals in Argentina, Brazil, Chile, Colombia, and Mexico. A selected sample of 1,505 patients (mean age 35.8 years, 59% women) was screened with the M.D.Q and additionally examined with structured interviews. The comparison in the 13 symptoms domains from M.D.Q between bipolar and non-bipolar patients showed differences statistical significance at level  $p = 0.05$  for euphoria, trouble concentrating, hypersociability and excessive spending. In addition, irritability, lack of need for sleep, pressured speech, racing thoughts and risky behaviors reached a level of significance of  $p = 0.001$ . Eighty six patients were positive in the M.D.Q screen. In the psychiatric interview, 85 patients were found to suffer from BPD, of whom 69 (82%) with bipolar II but only sixteen (18%) with bipolar I disorder. The sensitivity and specificity of the M.D.Q for detecting DSM-IV-diagnosed BPD are 91.7% (83.7% to 96.6%) and 99.4% (98.8% to 99.7%), respectively, in this ED population. The M.D.Q was found internally consistent (alpha 0.79) and a feasible screening tool. Several previous results could be confirmed, and under consideration of some limitations, the M.D.Q seems to be a valuable tool for identifying BPD in ED population.

#### **NR10-06**

#### **THE OHIO ARMY NATIONAL GUARD MENTAL HEALTH INITIATIVE: PREVALENCE OF DSM-IV DISORDERS**

*Chair: Marijo Tamburrino M.D.; Author(s): Philip Chan, M.S., Marta Prescott, M.P.H., Joseph Calabrese, M.D., Israel Liberzon, M.D., Renee Slembariski, M.B.A., Emily Goldmann, M.P.H., Edwin Shirley, Ph.D., Thomas Fine, M.A., Toyomi Goto, M.A., Kimberly Wilson, M.S.W., Stephen Ganocy, Ph.D., Alphonse Derus, B.S., Mary Beth Serrano, M.A., James Sizemore, M.Div., Sandro Galea, M.D.*

#### **SUMMARY:**

**Objective:** To explore the lifetime and current prevalence of DSM-IV Axis I disorders among a subsample of the Ohio Army National Guard (OHARNG). **Method:** 1052 (40.2%) of 2616 OHARNG soldiers who completed a telephone survey were randomly invited to participate in the in-depth clinical cohort assessments using the Clinician-Administered

PTSD Scale and the Structured Clinical Interview for DSM-IV-TR. Of those invited, 11.9% ( $n=125$ ) declined. Of the remaining 952, 21 (2.3%) did not attend their scheduled interview, and the goal of 500 was met before the remaining 406 (43.7%) were contacted. Interviews occurred in neutral settings such as private library rooms, between November 2008 and December 2009. **Results:** The prevalence of at least one DSM-IV disorder was 66.4% (332); substance use disorders were the most prevalent (52.2%), followed by mood disorders (30.0%) and anxiety disorders (22.0%). The prevalence of at least one current disorder was 25.0% ( $n=83$ ); alcohol abuse (28.2%), M.D.D (22.4%) and alcohol dependence (20.4%) were the most common. Deployed soldiers had a higher lifetime prevalence of alcohol use disorders (53.0% vs. 39.5%,  $p=0.0049$ ) and PTSD (6.8% vs. 2.5%,  $p=0.0447$ ) compared to those never deployed. Women were more likely than men to have any mood disorder history (43.3% vs. 28.2%,  $p=0.0163$ ). **Conclusions:** Alcohol abuse and M.D.D were the two most common lifetime disorders, similar to findings in the general population. However, the prevalence of alcohol abuse in the OHARNG was twice the rate in the general population. The fourth most common disorder in this study was drug use compared to specific or social phobia in the general population. Women were more likely to have mood disorder history, as expected from other general and military study populations. However, we did not find the expected lower prevalence of substance abuse in women. Clinicians should ask patients about military service, and carefully screen for substance abuse.

#### **NR10-07**

#### **SHOPLIFTING BEHAVIOR IN A GROUP OF ELDERLY PATIENTS IN A PSYCHIATRIC OUTPATIENT SERVICE**

*Chair: Matt Robillard M.D.; Author(s): David Myran M.D. FRCP (C) David Conn MB FRCP (C)*

#### **SUMMARY:**

**Purpose:** The study was designed to detail the demographic, phenomenological, treatment response and legal disposition data of a group of elderly patients with shoplifting behaviour or kleptomania. **Method:** Psychiatrists in the Department of Psychiatry at an academic teaching hospital affiliated with the University of Toronto were canvassed to see if they were providing care to elderly patients with a diagnosis of kleptomania or had patients whom were shoplifting. A chart review was done on these outpatients and then the information was collected and analyzed. **Results:** The sex ratio of the sample was predominantly female. Within the sample

there was one patient who had antisocial personality disorder, one patient had dementia and the remainder of the same had a major mood disorder. Onset of shoplifting behavior was often in the patient's twenties. The objects shoplifted included clothes, electronic devices and food. The course of the shoplifting behavior was chronic in nature. There was hoarding behavior noted in some of the cases. None of the patients had attempted suicide. None of the patients were charged or prosecuted. Patients often showed an unwillingness to get help for these symptoms and wished to deal with it on their own. Trials of SSRI's did not seem to help the behavior. In the case of one patient, adding a mood stabilizer and discontinuing the SSRI appeared to have arrested the shoplifting behavior. Conclusions: Shoplifting behavior was not common in the psychiatric outpatient services at a large urban academic teaching hospital in Toronto. Shame within person or family may account for underreporting. Onset of shoplifting behavior tended to be early onset and was chronic in nature. It was unrelated to medical conditions such as Parkinson's disease, substance abuse or cancer. None of the patients were holocaust survivors. One new clinical finding was that the main locus of distress for the shoplifting behavior was not in the identified patient but was in the family. Most common psychiatric illness was a mood disorder but the shoplifting events were not always clearly linked to mood or psychotic symptoms at the time of offence. Pharmacologic management did not seem to contribute or alleviate the shoplifting behaviour in most of the individuals.

**NR10-08**  
**GENERAL PRACTITIONER'S SATISFACTION WITH THE IMPLEMENTATION OF A C-L PSYCHIATRY SERVICE IN ULSM, PORTUGAL**

*Chair: Author(s): Cassilda Costa, M.D. Fátima Ferreira, M.D. Rosa Quelhas Ferreira, M.D.*

**SUMMARY:**

Background: Matosinhos Local Health Unit (ULSM) in Portugal has a model of organization consisting on the articulation between the general hospital and the center of community care (ACES Matosinhos) joining four community health care centers (CHCC). Since 2009, around 50% of the clinical activity of the Psychiatry Service was done in the CHCC, through the interaction with general practitioners (GPs) and general psychiatry outpatient clinics. Traditionally, the GPs' referral to and communication with psychiatrists was made through electronic or written methods. In ULSM, digital clinical records are shared by these two specialties, allowing a better communication of

clinical information. Clinical case discussion is an established practice offering important advantages such as the possibility of maintaining the patient's care in the GPs' clinic. Aims: The authors aim with this presentation to describe the functioning model of the ULSM Psychiatry Service and reflect on it and on its results, particularly evaluating the satisfaction of GPs with the implementation of the model. Methods: In January 2011 satisfaction questionnaires were sent to all the GPs of CHCC in an enclosed letter. Participation was voluntary; the questionnaires were self-rated and returned through mail, preserving confidentiality. The topics evaluated the frequency of referrals to psychiatry, satisfaction with the criteria for those referrals, with the administrative procedures, with the psychiatric and psychology staff, qualities and deficiencies of the model, suggestions of change and general satisfaction with the model. Results: 100 questionnaires were sent to all the GPs in the CHCC. Analysis included 59 questionnaires using SPSS. The participation varied in each CHCC, from 19 to 29%. The majority of the GPs referred patients once or twice a month. 28 considered the work of the psychiatrists "very good", 38 said the model was "appropriate" and 43 of the 59 considered that the patients benefited from the close articulation between GPs and psychiatrists. Conclusions: Acceptance of this model isn't always consensual to all parties involved. Implementation of these services requires knowledge of the needs of the general population and doctors and should ideally be done gradually, taking into account the need of adjustments according to the monitoring of satisfaction. From our results it's clear that GPs considered that the articulation and discussion of the cases between these two specialties was beneficial for the patients.

**NR10-09**  
**PROFILE AND IMPACT OF PHYSICIAN ASSISTANTS IN PSYCHIATRY**

*Chair: Sheila Mauldin Other Author(s): Sheila Mauldin, MNM, Scott E. Arbet, Ph.D., Janet J. Lathrop, MBA*

**SUMMARY:**

Profile and Impact of Physician Assistants in Psychiatry Sheila Mauldin, MNM, Scott E. Arbet, Ph.D., Janet J. Lathrop, MBA, National Commission on Certification of Physician Assistants (NCCPA), Johns Creek, Ga., USA. Objective Prior to the introduction of its new Certificate of Added Qualifications program for certified PAs specializing in psychiatry, the NCCPA conducted a practice analysis to study the knowledge and skills used by those PAs and the functions they perform within the specialty. This study presents the findings from that

analysis, providing insight into the role that certified PAs are fulfilling in psychiatry and into the demographic and practice characteristics of those PAs as compared to the larger population of certified PAs. This information will be useful to those considering incorporating PAs into a psychiatry practice and to those concerned about workforce issues. **Method** The practice analysis was conducted in 2010 as a two-stage process involving focus groups and an online survey distributed to all certified PAs (n=71,351); responses were received from 16,289 (23%). **Results** The study illuminates characteristics such as employment setting, number of clinical hours worked, inter-specialty mobility, and a number of other practice profile factors. It also quantified the frequency and importance of the application of over 300 knowledge and skill areas. **Conclusions** By understanding the role certified PAs are currently fulfilling in psychiatry and the demographic and professional profile of those PAs, employers, physicians and policymakers will be better positioned to influence the psychiatry workforce and address current and future provider shortages.

**NR10-10**  
**FACTORS ASSOCIATED WITH RE-ADMISSION TO A PSYCHIATRIC UNIT**

*Chair: Cheryl Ann Kennedy M.D.; Author(s): Saima Latif, M.D., Nicole Guanci, M.D., Donald Ciccone, Ph.D.*

**SUMMARY:**

**Objective:** Hospital administrators and doctors are under increasing pressure to reduce the cost of inpatient psychiatric treatment while, at the same time, maintaining quality of care. One factor contributing to the cost of psychiatric treatment is a rapid relapse in symptoms requiring re-admission to hospital. To examine this issue, we compared patients who required psychiatric readmission within 5 months to a similar group of patients who did not. Our aim was to identify factors that might allow us to reduce the risk of frequent readmission. **Method:** Data were obtained by reviewing charts for a consecutive series of inpatient admissions from July through October 2009 (N=357). The unit has 34 beds with 12 beds for involuntary admissions (civil commitment). The following variables were examined: demographic factors; administrative issues related to admission and discharge; and psychiatric factors (diagnosis at discharge, co-morbid substance use disorder, medications at discharge). **Results:** The overall mean length of stay (LOS) was 11.3 days during the study period compared to an expected LOS of 9.5 days (University Hospitals Consortium) and the 150 day re-admission rate was 13.4% (n=48/357). There was no significant difference in first admission LOS

between those that were readmitted versus those that were not. None of the demographic factors (age, gender, race, ethnicity) predicted re-admission. Voluntary versus involuntary (civil commitment) admission was significantly associated with increased risk of readmission (p<.01) as was the presence or absence of psychotic disorder diagnosis (p<.05). Patients discharged home were also less likely to be readmitted than those discharged to a boarding home (p<.01). Finally, those with a discharge diagnosis of substance use disorder were less likely to require readmission (p=0.02). **Discussion:** Patients with the most serious disorders (psychotic) were at the greatest risk for multiple admissions over the 5-month time frame of our study. Serious illness coupled with community placement appeared to pose the greatest risk of psychiatric readmission. Patients who were discharged home and thus had the benefit of increased social support were less likely to be readmitted than those who required boarding home placement. Psychiatric patients discharged to boarding homes may require an increased level of care if they are to avoid the risk of frequent readmission. Surprisingly, patients with a co-morbid substance use disorder were less likely to be readmitted within a 5-month time span. Whether these patients are able to avoid readmission in the short run (through self-medication) while having a higher rate of readmission in the long run is unknown and will require further research.

