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NEW RESEARCH ABSTRACTS

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NR1-01

MEDITATION AS TREATMENT MODALITY IN ACTIVE DUTY SERVICE MEMBERS PARTICIPATING IN RESIDENTIAL SUBSTANCE ABUSE REHABILITATION

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SUMMARY:
Objective: To evaluate the usefulness of meditation on state of change for attitudes toward drinking in an active duty population who are in residential treatment for alcohol and substance abuse. Method: IRB permission was gained to do anonymous survey using the Stages of Change Readiness and Treatment Eagerness Scale (SOCRATES) in active duty service members who were enrolled in a mindfulness based meditation education class. This class was a 4 class group meeting once a week for 90 minutes which involved teaching mindfulness-based meditation practice. The class provided educational materials on medication and an audio CD to facilitate practice though the week. Practice logs and journals were kept by participants Twenty service members were surveyed at the beginning of the 30 day residential program and at the end of the program. The meditation group was a voluntary class, that was in addition to the treatment curriculum of the substance abuse rehab program. Results: Significant improvement was made in recognition (17.1 to 32.3), ambivalence (8.4 to 12.7) and taking steps towards change in drinking behaviors (16.6 to 36.9), as assessed by the SOCRATES. Student T test showed results to be statistically significant for all subscales ($p < 0.001$). Conclusions: Using mindfulness breath-centered meditation may be a helpful treatment modality for service members who wish to recover from substance dependence and/or abuse. Randomized studies will be necessary to determine if the benefits described above are exclusively due to the effects of participation in meditation class.

NR1-02

STRAWS: SCHEDULED TAPER RECOMMENDED FOR ALCOHOL WITHDRAWAL SYNDROME

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SUMMARY:
Objective: To compare the safety and efficacy of using a scheduled benzodiazepine taper versus as-needed dosing for alcohol withdrawal syndrome (AWS). Methods: At RWJUH, a policy was recently ratified to standardize the screening and treatment of alcohol withdrawal syndrome (AWS). We conducted a retrospective study to assess the efficacy and safety of the current management of individuals diagnosed with AWS according to the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition. Inclusion criteria included patients assessed by the consultation-liaison service with an Axis 1 diagnosis of AWS who were recommended to receive either (a) standard taper (fixed-schedule) of benzodiazepine versus (b) as-needed dosing (prn vital signs and/or evidence of tremor). Results: A total of 16 patients were consulted by the C/L team. Of those, 14 (87.5%) were in the scheduled taper group and 2 (12.5%) were treated with as-needed benzodiazepine alone. No patients were front loaded or received symptom-triggered therapy (CIWA). Of the 14 patients being tapered, 100% received Lorazepam. The mean duration of Lorazepam treatment was 6 days in the "scheduled taper" group versus 16 days in the "as needed" group. The number of patients who experienced withdrawal complications including delirium (6) and seizures (2) were greater in the "scheduled taper" group, likely reflecting milder forms of withdrawal being treated with as-needed benzodiazepines alone. Conclusions: Although milder forms of alcohol withdrawal, as evidenced by lower rates of complications, are often treated with as-needed dosing of benzodiazepines alone, benzodiazepine taper for alcohol withdrawal is safe, and is associated with a decrease in the quantity of medication and duration of treatment when compared to dosing as needed for abnormal vital signs and/or tremor.

NR1-03

CORRELATION BETWEEN CHRONIC COCAINE USE AND HYPOGLYCEMIA IN PATIENTS ADMITTED TO THE HOSPITAL

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SUMMARY:
Background: Cocaine intoxication has traditionally been associated with hyperglycemia due to elevated input from

the sympathetic nervous system. The mechanism of elevation is via inhibition of serotonin-norepinephrine-dopamine reuptake. The human body however cannot perpetually sustain the hyper metabolic state induced by cocaine toxicity and hypoglycemia may ensue. Although no definitive relationship has been established between cocaine and hypoglycemia, cocaine use can theoretically cause hypoglycemia through several proposed mechanisms. One such mechanism is that of prolonged adrenergic stimulation as a result of a chronic hyper metabolic state which can lead to adrenergic receptor desensitization and decreased sympathetic tone below baseline levels, thus inducing hypoglycemia. A similar mechanism may occur with regard to the receptors of counter-regulatory hormones (glucagons, norepinephrine, epinephrine, cortisol, growth hormone). Another mechanism speculated to decrease sympathetic tone is depletion of catecholamine neurotransmitters from prolonged stimulation. Lastly, cocaine use decreases appetite and chronic cocaine abusers can suffer from hypoglycemia due to malnutrition. Methods: A retrospective chart review was done for patients admitted to Bergen Regional Medical Center with the diagnosis of Cocaine Dependence with Physiological Dependence between January 2007 and January 2009. Data collected include demographic factors and axis III comorbidities. Patients with the diagnosis of Diabetes Mellitus, CAD, Obesity, Mood Disorder, Alcohol Dependence, Schizophrenia and patients who were on antipsychotic medication were excluded. Patients with DSM-IV diagnosis of cocaine dependence, between ages of 18-55, and patients with BMI less than 30 were included. Fasting blood glucose was compared for the possibility of hypoglycemia. Result: In a review of 177 patients' records, 22 patients showed fasting blood glucose levels below 70mg/dl. This value represented 12.4% of the patients studied and these patients were classified as hypoglycemic. 148 patients, or 83.6% of the sample, were found to have fasting glucose values between 70mg/dl and 125mg/dl. These patients were classified as euglycemic. 7 patients, constituting 4% of the sample, were found to have fasting glucose values over 125mg/dl. These patients were classified as hyperglycemic. Conclusion: Our analysis provides evidence that hypoglycemia is associated with chronic cocaine use.