**NR10-11**  
**STIGMA EXPERIENCES OF COMBAT VETERANS WITH PTSD FROM IRAQ AND AFGHANISTAN WARS**

*Chair: Dinesh Mittal M.D.; Author(s): Karen Drummond, Ph.D. Greer Sullivan, M.D. Patrick Corrigan, Psy. D Dean Blevins, Ph.D. Geoffrey Curran, Ph.D.*

**SUMMARY:**

**Objective** Public stigma devalues individuals based on their distinguishing characteristics, and some individuals may respond with self-stigma. This study explored the knowledge of and responses to public stigma among Operation Enduring Freedom and Operation Iraqi Freedom (OEF/OIF) combat Veterans with Post Traumatic Stress Disorder (PTSD). **Methods** Seventeen combat OEF/OIF Veterans diagnosed with PTSD from the Central Arkansas Veterans Healthcare System participated in four focus groups conducted by investigators well versed in qualitative methods. **Results** Participants perceived that the public stigmatizes combat Veterans with PTSD. The most common stereotypes were Veterans being dangerous/violent, crazy, and responsible for PTSD because they

volunteered for military service. While participants initially responded with some degree of self-stigma, later they predominantly resisted these stereotypes. Most felt that fellow combat Veterans best understood them. Conclusions Awareness of public stereotypes impacts help seeking. Peer-based programs may help combat Veterans with PTSD resist stigma.

**NR10-12**  
**THE IMPACT OF HOSPITALISTS ON ADVERSE INCIDENTS IN ACUTE PSYCHIATRY: A STUDY OF 5019 ADMISSIONS IN NORFOLK, UK FROM 2002-2010**

*Chair: Julian Beezhold M.D.; Author(s): Roberta Puvanachandra M.D. Adam Duckworth MBBS Anna Croxford MBBS James Currie MBBS Sumathi Kandasamy M.D. Jenny Thurston Pete Williams Andy Harris*

**SUMMARY:**

Background: The 'hospitalist' model of service delivery has grown immensely over the last 15 years in the US. Psychiatry in the UK has undergone a number of changes within that same timeframe, with a more recent trend towards dedicated acute inpatient psychiatry 'hospitalists'. Data from other specialties suggests that the hospitalist model of care can lead to improved patient outcomes. This study examines the impact of this change, in acute general adult psychiatry wards in Norwich, upon the quality of care received, using the incidence of adverse incidents as a measure. Method: Quasi-experimental controlled retrospective analysis of all admissions to acute inpatient working age adult psychiatric wards in Norwich UK from Sept 02 – Feb 10, using anonymised routinely collected data. Patient admissions were split into four groups: a control group (one inpatient psychiatrist throughout) and an intervention group (ten inpatient psychiatrists prior to Mar 2006 and one 'hospitalist' from Sept 2006); with each in turn split into two 42-month sections, pre- and post- date of intervention. Subjects: All 5019 patients admitted to acute psychiatric wards in Norwich (UK) from Sept 2002-Feb 2006 and Sept 2006-Feb 2010. Results: All Incidents/1000 patient bed days decreased by 6.8% ( $p < 0.05$ ) in the intervention ward and increased by 43.5% ( $p < 0.000$ ) in the control ward. This increase in incidents in the control ward may be accounted for by the increase in the proportion of involuntary admissions in the control ward, likely to be more disturbed, in the post intervention period of 204% ( $p < 0.000$ ). Yet the intervention ward saw an increase in involuntary admissions of 244% ( $p < 0.000$ ) during the same period. Conclusion: The introduction of a hospitalist model of care was associated with a significant reduction in

reportable adverse incidents during the same time period as a control ward saw a large increase, suggesting that a hospitalist model delivers real improvements in patient care.

**NR10-13**  
**IMPACT OF COVERAGE POLICIES ON PATIENT ACCESS TO PALIPERIDONE PALMITATE**

*Chair: Cynthia Mueller M.S.; Author(s): Joel Silver, MBA, Amy Bartels, M.P.H., Dilesh Doshi, Phar M.D.*

**SUMMARY:**

Objective: To understand how prescription drug utilization and coverage policies impact patient access to paliperidone palmitate (PP). Methods: Patient and claims level data from 08/01/2009 to 06/30/2011 were extracted from Wolters Kluwer ProMetis database. Data on patients who received rejections for prescription (Rx) claims for PP between 8/01/2009 and 12/31/2010 were analyzed. A  $\geq 6$ -month look-forward period was allowed to determine whether PP or another antipsychotic (AP) achieved approval. The interval in days to approval of PP after rejection and the reasons for rejection were described. Total approved claims and total rejected claims for that time period were also reported. Results were summarized using descriptive statistics. Results: The database contained 59,197 claims for PP; of those, 85.1% were approved and 14.9% were rejected. A total of 1737 patients received a rejection for a PP Rx, and 57.3% of those received approval for PP within an average ( $\pm$  SD) of 54 ( $\pm$  70) days of the rejection. PP was the first AP approved after the PP rejection for 637 of the 995 patients (64.0%). Of the 1737 patients, 31.3% received approval for another AP without receiving PP approval, and 11.5% had no further AP approvals. The reasons for PP rejection in those patients who eventually received PP (995) included benefit design issues (45.5%), prior authorization requirements (19.7%), clinical/duplication issues (15.0%), missing or incorrect data (13.2%), processing errors (3.4%), and patient coverage issues (3.1%). Of the 45.5% having benefit design issues, the primary reasons were patient attempted to refill too soon (39.7%), product was not covered (29.1%), plan limitations were exceeded (25.2%), and claim needed to be submitted to another processor or primary payer (4.4%). Conclusion: The overall rejection rate for PP in the time period studied was relatively low. For patients who did receive a rejection, nearly 60% were eventually approved, and the majority of those occurred without the patient moving to another AP in the interim. The most common reasons for rejection were benefit design issues. Funded by Janssen Scientific Affairs, LLC

**NR10-14**  
**MANAGED CARE COST SAVINGS**  
**ASSOCIATED WITH THE USE OF LONG**  
**ACTING INJECTABLE FORMULATIONS**  
**OF ANTIPSYCHOTIC AGENTS IN**  
**SCHIZOPHRENIA**

*Chair: Jay Lin Ph.D.; Author(s): Bruce Wong M.D., Steve Offord Ph.D., Dario Mirski M.D.*

**SUMMARY:**

Background: Compliance to oral antipsychotic agents has been estimated to be less than 50% in some studies. Second generation depot agents were developed with the primary intent to improve compliance to medications in schizophrenia patients. We examined the managed care cost implications in real practice of the use of depot antipsychotic agents. Method: Schizophrenia patients were identified from the MarketScan™ Commercial database, a US national health plan database, between 1/1/2005 and 9/30/2010. Index events were patients initiating treatment with depot antipsychotics compared to patients initiating treatment with an oral antipsychotic. The 12 month post-index costs for inpatient and outpatient care were compared. Incident oral antipsychotic use was chosen as a comparison to incident depot use as it is likely to be a more costly time period of schizophrenia care. Patients were required to be  $\geq 13$  years at the index event and have  $\geq 12$  months of continuous health plan coverage prior to the index event. Changes in healthcare costs representing reimbursed payment were measured from the healthcare claims in the database. Medication Possession Ratio (MPR) was used as a measure of drug compliance. Data is expressed as mean  $\pm$  standard deviation. Statistical analysis was undertaken in SAS. Results: 3,004 patients met inclusion criteria. 394 patients initiated depot agents and 2,610 oral agents with a mean age of  $41.7 \pm 15.5$  and  $37.1 \pm 15.9$  years. The median MPR prior to the initiation of depot agents was 0.28. Between the 12-month of follow-up and baseline periods, the change in schizophrenia-related hospital costs of depot agents vs. oral agents was  $-\$5,981 \pm \$16,554$  vs.  $\$758 \pm \$14,327$ ,  $p < 0.0001$ . The depot group was associated with both larger reductions in the mean number of hospital admissions,  $-0.60 \pm 1.37$  vs.  $0.05 \pm 0.99$ ,  $p < 0.0001$  and mean length of stay for hospital admissions  $-7.46 \pm 20.68$  vs.  $0.60 \pm 12.49$ ,  $p < 0.0001$ . Changes in the cost of outpatient care also favored depot agents,  $\$134 \pm \$8,280$  vs.  $\$658 \pm \$3,260$ ,  $p = 0.023$ . The cost of psychiatric medications were higher in the depot group during the post-index period,  $\$4,132 \pm \$4,533$  vs.  $\$2,562 \pm \$2,714$ ,  $p < 0.0001$ . Conclusions: In managed care, switching

patients to depot antipsychotic agents to manage schizophrenia is less costly overall than the management of newly diagnosed schizophrenia patients with oral agents. The cost savings coming from reductions of hospitalizations and outpatient care outweigh the cost increase from psychiatric medications.

**NR10-15**  
**RATES AND TIME COURSE OF**  
**EXTRAPYRAMIDAL SYMPTOMS: A**  
**COMPARISON OF ORAL AND LONG-ACTING**  
**INTRAMUSCULAR (LAI) PALIPERIDONE**  
**RANDOMIZED CONTROLLED STUDIES**

*Chair: Srihari Gopal M.D.; Author(s): Larry Alphas, M.D., Ph.D. David Hough, M.D. Yanning Liu, Ph.D. Isaac Nuamah, Ph.D. Adam Savitz, M.D., Ph.D.*

**SUMMARY:**

Objective: To determine if there is a difference in either the incidence or time course of EPS-related adverse events (AEs) with oral vs LAI paliperidone. Methods: Analysis included pooled data (safety analysis set;  $n = 2256$  for non-placebo treated patients) from paliperidone studies in adult patients with schizophrenia that were randomized, double-blind and placebo-controlled (3 oral [6-weeks each]; 4 LAI [13-weeks each]), and included comparable doses (LAI doses 25-150 mg eq [US doses 39-234 mg]; oral doses 3-15 mg). EPS-related AEs were categorized using MedDRA EPS group term as: 1) tremor 2) dystonia 3) hyperkinesia 4) parkinsonism and 5) dyskinesia. Their incidence rates along with time of onset were summarized (LAI vs oral). Investigators, blinded to treatment, assessed patients for dyskinesia via AIMS (Abnormal Involuntary Movement Scale), akathisia via BARS (Barnes Akathisia Rating Scale) and parkinsonism via SAS (Simpson Angus Rating Scale). Mean values for these EPS scales over time were plotted graphically by administration route and dose. Results: Mean reductions (SD) from baseline to endpoint in EPS-scale scores were larger in the pooled LAI studies (AIMS:  $-0.10[1.27]$ ; BARS:  $-0.09[1.06]$ ; SAS:  $-0.04[0.20]$ ) than pooled oral studies (AIMS:  $-0.08[1.32]$ ; BARS:  $-0.03[1.24]$ ; SAS:  $-0.0[0.23]$ ). These differences favored LAI for BARS ( $P = 0.023$ ) and SAS ( $P < 0.0001$ ) but not AIMS ( $P = 0.49$ ). Anticholinergic use (to treat EPS) was also lower in LAI (12%) vs oral studies (17%). The incidence for all categories of spontaneously reported EPS-related AEs was highest in the first 8 days of treatment; it was generally lower for LAI vs oral in the pooled data. Graphical plots over time showed EPS scores increased between days 8-15 in the LAI, but not oral studies. Overall mean values for EPS scores were comparable for both treatment formulations without

evidence of a dose response. Conclusions: Incidence of spontaneously reported EPS-related AEs was similar following approximately 90 days exposure with LAI and 40 days of oral paliperidone, at comparable doses. Greater improvement in EPS-scale scores and lower anticholinergic medication use was seen with LAI than oral paliperidone. At the comparable doses used in the pooled studies, LAI paliperidone did not lead to higher incidence of EPS than oral paliperidone.

#### **NR10-16**

### **NO AXIS I DIAGNOSIS IN PATIENTS HOSPITALIZED DUE TO A SUICIDE ATTEMPT OR CRISIS**

*Chair: Amresh Shrivastava M.D.; Author(s): Satyadhar Mitta. M.D., Nilesh Shah, M.D., DPM, DNB*

#### **SUMMARY:**

Amresh Shrivastava, Satyadhar Mitta, Nilesh Shah  
Introduction Suicide attempt and ideations are responsible for about three fourth of acute psychiatric hospitalization. This poses a considerable challenge for clinical administrative and financial aspects. The main obstacle for clinicians continues to make a decision for hospitalization in the event of a crisis. Suicide behavior is complex and multifactorial in origin. Though mental illnesses are common in suicide (>90%), psychosocial factors also play a significant role. Present study attempts to examine underlying causes or factors amongst the hospitalized subjects due to suicide behavior. Method The study design was a retrospective chart review in a naturalistic setting. We conducted a clinical audit and screened 500 inpatient records. We reviewed consecutive 100 patients admitted for management of attempted suicide. We recorded clinical details and data was analyzed. The audit was conducted at the Hillingdon hospital PCT, Uxbridge. London UK Results: We screened 500 inpatient records and reviewed consecutive 100 patients admitted for management of attempted suicide. Data revealed that a majority of patients were young between 20-40 years (69%). Eighty five percent patients had one or the other primary psychiatric diagnosis, and 15% did not have any psychiatric diagnosis. Amongst those who had one or two psychiatric diagnosis, a primary diagnosis of Depressive disorder 24% alcohol abuse 15% and polydrug abuse 8% was found. Further other causes were: recurrent depressive disorder 7%, reaction to stress 7%, adjustment disorder 6%, anxiety disorder 6%, Personality disorder 4% bipolar disorder 3%, schizophrenia and related psychosis 10%, persistent mood disorder 2%, opiate dependence 1% and learning disability 1%. The patients with no axis 1 diagnosis

were somewhat younger, with lessor previous history of attempt, family history and psychiatric hospitalization. Discussion: absence of any psychiatric diagnosis in 15% and reaction to stress as a cause of suicide in 6% are significant findings. The individual's capacity to cope, presence of risk factors, protective factors and level of resilience determine suicide behavior. Those who do not have a mental illness may also suffer difficulty in coping with psychosocial situations. The premise that mental illnesses are leading causes of suicide needs re-exploration. Presence of only psychosocial stress as potential causes of suicide may explain a number of attempts as seen in 'relationship' problems and students suicide. Complexity of mental illness, psychosocial stress and suicide needs further investigation and carefully crafted research. Absence of Axis 1 diagnosis in a significant number of patients at an early age offers excellent preventive opportunity for further deterioration and possibly increase in psychopathology.

#### **NR10-17**

### **RISK OF DEVELOPMENT OF OSTEOPOROSIS DUE TO DEPRESSION IN THE ELDERLY INDIVIDUALS: A LITERATURE REVIEW**

*Chair: Umesh Vyas M.D.*

#### **SUMMARY:**

Educational Objectives: At the conclusion of this presentation, the participants will be able to understand, 1) The risk of development of osteoporosis, 2) Need for close monitoring and early assessment of risk, 3) Need for prophylactic treatment to avoid complications due to development of osteoporosis. Introduction and Hypothesis: Fifteen percent of elderly individuals report clinically significant depression due to variety of reasons. Osteoporosis is a disorder of bone metabolism which can be caused by multiple factors. The elder population has multiple risk factors for development of low Bone Mineral Density (BM.D.). Data supports that SSRI causes low BM.D.. There are numerous mediating processes, factors and causes that may contribute to relationship between depression and low BM.D., therefore it has been suggested that depression may be an unrecognized risk factor for development of osteoporosis in this patient population. Low BM.D. is a common condition among the elder population; prevalence of osteopenia and osteoporosis is expected to increase due to increasing elder population. Low BM.D. is associated with increased risk for debilitating fractures, particularly in hip, vertebrae and distal forearm. There is a growing body of evidence that depression impact the risk for fractures in the older population. Most studies support that depression is

associated with increased risk for both low BM.D. and fractures. There are many risk factors for low BM.D., but some are unalterable. Therefore it is crucial to identify modifiable risk factors to reduce the public health burden of osteopenia, osteoporosis and fractures, and complications associated with them. Objective: A literature review was performed to extract evidence and to evaluate risk of Osteoporosis in depression. Method: Pubmed.gov was searched by using pre-determined key word: "Depression AND Osteoporosis". Results: Current available evidence supports that there is a definite increase of development of osteoporosis due to various factors, pathways and medications used in treatment of depression. Conclusion: Evidence exists that patients with depression are at an increased risk of development of low BM.D. due to various factors, and hence increased risk for development of Osteoporosis. These patients may benefit from close monitoring, early assessment of risk, and preventive measures such as prophylactic treatment to avoid complications.

#### NR10-18

### VARIABLES ASSOCIATED WITH FALLS AMONG PSYCHIATRIC INPATIENTS: THE INSTITUTE OF LIVING FALLS INTERVENTION INITIATIVE

*Chair: Ellen Blair B.S.N.; Author(s): Bonnie L. Szarek, R.N., Stephen B. Woolley, DSc, Theodore F. Mucha, M.D., Olga Dutka, MSN, MBA, Harold I. Schwartz, M.D., John W. Goethe, M.D.*

#### SUMMARY:

Objective: To (1) examine variables associated with falls and (2) pilot an intervention to identify patients at greatest fall risk. Method: The authors prospectively examined all psychiatric inpatients 8/2010-9/2011. Demographics, diagnoses, and medications of patients with versus without a fall were compared using bivariate analyses and logistic regression. All medications received within 24 hours prior to the fall were recorded. We then identified a stratified, matched random sample (without replacement) and for these patients recorded all medications received the day after admission. Medications for both groups were compared using t-tests for number of medications and the McNemar statistic for specific medications. Results: Among 4426 admissions there were 160 falls (representing 130 patients of whom 17% had >1 fall): 31% occurring in patients age >64. Eight percent occurred on the day of admission, 24% between 1-3 days, 32% during 4-7 days, and 36% at >7 days. Falls occurred throughout the day: 25-30% during the three shifts between 6AM and midnight and approximately 18% between

midnight and 6AM. Patients who fell were more likely to be older (OR=3.2) and to have a length of stay in the upper quartile (>11 days); they were also more likely to have a diagnosis of dementia (OR=1.9), schizoaffective disorder (SA) (OR=1.9), or bipolar disorder (BP) (OR=1.6). Regression showed that after controlling for confounding age and LOS were each associated with 2-3-fold increased risk of falls and that BP, dementia and SA with 60-100% increases in risk. Compared with the matched sample, those who fell received a significantly greater number of psychotropics, and were more often given antipsychotics, anticonvulsants, and benzodiazepines (all p<.001). Specific medications associated with an increased risk of falling included clozapine (p=.001), haloperidol (p=.006), olanzapine (p=.016), diphenhydramine (p=.006), and benztropine (p=.003). Conclusions: This study adds to the existing literature on patient falls in that it simultaneously examined patients of all ages and controlled for variables not previously assessed (e.g., diagnosis). Some findings are consistent with previous studies (e.g., the association with age) while others are, to our knowledge, newly identified associations with increased risk of falling (e.g., diagnosis of SA). In addition, the multidisciplinary team approach has enhanced the development of interventions to reduce falls. Educational Objectives Practice Gap: Although patients falls is a well-known clinical complication few studies to date have led to a model intervention for fall reduction. Objectives: At the conclusion of this session participants will be able to list variables associated with increased risk for falls. References: Knight M, Coakley C: Fall risk in patients with acute psychosis. J Nurs Care Qual 2010; 25:208-215. Wilson NM, Hilmer SN, March LM, Cameron ID, Lord SR, Seibel MJ, Mason RS, Chen JS, Cumming RG

#### NR10-19

### SUICIDE RATES AND ITS RELATIONSHIP WITH QUALITY OF LIFE INDICATORS

*Chair: Jaime Santander M.D.; Author(s): Jorge Rodriguez, M.D.*

#### SUMMARY:

Introduction: Suicide is a complex phenomenon, with multiple known risk factors and differences in rates between countries. Increased risk is commonly attributed to economic difficulties and poorer quality of life, however, some studies show opposite results. Objective: To compare suicide rates in different countries published to date, with some economic and quality of life indicators. Methods: We correlated suicide rates of 82 countries published by the World

Health Organization with the purchasing power parity (PPP) and the human development index (HDI) for the year 2008 published by the World Bank and United Nations respectively. Results: A total of 82 countries with suicide rates published on the website of WHO statistics met the inclusion criteria. When comparing the overall suicide rates with the PPP for each country in 2008 obtained a positive correlation ( $\rho = 0.360$ ,  $p < 0.01$ ). When we compared suicide rates with HDI, we obtained a positive correlation ( $\rho = 0.366$ ,  $p < 0.01$ ). Conclusion: The positive correlation observed that while better economic and quality of life indicators it could have higher suicide rates, contradicts many previously published studies. Multiple factors could be involved in this result, so it is needed more research to better understand the phenomenon of suicide worldwide but also those related to quality of life.

**NR10-20**
**THE CONFIRMATORY FACTOR ANALYSIS OF THE SUICIDE TRIGGER SCALE (STS-3): A MEASURE OF A HYPOTHESIZED SUICIDE TRIGGER STATE**

*Chair: Zimri Yaseen M.D.; Author(s): Yaseen, Zimri, M.D., Galynker, Igor, M.D., Ph.D.*

**SUMMARY:**

Objective: Although studies have defined the chronic risk factors for suicide, acute factors involved in an imminent suicide attempt have yet to be determined. The Suicide Trigger Scale is currently under investigation in the hopes of defining these factors that may influence individuals immediately preceding a suicide attempt. This study aims to reaffirm the internal consistency of the construct of a 'suicide trigger state' by replicating factor analysis of the data gathered with the Suicide Trigger Scale (STS) whilst establishing predictive validity for imminent future attempts. METHODS: The 42-item STS-3 was administered to 176 adult psychiatric patients with suicidal ideation or attempt in the psychiatric emergency room at Beth Israel Medical Center during a semi-structured interview. Demographic and clinical information was collected and multiple psychometric scales were administered including the Columbia Suicide Severity Scale (CSSR-S) and the Beck Suicide Severity Scale (BSS). Multiple statistical methods were used to explore the scale's structure as well as construct and predictive validity. RESULTS: Cronbach's alpha (0.94) demonstrated excellent internal consistency. Factor analysis yielded a three-component solution with good agreement, similar to the previous analysis. The STS subscales were Frantic Hopelessness,

Ruminative Flooding, and Near-Psychotic Somatization with Cronbach's alphas of 0.896, 0.796, and 0.764, respectively. Convergent validity was demonstrated between frantic hopelessness and depression;  $r = .260$ ,  $p < 0.01$  and between psychotic somatization and paranoia;  $r = .159$ ,  $p < 0.05$ . A significant association was observed between increases in STS scores and future suicide attempts within the first year ( $p < .05$ ). CONCLUSION: Consistent with previous analyses, the STS-3 and is an internally reliable instrument possessing three stable subscales that measures a distinct and novel clinical entity, provisionally termed the "suicide trigger state". Rising scores on the STS-3 associate with future suicide attempts within the first year.