NR1-04

SAFETY AND EFFICACY OF VARENICLINE IN SCHIZOPHRENIA: PRELIMINARY DATA

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SUMMARY:
Varenicline was approved in 2006 for treatment of tobacco dependence. In 2009 the FDA issued a warning about possible adverse effects including depression and suicidal thoughts and actions. Although increases in depressed mood and suicidal ideation have not been observed in controlled trials or large observational studies, people at high risk for these outcomes, those with major mental illness, have not been studied systematically with varenicline. Objective: To evaluate the safety and efficacy of varenicline when used for treatment of tobacco dependence in stable, treated, outpatient smokers with schizophrenia. Methods: We conducted a 12-week, open-label, smoking cessation trial prior to a 40-week randomized double-blind, relapse-prevention phase in subjects able to quit smoking during the open phase. Subjects were nicotine-dependent adults with schizophrenia or schizoaffective disorder who were on a stable antipsychotic medication regimen, who smoked = 10 cigarettes a day, and who had no inpatient hospitalization for suicidal ideation in the 12 months prior to enrollment. Results described are from the first 86 subjects in the study enrolled in a cohort whose group completed open phase. Data were collected from May 5, 2008 to October 2, 2009. Results: 45.4% of those enrolled (39 of 86) achieved =2 weeks biochemically verified continuous tobacco abstinence at the end of the open phase. Significant changes in ratings of clinical symptoms during the open trial phase from baseline to week 12 or drop-out were not observed. Brief Psychiatric Rating Scale (BPRS) (53.8 (15) Baseline, 52.8 (14.6) week 13, p= 0.49), Scale for Assessment of Negative Symptoms (SANS) (44 (16.4) Baseline, 46 (16.4) week 13, p=0.25). Calgary Depression Scale (CDSS) (4.2 (3.3) Baseline, 4.0 (4.2) week 13, p=0.63). There is an early indication that varenicline may be associated with improvement in psychotic symptoms, BPRS Psychosis sub-scale (10.4 (5.6) Baseline, 9.6 (5.0) week 13, p< 0.04). Conclusions: These early, open-label findings suggest that 12 weeks of varenicline treatment is effective for smoking cessation in schizophrenia and is not associated with significant worsening in psychiatric symptoms. Supported by R01 DA021245. Study medication provided by Pfizer.

NR1-05

CLINICAL CORRELATES OF ATTRITION AT A RESIDENTIAL SUBSTANCE ABUSE THERAPEUTIC COMMUNITY PROGRAM

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SUMMARY:
Objective: Despite studies demonstrating improvement in substance abuse outcomes in long term residential treatment programs, attrition rates remain high and little is known about factors associated with attrition. We investigated clinical variables that correlate with attrition at a modified residential therapeutic community program for substance abusers. Methods: We conducted a retrospective chart review of residents at a 2-year modified residential therapeutic community program for substance abusers. Approximately 400 residents enrolled in the program in 2006, of which 189 randomly selected charts were reviewed. Follow-up data were up to 2 years from time of enrollment. Statistical analyses were performed using SPSS. Results: Of the 189 study subjects, 78% were male, 62% were African-American and 35% were Caucasian. Thirty-three percent of subjects were homeless at time of admission. Cocaine (73%) was the most common primary drug of addiction followed by alcohol (14%), opioids (9%), and cannabis (4%). Forty-eight percent of participants had history of felonies; 21% had misdemeanors; 34% had violent offenses; and 44% had drug offenses. Nine percent of subjects reported a history of psychiatric care at intake. Thirty percent of residents completed the 2-year program. Logistic regression analyses showed a significant correlation of attrition with history of violent offenses (p=0.004) and misdemeanors (p=0.033), and a trend association with history of drug offenses (p=0.057) and psychiatric care (p=0.061). Conclusions: In this population of substance abusers, having a history of violent offenses or misdemeanors was correlated with dropout from the 2-year residential program. It also appears that a history of drug offenses or psychiatric care may be associated with attrition. Specific treatment approaches tailored to patients with criminal or psychiatric history may be required to address attrition in residential programs.