**NR10-21**
**IMPROVING THE CARE OF PATIENTS WITH PSYCHIATRIC DISABILITIES IN THE COMMUNITY WITH PROACTIVE STRATEGIES TO PROMOTE TREATMENT ADHERENCE**

*Chair: Margaret Hendriks B.S.N.; Author(s): Rathi Mabendran, MBBS., MMed(Psych)., FAMS*

**SUMMARY:**

Introduction: Non adherence to prescribed antipsychotic medications increases the risk of psychiatric illness exacerbation and rehospitalization (1). At the Institute of Mental Health, a large 1800 bedded tertiary psychiatric hospital, an average of 250 patients with Schizophrenia and Delusional Disorders are discharged monthly. Our previous data revealed that only 78.4% of patients attended their clinic appointment 2 weeks after their discharge. This paper describes the proactive case management strategies that were employed from March 2010 to improve care and increase the outpatient clinic attendance of discharged patients. Method: Case Managers assessed their patients for their risk severity, biosocial and psychological needs upon their hospitalization and develop a care plan with the multidisciplinary team. When the patient is discharged, the case managers phoned the patients within 48 hours. This was followed with regular weekly and monthly telephonic case management support and meetings when the patients came to the clinic for their psychiatric review. The telephonic case management included psycho education and supportive counseling to the patients and their families and linking them to clinical and community services that they may require. Data mining of patients who were discharged and received these services from March 2010 to May 2011 was done and the results analyzed with SPSS version 18 and Microsoft Excel program. Results: A total of 3398

patients (1589 males and 1809 females) were discharged. 88% were aged between 18 years and 60 years, and 70% received inpatient care for a maximum of 3 weeks. Patients' compliance to follow-up treatment after discharge improved from an initial baseline of 78.4% to 90.2% within 14 months of implementing the system. The number of patients defaulting treatment also dropped from 22% to 10%. Conclusion: The improved percentage of patients complying with medication and treatment is encouraging. Therefore to promote patients' adherence to medication and treatment it is necessary to employ educational, behavioral and affective strategies as well as longer interventions and alliances with therapists (2). Literature reference: 1. Lacro, J.P., Dunn, L.B., Dolder, C.R., Leckband, S., Jeste D.V. Prevalence of and risk factors for medication non adherence in patients with Schizophrenia: a comprehensive review of recent literature. *J Clin Psychiatry*. 2002 Oct;63(10):892-909 2. Dolder, C.R., Lacro, J.P., Leckband, S., Jeste D.V. Interventions to improve antipsychotic medication adherence: review of recent literature. *J Clin Psychopharmacol*. 2003 Aug;23(4):389-99.

**NR10-22**  
**IMPACT OF A COORDINATED, COMMUNITY-BASED, BEHAVIORAL HEALTH, CRISIS SYSTEM OF CARE ON THE ACUTE PSYCHIATRIC ADMISSION RATE FROM A SPECIALIZED BEHAVIOR**

*Chair: Kathleen Crapanzano M.D.; Author(s): Jerry Heintz, M.D. Jan Kasofsky, Ph.D. Glenn Jones, Ph.D.*

**SUMMARY:**

**OBJECTIVE:** To evaluate the effectiveness of a coordinated, community-based response to behavioral health crises as measured by comparing psychiatric hospitalization rates of people presenting to a specialized behavioral health, community-based hospital emergency room versus a social work supported general emergency room. **METHOD:** In response to a documented increase of psychiatric crises experienced by a public emergency room in the post-Hurricane Katrina receiving community of Baton Rouge, Louisiana, and coincident with a statewide shortage of acute psychiatric inpatient beds, a coordinated crisis system of care was created. Psychiatric admissions from a large public emergency room, supported by psychiatric social workers in the two years prior to this program being instituted, were compared to admission rates in the year after a coordinated approach was established and included a dedicated psychiatric emergency room. **RESULTS:** The rate of individuals placed in inpatient

care was significantly lower with the coordinated approach of physicians and social workers within the specialized emergency room, the local public mental health clinics and law enforcement ( $p < 0.05$ ). **CONCLUSIONS:** Previous research documents the effectiveness of psychiatric emergency services as being beneficial to de-escalate /resolve crises, prevent long term hospitalization, and relieve pressure on inpatient units. This study confirms this finding and further documents how a coordinated community crisis response system is fundamental to the successful discharge of people from the emergency room to non-hospital, community-based alternatives. It is anticipated that the reported findings will continue to improve as the coordinated, community-based, crisis system matures.

**NR10-23**  
**HOME TREATMENT FOR THE ACUTELY MENTALLY ILL IN RURAL SOUTHERN GERMANY AS AN ALTERNATIVE TO INPATIENT TREATMENT – AN ECONOMIC ANALYSIS**

*Chair: Karel Frasch M.D.; Author(s): Miriam Ott, Henriette Jabn, M.D., Annett Rauscher, Markus Jaeger, M.D., Isolde Munz, Thomas Becker, M.D., Reinhold Kilian, Ph.D.*

**SUMMARY:**

**Objective:** Home Treatment (HT), a home based multiprofessional psychiatric service for the acutely mentally ill which is still in its infancy in Germany, is hypothesized to be equally effective to traditional inpatient treatment (TAU). Our study compared HT (n=60) to TAU (n=58) in two patient groups (studied consecutively, similar diagnostic distribution: schizophrenia n=25 HT, n=21 TAU; affective disorders n=26 in both groups) with regard to clinical effectiveness (HoNOS, PANSS, HAM.D.-21 at admission vs. discharge). We found HT to be equally effective with regard to HoNOS and PANSS scores; as to HAM.D.-21 scores, HT patients improved significantly more than the TAU group. This study aimed to analyse the cost-effectiveness of HT in comparison to TAU. **Method:** Statistical analysis of treatment effects was performed by mixed effects regression models with random time effects and a fixed treatment x time interaction. Selection bias was controlled by the propensity score method. For economic analysis, total direct costs have been adjusted for propensity scores. Incremental cost effectiveness ratios (ICER) have been conducted for adjusted outcome variables and adjusted costs. Nonparametric bootstrapping has been applied for estimating ICER variance. Cost effectiveness acceptance

curves CEAC have been computed for the interpretation of CEA results. Results: Regression coefficients for time x treatment interaction effects revealed a greater improvement in depressive symptoms for patients in the HT group ( $b = -5.71$ ;  $p < 0.001$ ). Total adjusted treatment costs did not significantly differ between treatment groups. ICER for the improvement of depressive symptoms indicates a saving of 314,3 € with each increase of the treatment effect by one unit of the HAM.D.-21. CEAC reveals a 82,5 % probability of HT to be cost-effective in comparison to TAU at a maximum willingness to pay of 500 € for an improvement of the HAM.D.-21 by one unit. Conclusions: In our patient sample, HT turned out to be a feasible and clinically effective intervention across diagnostic groups with an emphasis on schizophrenia and affective disorders, especially with regard to depressive symptoms (superior improvement in the HT group). As to economic issues, we found a trend towards cost-effectiveness with regard to depressive symptoms in comparison with TAU which may be due to small sample size and high variance on the one hand and to the course of the willingness to pay curve on the other. Further controlled studies with larger patient groups and longer observation periods are required to find out about cost-effectiveness of HT vs. TAU, especially with regard to long term course. Educational objectives: At the conclusion of the session, the participant should be able to 1) recognize HT as a feasible and at least equally effective treatment option compared with inpatient treatment 2) name the results of our study and discuss its limitations / implications for further research

**NR10-24**  
**A STATEWIDE TELEPSYCHIATRY PROGRAM TO IMPROVE ACCESS, AFFORDABILITY AND QUALITY CARE**

*Chair: Meera Narasimban M.D.; Author(s): Meera Narasimban, M.D., Benjamin Druss, M.D., M.P.H., Steve Marcus, Ph.D., Julie Royer, Von Silke, Ph.D., Zhao Liping and John Magill*

**SUMMARY:**

Aim: 1. Evaluate the impact of telepsychiatry on length of stay, ED recidivism, outpatient follow-up. 2. To study the impact of community and individual level moderators 3. To conduct a budget impact analysis of the telepsychiatry projects Method: The telepsychiatry services offered by the SCDMH currently provides consults at 25 ED's (rural and urban) in the state of South Carolina, 3 more are awaiting equipment, 9 others are in the contractual stage and so far >8400 patients have been served since March 2009. This

program provides emergency psychiatric care access 24 hours a day, seven days a week, the psychiatrist provides assessment and recommendations for initial treatment and works closely with the ED doctor in identifying resources in the community to help the patient with follow-up care, a necessity for many patients that reduces the need for re-hospitalization and improves quality of life for the patient and his or her family. Results: Telepsychiatry group had fewer inpatient admissions (9.2% vs 19.4%, shorter length of stay 3.8 vs 5.3 days, lower costs \$1211 vs \$378. The 30 and 90 day follow-up at the outpatient mental health center were 43.6% vs 30.2 and 52.5% vs 39.1%,  $p < 0.0001$ . Conclusions: This statewide telepsychiatry initiative has proved to be a promising strategy for improving care and outcomes of mental health Emergency Department (ED) visits by increased access to emergency psychiatric consultation, facilitated appropriate treatment and increased discharge activities by providing quality care on the one hand and reduced length of stay on the other hand. Funded by Duke Endowment and National Institute of Mental Health R01

**NR10-25**  
**GIVING BAD NEWS: COMPARING FIRST AND THIRD YEAR MEDICAL STUDENT SKILLS USING STANDARDIZED PATIENTS**

*Chair: Kristi Williams M.D.; Author(s): Denis J. Lynch, Ph.D., Constance J Shriner, Ph.D.*

**SUMMARY:**

Giving bad news has been identified by physicians as one of the more difficult and unpleasant tasks in their practice. It is important that the medical school curriculum include training in this basic skill. This study compared skill in giving bad news by first year medical students with that of third year students who had received formal training in how to give bad news. First year medical students ( $N=129$ ) and third year medical students ( $N=131$ ) role-played with standardized patients in a situation requiring the delivery of bad news. Observers completed a checklist developed to determine student skill in giving bad news. Overall, third year students did better in a number of checklist items, including giving a "warning shot" ( $X=21.4$ ,  $P=.0001$ ), giving information in small chunks ( $X=13.02$ ,  $P=.0001$ ), and conveying realistic hope ( $X=14.07$ ,  $P=.0001$ ). However, first year students performed better in basic skills such as assessing social support ( $X=51.46$ ,  $P=.0001$ ), asking about concerns and feelings ( $X=21.50$ ,  $P=.0001$ ) and summarizing the discussion ( $X=37.59$ ,  $P=.0001$ ). Although other factors, (e.g. being further advanced in their medical school training) may have

played a role in the superiority of the third year students, it is likely that the specific formal training in delivering bad news was a key component; however, first years excelled in some basic interviewing skills. Therefore, the authors recommend that basic interviewing skills should be reviewed and reinforced throughout the medical school curriculum so students maintain abilities such as asking about thoughts and feelings and discussing available support.

**NR10-26**  
**CAN PERCEPTIONS ABOUT PSYCHIATRISTS CHANGE? A STUDY AMONGST MEDICAL STUDENTS IN A PSYCHIATRY ROTATION**

*Chair: Rathni Mahendran, M.B.B.S Author(s): Kua EH FRCPsych, M.D. Birit Broekman, M Med E Abidin, Ph.D.*

**SUMMARY:**

Psychiatrists do face stigma in the work they do. Among study findings are descriptions of psychiatrists as “bright but cold and reserved” and “having an image problem”. These stereotypes and stigma do affect medical students’ views and willingness to care for the mentally ill. We studied attitudinal change amongst medical students before and after a psychiatry rotation using a 30 item Attitudes towards Psychiatry (ATP 30) questionnaire. The study had Ethics Board approval (NHG DSRB A). In the questionnaire there are several items relating to psychiatrists which were identified for analysis. Using SPSS (version 16) for statistical analysis, mean and standard deviations were calculated for continuous variables and frequencies. Differences between baseline and last day of the rotation were tested by Paired test and Wilcoxon signed-rank test. 146 students participated. These were significant improvement in overall pre- and post-rotation ATP scores (35.8 vs 39.7,  $p$  0.0002). The majority of the students reported the psychiatry training valuable ( $p$  0.000). However for individual items relating to psychiatrists, the findings were mixed. At the end of the posting students rejected items relating to performance such as “psychiatrists talking but doing very little ( $p$  0.001), not being able to do much for their patients ( $p$  0.005) and not being equal to other doctors ( $p$  0.003). But they did not change their views that “psychiatrist were as stable as other doctors and that “psychiatrists had less satisfaction from their work”. These findings are critical for teaching and mentoring and need to be acknowledged and discussed as negative perceptions remain despite close contact with students. In the long term these perceptions may impact relationships with peers in the psychiatry field and approaches to recruit into the field. Importantly they might also affect how the mentally ill are treated

and the referral for psychiatric care.