NR1-06

COLLECTIVISTIC AND SOSIOTROPIC TENDENCY OF PATIENTS WITH ALCOHOL DEPENDENCE IN KOREA

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SUMMARY:
Objective: The purpose of this study was to investigate collectivistic and sociotropic tendency of patients with alcohol dependence (AD) in Korea. Method: The subjects were 54 patients who met DSM-IV criteria for AD and 57 normal controls (NC). We administrated the questionnaires about demographic factors, individualism-collectivism(INDCOL), familialism, self-esteem, sociotropy-autonomy (Personal Style Inventory ; PSI).
Results: 1.) The education level and marital status in AD group were significantly lower than those of NC group. There was no difference in age, sex, religion between two groups. 2.) Among the subscales of PSI, score on sociotropy was significantly higher in the AD group than in the NC group ($p<0.05$). 3.) Self-esteem was significantly lower in the AD group than in the NC group ($p<0.01$). 4.) There was no significant difference in the INDCOL score between two groups. Conclusions: These results suggest that sociotropic tendency and low self esteem are related to patients with AD in Korea.

NR1-07

SEXUAL DYSFUNCTION IN PATIENTS DIAGNOSED WITH SUBSTANCE USE DISORDER

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SUMMARY:
Objective: To assess the impact of illicit drug abuse on male sexual function.
Method: Patients aged between 18-65 years with the diagnosis of substance use disorder according to DSM-IV-TR in Ankara Numune Training and Research Hospital Alcohol and Substance Treatment Department during March 2008 – August 2008 were enrolled in the study. Sexual functioning was evaluated using International Index of Erectile Function Questionnaire (IIEF) for male patients and The Female Sexual Function Index (FSFI) for female patients. Age and sex matched healthy volunteers without any mental and physical disorder were included as the control group. Results: 111 patients who met the study criteria (91% male (n=101)) and 43 healthy control group were included in the study. Twenty-six percent of participants have alcohol (n=40), 19.5 % opioid (n=30), 13 % mixed substance (n=20) and 13.6 % cannabis use

disorder (n:21). Median age of the patients was 32 (min=19, max=63). Total median scores of IIEF were found as: in alcohol users 55.0 (min=10, max=74), in opioid users 21.0 (min=5, max=62), in mixed substance users 35.0 (min=5, max=63), in cannabis users 48.50 (min=11, max=70) and 58.0 (min=31, max=71) in control group. According to IIEF total median scores, there was no significant difference between alcohol users and control group (P>0.005), IIEF median scores of opioid, mixed substance and cannabis users were significantly less than control group (P=0.00, P=0.00, P=0.014). Opioid users have significantly lower scores compared to control group among all subscale scores (P =0.00). Alcohol users had statistically lower scores on sexual desire and general satisfaction while cannabis users had lower scores on erectile function, sexual satisfaction and sexual desire compared to the control group. (P<0.005). Erectile dysfunction (ED) was reported in 69.3% and orgasmic dysfunction was reported 77% of all abusers. 96.3% (n=26) of the opioid users had reported erectile dysfunction, 88.9% (n=24) orgasmic dysfunction. 80% of the cannabis users (n=16) had erectile dysfunction and 70 % (n=14 orgasmic dysfunction. 88.2% of mixed substance users and 56.8% of alcohol users have erectile dysfunction. Conclusion: In our study orgasmic disorder was associated only with opioid use but not associated with other drug and alcohol use. Drug male abusers were prone to have ED, decreased sexual desire, and sexual satisfaction compared with healthy controls.

NR1-08

SUBSTANCE USE AND TRAUMA: A RETROSPECTIVE CHART REVIEW OF TRAUMA PATIENTS IN THE URBAN SOUTH

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SUMMARY:

It is well known that substance use poses a significant burden to individuals and societies throughout the world, causing it to remain an important area of research and clinical concern. Recent epidemiological studies have shown a significant association between substance use and injury among patients admitted to trauma centers. There is, however, limited information available in the literature concerning this relationship between substance use and trauma in the southern part of the United States. An IRB approved retrospective chart review of over 2000 surgical trauma patients is planned. Thus far, over 800 charts have been reviewed with data collected from the national trauma registry database in addition to the medical record. Blood alcohol level (BAL) and urine drug screen (UDS) results were collected along with demographics (age, sex, race), mechanism of injury (penetrating versus blunt), and outcome measures including Glascow Coma Scale (GCS), length of stay (LOS), and deaths (immediate versus total). The data has been examined to determine the incidence of BAL positive as well as the incidence of positive urine drug screen results for substances including cocaine, benzodiazepines, barbiturates, opiates, methadone, amphetamines, and cannabanoids. The preliminary data was analyzed using Fisher's exact T-test and ANOVA analysis to determine significant differences among alcohol positive and negative groups and among UDS positive and negative groups. Finally, the percentage of patients testing positive for either alcohol or drugs was determined for the counties in South Carolina with the highest number or trauma patients. Our preliminary data shows that 40.1% of surgical trauma patients tested positive for alcohol and 55.6% tested positive for at least one substance on urine drug screen at time of presentation. Younger age appears to be a significant factor in both alcohol- and drug-positive groups, but male sex was only significant in the alcohol group. No significant differences in race were identified in either group. Both positive alcohol and drug screening appear to be associated with higher risk of penetrating trauma and with lower Glascow Coma Scale scores. Although many studies have shown high incidences of substance use in trauma patients, questions regarding psychiatric follow up and assessment remain. We aim to identify how our patients with substance use disorders are at higher risk for trauma.