**NR10-27**  
**AN APPROACH TO IMPROVE MONITORING FOR METABOLIC SYNDROME IN PATIENTS TREATED WITH ANTIPSYCHOTICS, A QUALITY IMPROVEMENT PROJECT FOLLOW-UP**

*Chair: Deepa Hasija M.D.; Author(s): Manoj Puthiyathu M.D., Anita Jothy M.D., Imran Jamil M.D., Amel Badr M.D., Joray Wright MS III, Ross University School of Medicine*

**SUMMARY:**

**ABSTRACT** The metabolic syndrome is highly prevalent in psychiatric patients treated by antipsychotics and represents an enormous risk factor for development of dyslipidemia and glucose intolerance and subsequently increases the risk of cardiovascular diseases and diabetes. Clinical attention must be given to monitoring for this syndrome. The correlation between the use of antipsychotics and new-onset metabolic syndrome has been widely documented in younger and middle-aged schizophrenic and bipolar patients. Objective To assess physician compliance with screening patients who are being treated with antipsychotics for metabolic syndrome at Bergen Regional Medical Center’s (BRMC) outpatient clinic. Our goal was to (1) assess compliance by ordering at least one lipid panel and one liver function test per year and then (2) propose various protocols to implement in order to improve screening of these patients, such as annual lipid panels, measuring blood pressure, measuring fasting blood glucose levels, and follow up with the risks associated with these medications for necessary required steps to improve quality of service. Method Our study involved a retrospective chart review consisting of 200 randomly-chosen patient charts seen in the outpatient clinic at BRMC from January 2010 to December 2010. We assessed 1) overall physician compliance rate in screening patients, 2) whether or not physicians were more likely to screen patients who visited the clinic more frequently. Results Our analysis found that the compliance rate for lipid panels was 32% and for liver function test was 51%. This was a slight increase from the year 2009. There are many factors that contribute to poor physician compliance with screening for metabolic syndrome. Physicians, patients, and facilities all contribute to poor screening. We proposed measures to address each of these factors, including modified progress notes and patient reminder cards.

**NR10-28**

**THE POWER OF EXPECTATION BIAS**

*Chair: Janet Williams D.S.W.; Author(s): Danielle Popp, Ph.D. Kenneth A. Kobak, Ph.D. Michael J. Detke, M.D., Ph.D.*

**SUMMARY:**

Background: Researchers have identified several sources of bias in clinical trials that may lead to increased placebo response and decreased signal detection. One such bias, expectation bias (EB), is of particular concern in CNS clinical trials due to the subjective nature of many (including primary) outcomes. EB occurs when an individual's expectations about an outcome influence one's perceptions of one's own or others' behavior. In psychiatric clinical trials, both raters and subjects may enter the trial with expectations for the outcome. Rater EB may occur when raters expect that subjects will improve (or fail to improve) over the course of the trial. Subject EB may occur when subjects themselves expect to get better and/or report improvement to please the rater. Finally, in traditional trial designs, rater and subject expectations may interact to create an alliance, resulting in increased placebo response and possibly decreased drug-placebo separation. Double blind studies are designed to control for EB by blinding the subject and the clinical rater to whether the subject is taking placebo or drug. However, other unblinded factors, such as visit sequence and rater-subject relationship, may also affect placebo response. Methods: We review eight published studies that illustrate the problem of rater and subject EB across several therapeutic areas. Results: Results of studies examining rater EB suggest that rater expectations can affect subject diagnosis and also decrease inter-rater reliability when subjects do not behave according to pre-conceived expectations. Results of three studies of subject EB suggest that subject expectations regarding their likelihood of receiving active treatment can increase placebo response and affect study outcome. Finally, studies of the interaction of both rater and subject expectation find that placebo response increases linearly with the number of follow-up visits, and that having a different rater for baseline, endpoint, and sequential visits may decrease placebo response. Conclusions: EB may have an effect when raters' scores and subjects' reports are influenced by the expectation of improvement. The studies reviewed here suggest that patient expectations, rater expectations, and rater-patient relationships can increase placebo response and decrease signal detection. Taken together, these results suggest that using raters who are blinded to study protocol details, including inclusion/exclusion criteria and study visit number, may yield better signal detection and

lower placebo response. Blinding to protocol details and study visit number eliminates the possibility that clinical ratings will be affected by an expectation of improvement as treatment progresses. Further, using a different rater at baseline, endpoint and for consecutive visits controls for the possibility of a relationship (sometimes referred to as relationship bias) between rater and subject that could influence ratings.

**NR10-29**

**A QUALITY IMPROVEMENT PROJECT  
ASSESSING THE REPETITION OF  
LABORATORY TESTING IN PATIENTS  
ADMITTED THROUGH THE PSYCHIATRIC  
EMERGENCY ROOM TO THE INPATI**

*Chair: Deepa Hasija M.D.; Author(s): Sarah Sheikh M.D., Amel Badr M.D., Sylvia Edwards MS III (Ross University)*

**SUMMARY:**

Introduction: It has been the common practice in hospitals to have one set of laboratory studies drawn in the emergency room as part of medical clearance in order for a psychiatrist to evaluate a patient to determine the patient is acutely free of medical illness and is stable enough to be admitted into a psychiatric unit. In the emergency room, a psychiatric panel of blood work is drawn which usually includes basic chemistry, comprehensive metabolic panel, a toxicology screen and blood alcohol level. When a patient is admitted from the psychiatric emergency into an inpatient unit, they have some repeat blood work done which was not done in the emergency room which is needed to complete proper medical workup. In this process, certain laboratory work is repeated which might be un-necessary. Objectives: To assess the frequency of repeating laboratory studies in patients who have had blood drawn in the psychiatric emergency room and have repeat blood-work when they get admitted to an inpatient psychiatric unit. Method: We conducted a retrospective chart review of 145 patients who were admitted from emergency room to the inpatient psychiatric unit from May 2010 to June 2010. If the first set of the psychiatric panel was drawn in the emergency room and the lab values were within normal range then the same blood work should not have been drawn in the psychiatric inpatient unit. Results: Out of the 145 patient's charts that were reviewed, 15 patients had repeat laboratory work that was unnecessary. However, most of these patients did have laboratory work done in the inpatient units that included thyroid function tests, lipid panels, valproic acid level, etc. If the additional laboratory work could have been added on to the initial blood work, this could save the time and money for the

hospital and patient. Repeat blood work necessitates the nursing staff to spend additional time to draw blood on the unit, the patient is subjected to another blood draw that could have been prevented, and also can reduce healthcare expense if unnecessary lab work is minimized.

### NR10-30

#### PRO DEPRESSION SCALE DEVELOPMENT: A NEW DEPRESSION SCALE, THE ROSENBERG MOOD SCALE

*Chair: Leon Rosenberg M.D.; Author(s): Howard Hassman, D.O.*

#### SUMMARY:

A new Depression Rating Scale, the Rosenberg Mood Scale (RMS) is presented. According to the 2009 FDA Guidance for Industry regarding Patient Reported Observations (PROs) “sponsors should provide documented evidence of patient input during instrument development.(1.)” Previous work on a PRO depression scale includes two poster sessions comparing the McManus Rosenberg Rating Scale for Depression, the MRRS-D, and the MRRS-D-SR-FC (self-rated with Forced Confirmation) with other scales in 2005 (2.) and 2008 (3.), and 10 interviews that were conducted in 2011 with experts such as David Sheehan and Stuart Montgomery to assess opinions about the MRRS-D-FC. As a result, that previous self-rated scale, the MRRS-D-SR-FC has been replaced with this new PRO Depression Rating Scale, the RMS. (“It is expected that the instrument will change as data is collected.(1.)”) 14 characteristics of PRO instruments reviewed by the FDA include concepts being measured, response options and recall period. This work includes early data on Response Options on the RMS. The primary author established a conceptual framework that severity is equal to frequency since DSM-IV criteria for a Major Depressive Episode is based upon frequency (“depressed mood most of the day, nearly every day.(4.)”). Frequency of symptoms remains the sole measure of this PRO’s severity; item response options needed to be developed to capture frequency of symptoms. We have chosen to use a 7 point Likert Scale with interval constancy and tested it a diverse patient and a diverse clinician group in response to the FDA Guidance for Industry regarding PROs in this preliminary study of item response options in the RMS and other existing scales. Complete statistical analysis is in progress. 1. Guidance for Industry Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims. Office of Communications, Division of Drug Information, Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51,

Room 2201, Silver Spring, M.D. 20993-0002. 2. A New Depression Rating Scale, NCDEU 2005 3. A New Self Rated Depression Rating Scale, NCDEU 2008 4. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision, Washington, DC, American Psychiatric Association, 2000.

### NR10-31

#### PREDICTORS OF SUICIDAL IDEATION IN A PROSPECTIVE STUDY OF BODY DYSMORPHIC DISORDER

*Chair: Katharine Phillips M.D.; Author(s): William Menard, BA, Eugene Quinn, Ph.D., Robert L. Stout, Ph.D.*

#### SUMMARY:

Objective: Body dysmorphic disorder (BDD) is a common and severe disorder. Individuals with BDD have been found to have high rates of suicidal ideation, with 45% of clinical samples reporting current suicidal ideation and approximately 80% reporting lifetime suicidal ideation. Lifetime suicidal ideation that is attributed primarily to BDD symptoms has been reported by 55%-68% of clinical samples. Rates of suicide attempts and completed suicide also appear markedly elevated. In cross-sectional/retrospective studies, higher rates of suicidal ideation are significantly associated with more severe BDD symptoms and with comorbid major depressive disorder. However, cross-sectional data have limitations, and prospective studies that examine predictors of suicidal ideation are needed. To our knowledge, this report is the first to prospectively examine predictors of suicidal ideation in BDD. Methods: Prospective mediational analyses examined predictors of suicidal ideation in 111 subjects with BDD over 3 years of prospective follow-up. Subjects were participants from the northeastern United States in a prospective longitudinal study of the course of BDD who were ascertained from a wide variety of sources. Subjects were interviewed annually with measures of BDD severity, depression severity, and frequency of suicidal ideation. Results: During each year of follow-up, 41% -51% of subjects experienced suicidal ideation. Greater BDD severity in year 1 significantly predicted a higher frequency of suicidal ideation in year 3 (beta = 22.02, p<.0001). In addition, BDD severity in year 1 significantly predicted depression severity in year 2 (beta = .56; p<.0001), and depression severity in year 2 significantly predicted suicidal ideation in year 3 (beta = 19.77, p<.0001). The MacKinnon test indicated that depression severity significantly mediated the relationship between BDD severity and suicidal ideation (MacKinnon z = 3.606, p < .01). However, BDD severity in year 1 remained a significant predictor

of suicidal ideation in year 3, even after controlling for the effect of depression severity in year 2. Conclusions: In prospective analyses, greater BDD severity directly predicted the development of greater suicidal ideation. The relationship between BDD severity and suicidal ideation was partially, but not completely, mediated by severity of depressive symptoms. Examination of additional potential mediators is needed. Funding Source: NIMH and American Foundation for Suicide Prevention. Educational Objective: At the conclusion of this session, the participant should be able to recognize that suicidal ideation is frequent in BDD and that both BDD severity and depression severity predict the frequency of suicidal ideation in individuals with this disorder.

**NR10-32**  
**GENDER DIFFERENCES IN BODY**  
**DYSMORPHIC DISORDER**

*Chair: Himanshu Tyagi M.D.; Author(s): Anusha Govender  
 Lynne M Drummond MRCPsych*

**SUMMARY:**

Background Gender is unequivocally tied to self-perception of one's own body image. However, disorders of body image do not usually have gender specific approaches to treatment, mainly due to a relative lack of evidence for similarities and differences between genders. This study investigated gender similarities and differences in patients with Body Dysmorphic Disorder (BDD). Method We conducted a retrospective case note analysis of all patients with BDD who were assessed at a specialised national and regional centre for BDD in South West London in last four years. Routinely collected standard measures at the time of assessment i.e. Yale Brown Obsessive Compulsive Scale (YBOCS-BDD), BDD Checklist, BDI, MADRS, Disability and sociodemographic information were collated and analysed with respect to gender. Results Our study found fewer differences than similarities between the two genders. However the gender differences noted were interesting and important. Males were more likely to present late for treatment. Compared with their female counterparts, they were also less likely to be in a stable relationship. Comorbid substance use was also reported to be higher in the male population in our sample. Differences were also noted in the patterns of avoidance responses, neutralisation behaviours, rituals and the reported frequency of mirror gazing and mirror checking behaviours. Body dissatisfaction checklist information suggested that although both sexes are equally likely to be preoccupied with their facial features, significant differences are

present in their preoccupation towards other body parts. Men, overall, were less likely to mention the option of having a plastic surgery in the assessment and diagnostic interview.

**NR10-33**  
**TRAUMATIC LOSS IN HURRICANE**  
**SURVIVORS: HEART RATE VARIABILITY**  
**(HRV) CHANGES IN DEPRESSION, NOT PTSD**

*Chair: Phebe Tucker M.D.; Author(s): Hattie Jeon-Slaughter,  
 Ph.D. Qaiser Khan, M.P.H. Theresa Garton, M.D.*

**SUMMARY:**

Objective: To assess emotional distress and autonomic dysregulation due to depression/traumatic loss and PTSD in relocated Katrina survivors. Method: Survivors (n=34) and demographically matched Oklahoma controls (n=34) were assessed for psychiatric diagnoses (SCID-IV), symptoms of PTSD (CAPS-1) and Depression (BDI), psychosocial disability (SDS) and power spectral analysis HRV in response to trauma reminders. Wilcoxon rank sum, MANOVA and Spearman correlation tests compared group measures. Results: PTSD rates were 38% in survivors (Katrina-related) and 12% in controls. Survivors had higher PTSD and depression symptoms (within diagnostic ranges) more psychosocial disability, higher resting heart rate (80.8 vs. 74.9, p=0.05), lower parasympathetic (H.F.n.u.) baseline HRV activity (p=0.04), less vagal reactivity with trauma cues (p=0.04), and higher baseline sympathetic (LF/HF) activity (p=0.04) than comparisons. Survivors with depression (n=12) and with comorbid depression and PTSD (n=7), but not those with PTSD (n=13) had flattened parasympathetic reactivity to trauma cues. HRV measures correlated with depressive (p=0.01) but not PTSD symptoms (p>0.05). Conclusions: Hurricane exposure and relocation were associated with psychiatric morbidity and autonomic dysregulation. Of note, HRV reactivity to trauma reminders was dysregulated among survivors with depression, but not PTSD, despite inclusion of physiologic reactivity in diagnostic criteria for PTSD. Results suggest that survivors with depression/traumatic loss should be evaluated for emotional and health issues related to autonomic nervous system reactivity. Implications of our findings are discussed in relation to higher myocardial infarct rates in New Orleans after Katrina.

**NR10-34**  
**STRESS INDICATORS IN THE SKELETAL**  
**REMAINS OF A LATE POST-CLASSIC MEXICA**  
**POPULATION**

*Chair: Jacqueline Cortes M.D.; Author(s): Gerhard Heinze Martin M.D. and Arturo Jorge Ramirez Padilla M.D.*

**SUMMARY:**

Introduction: Mexicans lived under great pressure; their daily life had high emotional tension. They had nervous, neurotic personalities with constant fear, apprehension, and angst. Hypothesis: Various stress indicators were found in the skeletal remains of this Mexican population. Objective: Describe the stress indicators found in these skeletal remains. Methodology: one hundred and twenty (120) skeletons were classified by sex and age from a total of 124 Macehual skeletons, a late Post-Classic Mexican population between 1300 and 1521, in San Gregorio Atlapulco, Xochimilco de la Cuenca de Mexico, Residential Platform “El Japon”, belonging to the Osteology Laboratory in the Physical Anthropology Department of the National School of Anthropology and History. To be able to perform the necessary tests to describe stress indicators, those with most teeth were chosen. Results: The stress indicators found were: occlusal wear, caries secondary to occlusal wear, enamel hypoplasia, porous Hyperostosis in the frontal and parietal bones, porous superior orbital cribrum secondary to cortical wear, dental paradontosis, facial asymmetry, and dental calculus. Markers of occupational stress were also found, bone degeneration was found in upper extremities as they worked cultivating vegetables, they rowed for prolonged periods of time. Conclusion: according to the previously mentioned indicators, the Mexicans in general were subjected to stress due to their beliefs and lifestyle, but the Macehuals were subjected to even greater stress as they belonged to the lowest social sphere.

**NR10-35  
QUANTIFICATION OF THE PERMANENT IMPAIRMENT DUE TO MENTAL & BEHAVIORAL DISORDER IN INDIVIDUALS WITH POLY-TRAUMA, ACCORDING TO AMA GUIDES 6TH EDITION**

*Chair: Armando Miciano M.D.*

**SUMMARY:**

The study determined the Mental & Behavioral Disorder Impairment percentage rating (%MBD), according to the AMA Guides to Evaluation of Permanent Impairment, 6th Edition and examined the relationship between %MBD, health-related quality of life, and functional performance of individuals with Poly-trauma (PTM) history >two year. There has been no previous systematic research on the %MBD

from the AMA Guides. The retrospective study was done on 98 PTM subjects (41 men; ages 28-62) from outpatient rehabilitation clinic records. Main outcome measures used were %MBD, SF36-Mental Component Scale (SF36-MCS), and 50-Foot-Walk-Fastest (FWF). Subjects were stratified by %MBD, a mental & behavioral impairment assessment system from the AMA Guides 6th Ed., based on: Brief Psychiatric Rating Scale, Global Assessment of Functioning Scale, and Psychiatric Impairment Rating Scale. SF36-MCS measured the health-related quality of life (HR-QOL), while FWF measured the functional performance status (FPS). Clinical scores ranged: 5-20%MBD (mean 10.67%); MCS 7.5 to 64 (mean 32.8 normative score); and, FWF 2-30 seconds (mean 12.6), %MBD were mostly in the mild severity, functional performance levels acceptable, but HR-QOL low. There was a trend relationship of the %MBD to the HR-QOL and FPS. The study supports the medical necessity of providing psychotherapeutic support in individuals with Poly-Trauma to decrease their health burden. Further study on the correlation of %MBD, and SF36-MCS & FPS should be done.

**NR10-36  
PREDICTIVE VALUE OF 4 DIFFERENT DEFINITIONS OF SUBTHRESHOLD POST-TRAUMATIC STRESS DISORDER: RELATIONSHIP TO SEVERITY OF SYMPTOMS AND FUNCTIONING**

*Chair: John Kasckow M.D.; Author(s): Derik Yaeger, Ph.D. Kathryn M. Magruder, M.P.H., Ph.D.*

**SUMMARY:**

Background: Post-traumatic Stress Disorder (PTSD) is highly prevalent and is associated with marked psychiatric comorbidity and impairment across a number of psychosocial domains. Although subthreshold PTSD is not a formal diagnosis, it has been used in research to characterize individuals who report clinically significant trauma-related symptoms but do not meet full diagnostic criteria for PTSD. There is no agreed-upon “gold standard” to determine whether a particular definition of subthreshold PTSD accurately identifies patients. We have examined 4 distinct definitions of this subthreshold syndrome (based on Blanchard, Schnurr, Marshall, and Stein) with the aim of comparing the 4 in their ability to predict PTSD symptom levels and levels of functioning. Methods: The dataset came from a regional sample of 815 primary care veterans at 4 VAMC’s who had been assessed with the Clinician Administered PTSD Scale (CAPS) and were also administered the PTSD Checklist (PCL) and SF-36. We used multiple linear regression with

multi-level categorical variables to determine which of the 4 definitions of subthreshold PTSD (i.e., based on Blanchard, Marshall, Stein and Schnurr) predicted PTSD symptom scores and mental health functioning. The reference population comprised patients not meeting CAPs criteria for PTSD. Results: The prevalence of subthreshold PTSD ranged from 4.0% to 9.7% with the Marshall definition yielding the greatest number of cases. Furthermore, only the Marshall definition positively predicted PTSD symptom scores and negatively predicted mental functioning scores while taking into account the 3 other definitions. Conclusions: Based on our approach involving criterion validity, only the Marshall definition appears to predict PTSD symptom severity and mental functioning. Longitudinal study is also needed to better determine if these results are stable over time. The contents do not represent the views of the Dept. of Veterans Affairs of the US government.

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**NR10-37**  
**EFFICACY EXPECTATIONS ARE ASSOCIATED WITH RISK OF NEW ONSET PTSD IN NEW JERSEY NATIONAL GUARD TROOPS**

*Chair: Donald Ciccone Ph.D.*

**SUMMARY:**

Objectives. Recent studies using high risk cohorts, including members of the National Guard and firefighters, have found that lower levels of self-efficacy increase vulnerability to posttraumatic stress disorder (PTSD). The extent to which efficacy expectations influence risk, however, may vary depending on the severity of trauma exposure. High levels of efficacy may protect against PTSD when trauma exposure is low but not when trauma is more severe. At issue in the present study was an effort to (1) replicate the finding that National Guard troops with low efficacy expectations are at increased risk of PTSD after deployment; and (2) determine whether the association between efficacy expectations and new onset PTSD depends on the degree of trauma exposure. Method. A population sample of National Guard troops completed a health survey prior to military deployment and again upon returning home one year later. The survey included a screen for PTSD, a combat exposure questionnaire, and a measure of perceived military preparedness or efficacy. Those scoring at or below the 50th percentile on the preparedness questionnaire were classified as Low Efficacy while those scoring above the 50th percentile were classified as High Efficacy. Results. Guard members who screened positive for PTSD prior to deployment were excluded. Out of 864 remaining

participants, we identified 97 cases of new onset PTSD (11.2%). The percentage of cases among Guard members with Low Trauma Exposure and High Efficacy was 6.8% while for members with Low Exposure and Low Efficacy it was 13.1% ( $p < .05$ ,  $\Phi = .106$ ). In the case of High Trauma Exposure the rates were 6.3% and 19.8% for High and Low Efficacy, respectively ( $p < .01$ ;  $\Phi = .204$ ). Logistic regression was used to model post-deployment PTSD by controlling for extraneous factors, including education, pre-deployment PTSD symptoms and preexisting psychiatric illness. The adjusted odds ratio (AOR) with 95% confidence intervals (in parentheses) for troops with Low Exposure and Low Efficacy was 1.93 (CI= 0.96-3.86) while for troops with High Exposure and Low Efficacy the AOR was 3.03 (CI=1.54-5.95). Conclusions. Pre-deployment efficacy expectations significantly altered risk of new onset PTSD among members of the National Guard. Low Efficacy was associated with increased vulnerability while High Efficacy was associated with lower levels of risk. The effects of efficacy were similar regardless of whether troops reported High or Low combat exposure but the magnitude of the effect was greater for those with more severe trauma.