NR1-09

THE CONTRIBUTING FACTORS ON THE PROBLEM DRINKING OF WORKERS

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SUMMARY:

Objectives: Drinking problems among employees cause decreased productivity, injuries, and increased health insurance claims . In this study the relationships between 7 measures of alcohol-related psychosocial factors and employee's drinking problems were investigated. Methods: Cross-sectional data were collected from 898 employees living in Chuncheon city. Data from 678 employees were

subjected to final analysis. All subjects completed a set of self-report questionnaires that included the demographic data, problematic drinking behavior (AUDIT-K), expectations about the effect of drinking (Alcohol Belief Scale), a job stress questionnaire (Korean Occupational Stress Scale), and questions about the workplace drinking environment (e.g., the workplace subculture about drinking), social support, and self- esteem. Results: The AUDIT-K score was significantly and positively correlated with alcohol withdrawal experiences, expectations of the effect of drinking, workplace drinking environment, social support, and self-esteem. Analysis by binary logistic regression showed that sex, the amount of daily drinking, expectations about the effect of drinking, and characteristics of the subculture about drinking predicted problem drinking. However, job stress, which had been known to be a contributing factor for employee drinking problem was not related to problem drinking behavior in this study. Conclusion: Previous evidence indicates that job stress can contribute to alcohol problems among employed persons. However, this study does not support this linkage between job stress and alcohol problems. Instead, positive expectations about the effects of drinking and the degree of positive environment about drinking in the workplace contributed to the severity of employee alcohol problems in this study. These results have important implications for the development of preventive programs for employee alcohol abuse by changing the office subculture through educational programs that correct distorted expectations about the effects of alcohol.

NR1-10

COMPARISON OF BEHAVIORAL, PSYCHOLOGICAL CHARACTERISTIC FEATURES AND SEVERITY BETWEEN GAMBLERS IN LEGAL AND ILLEGAL GAMBLING PLACES

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SUMMARY:
Objective: Pathological gambling problem has become a serious social and national issue in Korea recently. About 3 to 4% of Koreans are estimated to be pathological gamblers. In particular, illegal gambling (the video slot machine game) used to be massively popular in residential areas and disappeared nationwide 4 years ago under strict governmental regulation. However it's now doing a brisk business in apparently illegal online gambling. This study investigated whether the pathological gambling severity, motivation, irrational gambling belief and depressive mood varied between gamblers in legal and illegal gambling places (the video slot machine game rooms). Methods: A sample of 890 adults was collected at legalized gambling places, illegalized gambling places, or normal general people and divided into three groupings: gambling in both legal and illegal gambling places(n=217), gambling only in legal gambling places (n=119), and gambling only in illegal gambling places (n=124). We had analyzed the differences of the prevalence of pathological gambling, the gambling motives for avoidance, monetary, excitement and socialization, the degree of irrational belief about gambling, severity of anxiety and depression among 3 groups. Results: The results revealed that the prevalence of pathological gambling was the highest in the both legal and illegal gambling places, and the lowest in the only legal group. Among the gamblers who gambled in the both legal and illegal places, the gambling motives for avoidance, monetary, excitement and socialization tended to be stronger and the degree of irrational belief about gambling, severity of anxiety and depression were higher than the other groups. Conclusion: These results suggest that for some people, easy access to gambling will be a risk factor for pathological gambling.

NR1-11

PSYCHIATRY RESIDENTS' ATTITUDES ON SUBSTANCE ABUSE: CHANGES IN ATTITUDES POST-SBIRT TRAINING

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SUMMARY:
Psychiatry residents encounter many patients with substance abuse problems. Substance abuse disorder is costly to health care if not treated and detrimental to a patient's overall health. Under-diagnosis or under-treatment of substance use disorder can further complicate medical and psychiatric illness. According to the literature (Chappel JN, Veach TL, Krug RS. The Substance Abuse Attitude Survey: An Instrument for Measuring Attitudes. Journal of Studies on Alchohol, Vol. 46, No. 1, 1985 and Ballon BC, Skinner W. "Attitude is a Little Thing That Makes a Big Difference": Reflection Techniques for Addiction Psychiatry Training. Acadmic Psychiatry, 32:3, May-June 2008) there is evidence that psychiatry residents