**NR10-38**  
**TRAUMA AND MENTAL ILLNESS AMONG AFRICAN AMERICAN MALE IN JUVENILE DETENTION**

*Chair: Kenneth Rogers M.D.; Author(s): Eunice Peterson, M.D. Julius Earle, M.D.*

**SUMMARY:**

Objective: African American males are confined in juvenile justice facilities more frequently than other demographic groups. Confinement in a detention facility raises significant issues for psychiatrists since 60% of youth detained in juvenile justice settings have a psychiatric illness. Many of these youth have unidentified and untreated trauma histories. The objective of this study is to identify the types and level of trauma experienced by African American males in a juvenile detention setting. Methods: African American males ages 12-18 detained in a juvenile detention facility were interviewed using the Youth Self Report (YSR) Scale and the Diagnostic Interview Schedule for Children (version IV). Additionally, all youth received a comprehensive psychiatric interview using Kiddie-Schedule for Affective Disorders and Schizophrenia (K-SADS). The parents of the youth were administered the Child Behavior Checklist (CBCL). The total, internalizing, and externalizing T scores were analyzed for both the CBCL and the YSR. A clinical

history was obtained from the parents. Results Seventy percent of youth met criteria for a psychiatric disorder. When using stringently defined behavioral symptoms (T-score=70; 2 SD above the mean on the CBCL) along with the presence of a psychiatric diagnosis, 40% of youth met the criteria for mental health service need. The most common disorders were anxiety disorders (55%), Affective Disorders (53%), and Disruptive Behavior Disorders (43%). This was the first detention for 62% of African American youth. Most youth (68%) were from urban areas while the remaining youth were from rural communities. There were no significant differences between the legal charges of African American and Caucasian youth on variables including types of legal charges or urban vs rural homes. On initial interview 47% of African American males reported experiencing a traumatic event. The events that were specifically asked about included physical/sexual abuse, being threatened or attacked by another individual, witnessing a crime or being a victim of a crime, or being in an accident. The parents of the youth identified traumatic events in 42% of youth. When data from both the parents and the youth were combined, 110 youth (60%) had been exposed to some type of traumatic event. These findings were consistent with the findings for the DISC-IV which found that 101 youth (55%) met criteria for an anxiety disorder with 87 youth (48%) meeting criteria for PTSD. There were also a number of youth who had a history of significant trauma, but did not meet criteria for PTSD or other anxiety disorders such as Acute Stress Disorder. Conclusions: These findings are likely underestimates of the level of trauma experienced by this population. Although they experienced multiple traumas, many youth did not meet criteria for PTSD. More work is needed to identify coping skills in this population.

**NR10-39**  
**FACTORS DETERIORATING DEPRESSION**  
**IN MOTHERS WITH CHILDREN IN**  
**SEPARATION-INDIVIDUATION PERIOD**

*Chair: Hyungin Choi M.D.; Author(s): Y. Wada Ph.D., A. Fujimori Ph.D., H. Yamamoto, H Nanri, T. Yamashita Ph.D., K. Fukui Ph.D.*

**SUMMARY:**

Purpose: The study was conducted to examine the development of depression and factors involved in its exacerbation in mothers with children aged 0 to 2 years. Methods: Data were collected during 0-year-old baby check-ups and a follow-up investigation in Japan, and 262 participants were included in the analysis. The first survey included the Zung Self-rating Depression Scale

(ZSDS), State Trait Anxiety Inventory, the Parental Bonding Instrument and the Borderline Scale Index, and the follow-up survey included ZSDS. Paired t-test was initially performed to investigate the development of the ZSDS scores. ZSDS scores of each of the surveys and the difference among them were then compared between the high/low anxiety traits, the high/low childhood maternal care groups, the borderline personality traits/lack thereof, and some additional personal factors with t-tests. Results: The average ages ( $\pm$  SD) of the children at each of the surveys were  $7.0 \pm 3.24$  months and  $21.8 \pm 2.35$  months, respectively. The ZSDS scores of each of the surveys were  $40.6 \pm 7.88$  and  $40.1 \pm 8.74$ , respectively, but demonstrated no significant difference of the 2 surveys. In the comparison analysis, low childhood maternal care group exhibited markedly higher depression scores in the follow up survey compared with the first. In contrast, high childhood maternal care, the high anxiety trait, the non-borderline trait and breast-feeding groups exhibited markedly lower depression scores in the follow up survey compared with the first. Conclusions: Masterson reported the rapprochement phase (15-22 months) during which the borderline mother is not able to support the child's individuation to defend against her own abandonment depression. Our finding shows that mothers with low childhood maternal care become more depressive during their children's separation-individuation period compared with the postpartum period. In the same manner, the mothers with borderline personality trait did not exhibit improved depression. It implies that they could feel loss of the complete union with their children.

**NR10-40**  
**INCIDENCE AND RISK FACTORS FOR**  
**PREGNANCY AMONG ADOLESCENT**  
**FEMALES IN COLOMBIA: A**  
**POPULATION-BASED COHORT STUDY**

*Chair: Wilma Castilla-Puentes M.D.*

**SUMMARY:**

Incidence and Risk Factors for Pregnancy Among Adolescent Females in Colombia: A Population-Based Cohort Study Objective: To estimate the incidence and risk factors of pregnancy among adolescent females in Colombia. Methods: A prospective 12-month cohort study was conducted from November 2010 to November 2011. At enrollment 2,202 of 2,500 eligible adolescents (88%) were interviewed. A questionnaire focused on psychosocial factors: psychiatric history, family structure, education, reproductive health, suicide behaviors, socioeconomic status and

childhood-adolescent trauma was applied to adolescent girls (10-19 years of age). Depressive symptoms were measured by the Center for Epidemiological Studies Depression Scale (CES-D), with scores > 16 indicative of elevated depressive symptoms. Conditional logistic regression was used to adjust for potential confounders. Results: Data from female adolescents from Duitama N=1,177, 54%; Tunja N=579, 26%; and Santa Marta N=446, 20% were analyzed. There were 19 pregnancies [95% confidence interval (CI) 11.43–29.67, for an overall incidence rate of 9 per 1000-year (1:116). Incidence rates were highest among adolescents 15-18 years of age (95%). In multivariate analysis, depression (OR 21.37, 95% CI 5.92–77.15); history of obesity (OR 20.36, 95% CI 7.03–58.94); being less than 6 years in school at the time of the interview (OR 5.46, 95% CI 0.81–36.73); physical abuse during childhood-adolescence (OR 7.07, 95% CI 1.96–25.51); a lifetime history of suicide attempt (OR 5.96, 95% CI 1.22–29.05); sexual abuse during childhood-adolescence (OR 5.21, 95% CI 0.77–35.13); living in a very poor household (OR 3.64, 95% CI 1.29–10.29); and being use of contraception (OR 2.06, 95% CI 0.69–6.13) were factors significantly associated with increased risk of adolescent pregnancies. Conclusion. These findings suggest that depression, obesity, lower education, history of suicide attempts, history of sexual/physical abuse, living in a very poor household and the use of contraception, were associated with adolescent pregnancy in Colombia. Our study supports the concept that important psychosocial factors contribute to the occurrence of pregnancy among adolescent females.

**NR10-41**  
**CONTINUOUS EXPRESSION OF GSK-3SS**  
**IN THE HIPPOCAMPAL DENTATE GYRUS**  
**INDUCES PRODEPRESSANT-LIKE EFFECTS**  
**AND INCREASES SENSITIVITY TO CHRONIC**  
**MILD STRESS I**

*Chair: Kerang Zhang M.D.; Author(s): Xi Song, M.M., Yong Xu, M.D., Pozi Liu, Ph.D., Ning Sun, M.M., Xin Zhao, Ph.D., Zhifen Liu, M.M., Zhongchen Xie, Ph.D., Jvyi Peng, M.B.*

**SUMMARY:**

Objective: Glycogen synthase kinase-3 (GSK-3) has been linked to prodepressant-like effects in rodents. However, the roles of GSK-3 $\beta$  and the hippocampal dentate gyrus in regulating these behavioral effects remain unclear. The aim of the present study was to explore the effect of overexpressing GSK-3 $\beta$  on mice exposed to chronic mild stress (CMS). Methods: We examined the effects of bilateral intra-hippocampal

injections of lenti-GSK-3 $\beta$ -overexpressing GSK-3 $\beta$  on behavioral performance in mice that were subjected to chronic mild stress (CMS). The expression levels of GSK-3 $\beta$  were persistently and markedly increased in the hippocampal following lenti-GSK-3 $\beta$  injections. Results: In mice that were previously exposed to CMS, pre-injection of lentivirus-expressing GSK-3 $\beta$  into the hippocampal dentate gyrus of the mice significantly decreased their sucrose preferences in the sucrose intake test and increased their immobility times in both the forced swim and tail suspension tests. Moreover, fluoxetine engendered similar antidepressant-like effects following chronic but not acute administrations under these conditions. When we observed cellular apoptosis in the hippocampal DG using a TUNEL approach, we found that lenti-GSK-3 $\beta$  mice exhibited many TUNEL-positive cells suggesting that overexpression of GSK-3 $\beta$  exacerbated the cellular apoptotic effects of CMS. After chronic administration of fluoxetine for 14 days, the number of apoptotic neurons in GSK-3 $\beta$ -overexpressing mice that underwent CMS was not different to that in control mice. Conclusions: To our knowledge, this study demonstrates that site-specific injection of a lentivirus that induces continuous expression of GSK-3 $\beta$  in the hippocampal dentate gyrus of mice elicits prodepressant-like effects and increases sensitivity to chronic mild stress. Furthermore, chronic administration of fluoxetine reverses the prodepressant-like effects and neuronal apoptosis in the hippocampal DG of GSK-3 $\beta$ -overexpressing mice.

**NR10-42**  
**CHILDHOOD TRAUMA, ATTACHMENT**  
**STYLE, AND DEPRESSION IN YOUNG ADULT**  
**WOMEN**

*Chair: Jena Bobish B.A.; Author(s): Deimante McClure, B.S., Christopher Miner, Ph.D., Lisa Cohen, Ph.D., Zimri Yaseen, M.D., Melissa Tandy, Igor Galynker, M.D., Ph.D.*

**SUMMARY:**

Introduction: Current literature on depression suggests that childhood trauma and attachment style may influence the adult presentation of depressive symptoms. We analyzed relationships among depression severity, childhood trauma and attachment in a sample of young adult women who met criteria for Major Depressive Disorder (M.D.D). We hypothesized that adult attachment style and a history of childhood abuse and/or neglect may predict the expression of depressive symptoms. Methods: 14 young females (64 % Caucasian) met criteria for M.D.D and were recruited for an fMRI study at Beth Israel Medical Center in New York City. Upon study entry, questionnaires assessing

clinical characteristics and early childhood experiences were administered. Depression severity, childhood trauma and attachment style were assessed by the Beck Depression Inventory II (BDI-II), the Childhood Trauma Questionnaire (CTQ) and the Relationship Style Questionnaire (RSQ). Following Kurdek (2002), we used RSQ data to create two orthogonal dimensions that index attachment, i.e., Secure/Fearful and Dismissive/ Preoccupied attachment. All measures were correlated pair-wise. Results: Subjects' mean age was 24 years (SD = 2.65). Mean BDI score was 32.0 (SD = 11.8). CTQ sub-scale mean scores were: Emotional Abuse = 13.93 (SD = 5.05), Physical Abuse = 11.43 (SD = 4.89), Sexual Abuse = 10.93 (SD = 7.41), Emotional Neglect = 13.79 (SD = 5.73 and Physical Neglect = 10.93 (SD = 3.85). For the two RSQ attachment dimensions, mean scores were -.62 (SD = 1.70) and .59 (SD = 1.32) on Secure/Fearful attachment and Dismissive/Preoccupied attachment, respectively. BDI-II totals correlated with CTQ Physical Abuse ( $r = .91, p < .0001$ ), CTQ Emotional Abuse ( $r = .82, p < .001$ ), CTQ Sexual Abuse ( $r = .76, p < .01$ ) and, negatively, with RSQ Dismissive/Preoccupied Attachment Style ( $r = -.56, p < .05$ ). Although Secure/Fearful attachment was not significantly related to any measure of neglect, abuse or depression, Dismissive/Preoccupied attachment also correlates negatively with CTQ Physical Neglect ( $r = -.60, p < .05$ ), CTQ Sexual Abuse ( $r = -.73, p < .01$ ), CTQ Physical Abuse ( $r = -.64, p < .05$ ), CTQ Emotional Abuse ( $r = -.53, p < .05$ ) and with the CTQ Summary Score ( $r = -.66, p < .01$ ). Discussion: In a sample of 14 young depressed women, we found that subjects with high scores on Dismissive/Preoccupied attachment tend to have low BDI totals and low CTQ scores. Given the polarity of the Dismissive/Preoccupied attachment dimension, findings indicate that subjects with high scores on the Dismissive end of this dimension tend to have low abuse, neglect and depression scores whereas those falling on the Preoccupied end of the dimension tend to have high abuse, neglect and depression scores. Results suggest that trauma and neglect predict depression severity whereas secure attachment may serve as a protective factor. With increased N, regression models may further elucidate these mediating relationship