have negative attitudes toward patients who abuse substances. As a result of the negative attitudes, diagnosis is delayed until late in the disease and treatment is applied with little hope of improvement. Studies have shown that various courses or training concerning substance abuse have changed psychiatry residents' attitudes in a more positive direction when working with this patient population (Karam-Hage M, Nerenberg L, Rower KJ. Modifying Residents' Professional Attitudes about Substance Abuse Treatment and Training. Am J Addict 2001; 10:40-47). This change in resident attitude towards working with a substance abuse population helps psychiatry residents provide appropriate and better care for those suffering with addictive disorders. Based on the literature that indicate that an educational training or course on substance abuse treatment has a positive influence on psychiatry residents' attitudes toward working with substance abuse population, the current study set out to explore if screening, brief intervention, and referral for treatment (SBIRT) training would change psychiatry residents' attitude when working with this patient population. SBIRT was initiated as a research project to help develop programs to improve resident education in substance abuse and diagnosis. SBIRT was developed as part of a larger SAMHSA training grant, a public health initiative to reduce risky use of alcohol and other substances in health care. Twenty-three psychiatry residents in an upstate New York residency training program were given the Chappel's substance abuse attitude survey (SAAS) pre- and post-SBIRT training. The current study predicts a change in psychiatry's residents' attitudes in a more positive direction after SBIRT training.

NR1-12

WITHDRAWAL AND ABSTINENCE-RELATED PSYCHIATRIC SYMPTOMS IN ABSTINENT METHAMPHETAMINE-DEPENDENT SUBJECTS

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SUMMARY:

Methamphetamine (MA) abuse is a growing problem that has reached epidemic levels worldwide. There are no FDA-approved medications to treat it, and current psychosocial treatment modalities have limited effectiveness. With respect to drug dependence in general, severe withdrawal symptoms are associated with propensity to relapse. This may also be true of MA dependence. Previous studies of MA withdrawal symptoms during abstinence have included few subjects and had a narrow scope of symptom focus. A better understanding of the time-course and range of physical, emotional, and psychiatric symptoms experienced by MA-dependent subjects during abstinence would help identify factors that may lead to relapse. Therefore, in a study of 56 MA-dependent subjects, we asked 1) whether initiating abstinence from MA withdrawal produces debilitating psychological and physical symptoms during the first week, 2) how craving for MA evolves during abstinence, and 3) whether psychiatric symptoms (e.g., depression, psychosis) are related to duration of abstinence up to 5 weeks. We observed a generally benign withdrawal syndrome that resolved completely within several days to 2 weeks of abstinence. Initially high levels of depressive and psychotic symptoms largely resolved with a week. However, craving for MA did not significantly decrease from the time that abstinence was initiated until the second week, and then continued throughout the fifth week at a reduced level. This symptom pattern may contribute to the high propensity to relapse among MA-dependent individuals. Based upon these findings, we suggest that medications which target craving during abstinence may be helpful to treat MA dependence.

NR1-13

ASSOCIATION STUDY BETWEEN PANIC DISORDER AND 5-HT1A GENE C(-1019)G POLYMORPHISM

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SUMMARY:

Objectives: Various studies suggest that serotonergic dysfunction is quite evident in panic disorder. In particular, allelic variations in the 5-HT1A receptor gene can be a predisposing factor for panic disorder. We investigated whether the C(-1019)G polymorphism of 5-HT1A receptor gene may play a role in the pathogenesis of panic disorder. Methods: Ninety-four patients with panic disorder were included in this study. Patients who have comorbidity with medical disease, mood disorders and other psychotic disorders were excluded. Concurrent agoraphobia was present in 70 (74.5%) of the patients. One hundred eleven healthy controls were recruited by local advertisement. The 5-HT1A receptor genotype for the SNP C(-1019)G was analyzed in patients and healthy

controls. For statistical analysis, allele and genotype associations with the SNP C(-1019)G were evaluated using the ?2 test or Fisher's exact test. The severity of the patients' symptoms was examined using the Spielberger State-Trait Anxiety Inventory (STAI), Panic Disorder Severity Scale (PDSS), Anxiety sensitivity index (ASI), Acute Panic Inventory (API) and Hamilton's Rating Scale for Anxiety (HAM-A). Effect of genotype on symptom severity was examined with ANOVA by comparing the mean scores of each genotype. Results: The distribution of the genotypes of the C/G polymorphism did not differ significantly from those predicted by Hardy-Weinberg equilibrium in controls(p=0.99) as well as the patients (p=0.98). No association between the C(-1019)G polymorphism and panic disorder was detected in either the allele frequency(?2 =0.541, p=0.462) or genotype distribution (?2 =0.617, p=0.734). No significant association could be observed in the subgroup of panic-disorder patients with agoraphobia (?2 =1.742, p=0.783) comparing the genotype distribution. Symptom severity differences were no significant statistical differences between genotypes in patients with panic disorder (STAI : F=0.481, p=0.619; API : F=0.025, p=0.975; ASI : F=0.091, p=0.913; PDSS : F=0.290, p=0.749; Ham-A : F = 0.062, p=0.940). Conclusion: There was no association between the C(-1019)G 5-HT1A receptor gene polymorphism and panic disorder. Further studies with other SNPs of 5-HT1A receptor and transporter gene and haplotype analysis will be needed to prove genetic factors underlying panic disorder.

NR1-14

ASSOCIATION STUDY BETWEEN PANIC DISORDER AND -874 A/T INTERFERON-GAMMA GENE POLYMORPHISM

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SUMMARY:

Objectives: Cytokines have been associated with the pathophysiology of psychiatric disorders, including schizophrenia, major depressive disorder and anxiety disorder. Interferon gamma (IFN-r) is an inflammatory cytokine playing a important role in both innate and adaptive immune responses. In animal studies, chronic administration of inflammatory cytokines has induced symptoms similar to depression and anxiety. We aimed to investigate whether the Interferon-gamma-874 A/T SNP may play a role in the pathogenesis of panic disorder.

Methods: One hundred and six patients with panic disorder were included among the patients admitted to Korea university hospital. One hundred forty-nine healthy controls were recruited by local advertisement. Patients with panic disorder who have comorbidity with medical disease, mood disorders or other psychotic disorders were excluded. Control groups were also excluded if they had any self-reported personal or familial psychiatric history. The genotype for the SNP Interferon-gamma-874 A/T was analyzed in patients and healthy controls. Genotype and allele frequencies were compared between groups by ?2 test. The severity of the patients' symptoms was examined using the Spielberger State-Trait Anxiety Inventory (STAI), Panic Disorder Severity Scale (PDSS), Anxiety sensitivity index (ASI), Acute Panic Inventory (API) and Hamilton's Rating Scale for Anxiety (HAM-A). Effect of genotype on symptom severity was examined with ANOVA by comparing the mean scores of each genotype. Results: The distribution of the genotypes of the Interferon-gamma-874 A/T polymorphism did not differ significantly from those predicted by Hardy-Weinberg equilibrium(p=0.98) in the controls as well as in the patients. No evidence of an association between the Interferon-gamma-874 A/T polymorphism and panic disorder was detected in either the allele frequency or genotype distribution (?2 =2.148, p=0.342). No significant association could be observed in the subgroup of panic-disorder patients with agoraphobia (?2 =1.851, p=0.396) comparing the genotype distribution. Symptom severity differences were no significant statistical differences between genotypes in patients with panic disorder (STAI : F=1.093, p=0.339; API : F=2.375, p=0.098; ASI : F=2.142, p=0.123; PDSS : F=2.134, p=0.124; Ham-A : F = 1.403, p=0.251). Conclusion: Our study result showed no association between the Interferon-gamma-874 A/T gene polymorphism and panic disorder.

NR1-15

COMPARISON OF ANXIETY-RELATED TRAITS BETWEEN EARLY AND LATE-ONSET PANIC DISORDER

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SUMMARY:

Objectives: It has been suggested that there are some

differences between early- versus late-onset panic disorders. However, it is still unclear that this distinction of early- versus late-onset panic disorder is a valid clinical classification. The aim of this study is to investigate possible differences of anxiety-related traits between early- and late-onset panic disorder. Methods: Two hundred thirteen out-patients were recruited and diagnosed with panic disorder by MINI international neuropsychiatric interview. We divided the patients into 2 groups: early-onset panic (n=177, panic onset<50 years of age) and late-onset (n=36, panic onset=50 years of age). Anxiety Sensitivity Index (ASI), ASI-dimensions, Beck Anxiety Inventory (BAI), Beck depression Inventory (BDI), State-trait anxiety Inventory (STAI-S, STAI-T), Hamilton Anxiety Scale (HAM-A), and Hamilton Depression Scale (HAM-D) were compared between two groups using the independent t-test. Univariate analyses were controlled for differences in age, sex, illness duration, education and marital status by using analysis of covariance. Results: There are significant differences between early- and late-onset panic disorders according to age, sex, and illness duration. Patients with late-onset panic disorder showed lesser severity of ASI ($p<0.034$), ASI-psychological ($p<0.022$), ASI-social ($p<0.023$), BAI ($p<0.022$), and HAM-A ($p<0.010$), STAI-T ($p<0.047$) than early-onset subjects. But comparison of ASI ($F=0.073$, $p<0.787$), ASI-psychological ($F=0.000$, $p<0.987$), ASI-social ($F=0.073$, $p<0.788$), BAI ($F=0.154$, $p<0.695$), HAM-A ($F=0.849$, $p<0.358$), and STAI-T ($F=2.419$, $p<0.121$) did not show any difference between two groups after controlling age, sex, and illness duration. We also found that there were no significant differences between two groups by the presence of comorbidity ($p<0.263$). Conclusion: These results suggest that early- and late-onset distinction of panic disorder may be a relatively arbitrary cut in the same disorder.