#### NR10-43

### A VIRTUAL STUDY DESIGN TO REDUCE "REAL WORLD" CHALLENGES OF A TREATMENT RESISTANT DEPRESSION STUDY IN A MANAGED CARE SETTING

*Chair: Bryce Kasuba M.A.; Author(s): Jay Lombard, DO Herb Harris, M.D. Ph.D. Lauren Novasitis, BS Rachel*

*Belani, BA Jared Steczak, BS Rachel Dicker, M.D.*

#### SUMMARY:

A Virtual Study Design to Reduce "Real World" Challenges of a Treatment Resistant Depression Study in a Managed Care Setting Background: Conducting depression clinical trials in non-research settings offers both challenges and opportunities. We describe methodology employed in the conduct of a clinical effectiveness trial that compares treatment guided by a pharmacogenomic test with Treatment as Usual in outpatients with Treatment Resistant Depression. The study is being conducted in a managed care environment, and it employs design features that enable the collection of patient-reported outcomes (PRO) data in a real-world setting with clinicians who are not generally experienced clinical researchers. Methods: The Principal Investigators will utilize claims data from a mental health managed care company to identify potential study participants, which includes both clinicians and the patients they treat. Care managers will contact clinicians and direct them to a website for electronic consenting; care managers, and/or study PI will be available to address questions during the consent process. Once clinicians provide consent and indicate willingness to participate, care managers will contact their patients identified through claims database. They will provide information for patients to access the web based informed consent and will answer any questions potential subjects have regarding the study. When electronic consent is provided, study entry criteria is confirmed by the care manager over the phone. Study subjects will visit their doctors at the Baseline Visit to provide a sample of their DNA. Clinician Subjects and Study Subjects will complete online assessments and follow-up visits are "virtual" i.e. Subjects will not be required to return to the clinicians office. Results: Study begins recruitment in December 2011 and 100 Subjects are expected to enroll by March 2012. Conclusion: Conducting clinical trials in non-research settings is challenging, but affords the opportunity to collect data relevant to real-world practice. While clinicians often are interested in being a part of research and offering innovative treatment to their patients, many barriers exist including training, ICH/GCP regulations, IRB submission processes and study sponsor agreements. This study design offers a novel paradigm to more quickly operationalize a clinical trial through electronic Informed Consent, close oversight through care managers (via online capture and reporting of PRO data) and rapid identification of study subjects using claims database information.

#### NR10-44

## RELATIONSHIP OF IMPULSIVITY AND SOCIAL SUPPORT TO NUMBER AND SEVERITY OF SUICIDE ATTEMPTS IN BIPOLAR DISORDER

*Chair: Deimante McClure B.A.; Author(s): AMR Lee M.D., J Bobish BA, S Kats, L Cohen Ph.D., II Galynker M.D., Ph.D.*

### SUMMARY:

Introduction: A number of studies suggest impulsivity as an important characteristic of bipolar disorder that may play a role in the disorder's high risk for suicidal behavior. Availability of social support is thought to be an ameliorating factor in suicide risk. In this study, we hypothesized that higher impulsivity and lower social support would be associated with a history of higher number and higher lethality of suicide attempts (SA) in our sample of patients with bipolar disorder. Methods: Patients diagnosed with Bipolar Disorder by SCID-P were recruited from the Family Center for Bipolar in New York City as part of a larger study of Family-Inclusive Bipolar Treatment. At study intake, impulsivity traits were assessed using the Barratt Impulsiveness Scale (BIS) and social support was assessed using the Interpersonal Support Evaluation List (ISEL-12). The Columbia Suicide Severity Rating Scale (CSSRS-S) was used to assess suicidal ideation (SI) and the history and lethality of SA. Results: Seventeen patients were recruited. Patients were diagnosed with Bipolar I (47.1%), Bipolar II (41.2%) and Bipolar NOS (11.8%). Patients were 65% male and 70% white, with a mean age of 38.78 (SD=12.06). 72% reported a lifetime history of SI. Five patients (21.4%) reported a history of SA, with three reporting one attempt, one reporting two attempts, and one reporting three attempts. Among attempters, mean lethality was 1.8 (SD=1.48), with 2 reporting a low level of lethality, 2 a moderate level, and 1 a high level. The non-planning impulsiveness subscale of the BIS (M=27.61, SD=5.68) was negatively correlated with number of SA ( $r=-.518, p=.033$ ), as well as with attempt lethality ( $r=-.621, p=.023$ ). In low scorers on non-planning impulsiveness, the tangible support subscale of the ISEL-12 (but not scores reflecting emotional support) correlated negatively with the intensity of SI ( $r=-.891, p=.003$ ) and the number of SA ( $r=-.730, r=.040$ ). Discussion: In our group of patients with bipolar disorder, lower non-planning impulsivity is associated with a higher number of SA and with more lethal attempts. This finding suggests that the suicidal behavior in this patient group may be premeditated rather than carried out impulsively. In addition, the finding that tangible social support was more related to suicidality than emotional support suggests the

importance of interventions focusing on concrete support in this high-risk population. Key Words: Bipolar Disorder, Impulsivity, Social Support, Suicidal Ideation, Suicide Attempt

## NR10-45 FACTORS IMPACTING MEDICATION REFUSAL AND ADHERENCE IN PREGNANT DEPRESSED WOMEN: MATERNAL AND NEWBORN OUTCOMES

*Chair: Deirdre Ryan M.D.; Author(s): Deirdre Ryan, M.D., Shaila Misri, M.D., Jasmin Abizadeh, B.A., Gillian Albert, B.Sc., Diana Carter, M.D.*

### SUMMARY:

Objective: Clinical evidence suggests that pregnant women with mood and anxiety disorders often hesitate to engage in pharmacotherapy due to fear of teratogenicity in the fetus. Specific demographic or psychosocial characteristics may differentiate women who adhere to antidepressant medication (AD) versus those who decline, resulting in varying mental illness trajectories. Methods: 59 pregnant women (18-34 weeks) were classified as adherers taking medication (n=30) or decliners not taking medication (n=29). Follow up occurred at 18, 22, 26, 30, 34 weeks and 1 month postpartum. Questionnaires assessed mood, anxiety, personality, social support, genetic vulnerability, addiction severity, mood disorders insight, alternative therapies, AD compliance. Qualitative interviews took place with the mothers and data was collected from neonatal charts (n=34). Results: Results are based on 50 women (30 adherers, 20 decliners) due to attrition. Adherers and decliners did not statistically differ in mean age, years of education, ethnicity, marital status, or household income (all  $p's > .25$ ). No differences in social support [ $t(45) = .295, p = .77$ ] or personality traits existed [ $F(5, 42) = 1.63, p = .17$ ]. Adherers had significantly better attitudes towards AD compliance [ $F(4, 34) = 5.68, p < .005$ ] and insight into their illness [ $F(3, 41) = 7.43, p < .001$ ]. Both groups did not differ in alternative therapy use [ $t(33) = -.360, p = .72$ ], their worrying [ $t(45) = .93, p = .36$ ] or the likelihood of having obsessions, compulsions or panic attacks [ $\chi^2(1) = 1.75, p = .19$  for Y-BOCS;  $\chi^2(1) = .62, p = .43$  for PDSS]. Both had similar lifetime regular alcohol consumption rates [ $\chi^2(1) = 3.09, p = .08$ ] but decliners were significantly more likely to have drunk to intoxication [ $\chi^2(1) = 4.64, p = .03$ ]. Depression [ $t(48) = -1.49, p = .30$ ] and anxiety [ $t(48) = 0.08, p = .94$ ] scores at study entry were not significantly different but adherers' HAM-D scores decreased on average by 6.8 points between the first and last visit and increased for decliners by 5.2 points. Likewise, HAM-A scores

for adherers decreased by 5.4 points and increased for decliners by 6.4 points. No apparent group differences in newborn characteristics existed (e.g. gestational age, weight, APGAR, etc.; all  $p$ 's > .35). Few babies were abnormal on physical measures of health at the time of birth (e.g. general appearance, skin, respiration, etc.). Nearly all were rated normal when re-assessed at discharge. Qualitative analysis revealed that adherers wanted a sense of control, could not function without AD and desired to be well for their child. Decliners worried about their fetus or infant being exposed to AD, did not believe they needed AD and wanted to avoid negative side effects. Conclusion: Pregnant women who adhere to AD differ on psychosocial characteristics from those who decline.

**NR10-46**  
**SYSTEMATIC LITERATURE REVIEW OF ECONOMIC COSTS IN THE US OF MAJOR DEPRESSIVE DISORDER IN ADULTS WHO ARE INADEQUATE RESPONDERS TO INITIAL TREATMENT**

*Chair: Eduard Vieta M.D.; Author(s): Julie Locklear, Phar M.D., MBA, Helena Granstedt, MSc, Evelina Zimovetz, MSc, Josephine Mauskopf, Ph.D., Raj Tummala, M.D., Berhanu Alemayehu, MS, Miny Samuel, Ph.D.*

**SUMMARY:**

**Objective:** Although antidepressant drugs are efficacious and widely prescribed, 50% to 70% of patients do not achieve remission after receiving treatment with at least 1 antidepressant of standard dosage and sufficient duration. Given that major depressive disorder (M.D.D) is highly prevalent and may result in ongoing impairment of psychosocial and occupational functioning and physical health, characterization of the economic costs of inadequate response to antidepressant treatment is warranted. Here, we present data from a systematic literature review of studies that report cost data for inadequate responders to SSRI or SNRI treatments in the United States. **Methods:** Using a predefined strategy, a search was performed in MEDLINE, EMBASE, the Cochrane Library, Econ Lit, the National Health Service Economic Evaluation Database, and the Health Economic Evaluation Database using a time frame of January 2000 to February 2011. Conference abstracts from January 2008 to February 2011 were also searched. Studies reporting costs and/or resource utilization associated with inadequate response to treatment of M.D.D were selected. In this literature review, inadequate responders include partial and nonresponders, those who switch

or augment their initial treatment, and those defined as having treatment-resistant depression (TRD, a condition to which inadequate response may eventually lead). **Results:** A total of 11 US-specific cost-of-illness studies were included (cost-years, 1994 to 2007): Of these, 10 examined direct health care costs, 6 reported indirect costs (e.g., lost productivity), and 7 were prospective. Partial and nonresponse definitions varied slightly across the 4 studies that reported costs by these outcomes; however, remission was consistently defined as a HAM-D17 score <8. Direct costs were higher for patients with partial or nonresponse than for patients who attained remission. Annual mean total health care costs ranged from \$3459 to \$3564 for partial responders; \$3324 to \$8661 for nonresponders; and \$1332 to \$2816 for remitters (4 studies). Productivity loss (i.e., indirect cost) was substantial?1.4 to 2.7 times higher for partial and nonresponders compared with remitters. The available evidence was insufficient to conclude with certainty that costs associated with nonresponse were higher than those with partial response. Patients who had treatment switches or augmentations incurred 38% to 54% higher costs than did patients who maintained their initial therapy (3 studies). Patients categorized as having TRD had the highest all-cause health care costs, ranging between \$8506 and \$10 377(4 studies). **Conclusion:** Systematic review of the literature from the US indicates that health care costs and lost productivity due to illness were higher for adults with M.D.D who had inadequate response to initial treatment compared with patients in remission, patients whose initial treatment was not switched or augmented, or patients defined as not having TRD.