NR1-16

THE EFFECT OF TEMPERAMENT AND CHARACTER ON THE TREATMENT OUTCOME AFTER 24-WEEK PHARMACOTHERAPY WITH ESCITALOPRAM IN PATIENTS WITH PANIC DISORDER

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SUMMARY:
Background: Personality traits are known to play an important role in the treatment outcome of anxiety disorders. However, few studies have reported the effect of temperament and character on the treatment outcome after long-term pharmacotherapy with selective serotonin reuptake inhibitors in patients with panic disorder (PD). Thus, we examined which temperament or character dimension could predict treatment outcome after 24-month escitalopram treatment in patients with PD. Methods: Data of the eighty-two patients (age = 42.2 ? 11.2yr; M/F = 48/34) who met DSM-IV criteria for current PD were eligible for the analysis. All the subjects received escitalopram during 24 months(final dosage = 12.2 ? 3.8mg). Remission criteria were as follows: 1) The Hamilton Rating Scale for Anxiety (HAM-A) score = 7; 2) The Clinical Global Impression-Severity (CGI-S) = 2; 3) The Hamilton Rating Scale for Depression (HAMD) = 7; and 4) essentially free of panic attacks. Personality was assessed using the Cloninger's temperament and character inventory-revised short form (TCI-RS). Results: Fifty-two patients with PD achieved remission. Demographic and baseline clinical data were not significantly different between the remitters and non-remitters. Non-remitters showed higher reward dependence than remitters, and logistic regression analysis revealed that higher reward dependence predicted non-remission after 24-month treatment with escitalopram for patients with PD (OR=0.248, CI = 0.07-0.85, p=0.026). Conclusion: This study shows that panic patients with high reward dependence are apt to be resistant to escitalopram treatment. Since long-term pharmacotherapy is needed for treatment of panic disorder, the present result suggests that development of therapeutic strategy for panic patients with high reward dependence is needed.

NR1-17

BRAIN GLUCOSE METABOLISM AND TEMPERAMENT AND CHARACTER IN PATIENTS WITH PANIC DISORDER: AN [18] FDG-PET STUDY

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SUMMARY:
Background: Panic disorder (PD) patients usually show abnormal [18F]FDG uptake in several brain areas. Some personality characteristics play a role in the development of PD. Especially, high harm avoidance is known to be

important in the pathophysiology of panic disorder. Thus, we examined the relationship between brain glucose metabolism using PET and Cloninger's temperament and character inventory(TCI) in patients with PD. Method: Fifteen patients with PD were compared to 20 normal control subjects using [18F]FDG-PET and TCI. Statistical analyses of PET data were performed using statistical parametric mapping (SPM) 2. The adjusted mean activities of regions of interest (ROIs) were calculated by the previously described method* from the clusters obtained from voxelwise t-statistics. Pearson correlation analysis was performed to examine the adjusted mean activities of each region and TCI scores. Result: There was statistically significant positive correlation (r = 0.516, p = 0.049) between the activity of the right superior frontal lobe and harm avoidance score in PD patients, and panic patients with high harm avoidance scores showed increased activities in the right superior frontal lobe. Discussion: This result suggests that increased activities of the right superior frontal lobe may reflect cognitive compensating process in panic patients who are prone to have high harm avoidance.

NR1-18

EFFICACY OF KOREAN-TYPE COGNITIVE-BEHAVIORAL GROUP THERAPY FOR SOCIAL ANXIETY DISORDER

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SUMMARY:
Objective: This study aims to evaluate the therapeutic effect of Korean-type cognitive behavioral group therapy (CBGT) for social anxiety disorder (SAD). Methods: Twenty-nine SAD outpatients participating in Korean-type CBGT were included in the study. Korean-type CBGT intensified the paradoxical intention, video feedback and Korean cultural receptivity process on the classical CBGT course. The main outcome measure was the self-reported version of Liebowitz Social Anxiety Scale (LSAS-SR). Results: After the treatment, the total score of LSAS-SR was significantly decreased (15.80±29.14, p=0.006, cohen's d=0.69), with both fear and avoidance subscale decreased (7.60±13.94, p=0.006 vs 8.30±16.31, p=0.009, respectively). The effect of CBGT was especially effective in generalized type (cohen's d=1.02). There were significant correlations between the effect of Korean-type CBGT (r=0.414, p=0.026). Accompanied pharmacotherapy did not arouse the difference of treatment response. Conclusion: Our study suggests that the Korean-type CBGT was effective in the SAD patients in reducing both fear and avoidance symptom regardless of subtype and pharmacotherapy.

NR1-19

ASSOCIATION OF THE C-1019G POLYMORPHISM OF SEROTONIN 1A RECEPTOR GENE AND ABNORMAL EATING BEHAVIOR IN KOREAN FEMALE ADOLESCENTS

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SUMMARY:
Objective: A few studies observed the increased 5-HT1A receptor binding in eating disorders. But no genetic association studies have addressed the relationship between 5-HT1A receptor polymorphism and eating behaviors in humans. The purpose of this study was to examine the relationship between C 1019G polymorphism in the serotonin-1A receptor gene and abnormal eating behavior in female adolescents. Methods: A total of 204 adolescent women after menarche, aged 16-17 years, recruited from two neighboring high schools for girls in Seoul, was invited to participate in this study. Polymerase chain reaction (PCR) was used to test 204 Korean female adolescent subjects for C1019G polymorphism in the serotonin-1A receptor gene (rs6295). The Bulimia Investigatory Test, Edinburgh (BITE) and the Eating Attitude Test (EAT) were administered to all subjects. Results: The total score of EAT was significantly different with respect to the three genotypes (CC,CG,GG; F=4.84, p=0.009). Both EAT (F=9.69, p=0.002) and BITE (F=5.22, p=0.023) scores were higher in G allele carriers than non-carriers. These results were conserved even after adjusting the degree of depression and anxiety. Dieting subscale of EAT was higher in G allele carrier (F=8.61, p=0.004). Conclusion: These findings suggest that C-1019G polymorphism in the 5-HT1A receptor gene is associated with eating behavior in Korean female adolescents.

NR1-20

AN OPEN-LABEL, RATER BLINDED 6-WEEK PILOT TRIAL OF ESCITALOPRAM FOR GENERALIZED ANXIETY DISORDER AMONG PATIENTS WITH HIV

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SUMMARY:
Objectives: To date there has been little information about whether SSRIs have a role in treating Generalized Anxiety Disorder (GAD) in HIV patients. As a preliminary study, we investigated the clinical utility of escitalopram for GAD in HIV patients in a 6-week, open-label, flexible-dose, prospective pilot trial. Methods: After screening, consenting, and a minimum of 4 week washout from preexisting antidepressants, 13 clinically stable HIV subjects taking anti-viral therapy received escitalopram (10-20 mg/day) for 6 weeks. The primary outcome was a change from baseline to end of treatment on the Hamilton Anxiety Rating Scale (HAM-A) scores. Secondary outcomes included changes in scores on the Mini Mental State Examination (MMSE), Sheehan Disability Scores (SDS), and responder ratings on Clinical Global Impression (CGI-S and CGI-I). Intent to Treat analysis with Last Observation Carried Forward approach was used for analysis. Results: The study participants (n=13) were 31% female with a mean age of 44.63 years. The dropout rate was 13%. The mean HAM-A score at baseline was 21.23 (SD=2.57), indicating moderate anxiety. There was a significant reduction in mean HAM-A scores from baseline to end of treatment (mean change -17.62, t=-14.35, p<0.01). Eighty-five percent of subjects were responders (CGI-I score of 1 or 2 at end of treatment). There were no significant changes in MMSE or SDS scores with treatment. The common side effects were nausea (n=3); dizziness (n=3), diarrhea (n=3) and dry mouth (n=2).There were no clinical significant interactions of escitalopram with existing antiviral therapy. The mean dose of escitalopram was 14.90 mg per day. Conclusions: Preliminary evidence indicates that escitalopram may have a role in the treatment of GAD in patients with HIV. Randomized, double-blind, placebo-controlled trials are necessary to determine the efficacy of escitalopram for GAD in HIV patients.

NR1-21

COGNITIVE MODULATION OF FRONTO-STRIATAL NETWORKS IN OBSESSIVE-COMPULSIVE DISORDER PATIENTS

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SUMMARY:
The obsessive-compulsive disorder (OCD) is a frequent psychiatric condition characterized by obsessions and/or compulsions. In these patients, attentional biases play a major role in the initiation and maintenance of the symptoms. We hypothesize that attentional dysfunction in fronto-parietal network may also affect processing within fronto-striatal regions and thus contribute to both cognitive as well as affective dysfunctions in OCD patients. Here, we tested with functional MRI (fMRI) whether OCD patients show altered attentional effects on the neural filtering of irrelevant visual stimuli in visual cortices. Sixteen OCD and sixteen matched controls scanned while they performed an easy or difficult detection task at fixation, while irrelevant colored visual stimuli were presented in the periphery. Our fMRI results reveal that patients with OCD show (i) an increased filtering of irrelevant information in visual cortex, (ii) a suppression of ventromedial prefrontal/orbitofrontal cortex (vmPFC/OFC) with increasing task difficulty (high attentional load), and (iii) an increased activity in ventral striatum at baseline. These findings suggest that hyper-vigilance seen in OCD patients might result in an increased attentional filtering in visual cortex. In addition, OCD patients showed a reduction of vmPFC/OFC activity during high load, as reported after successful psychotherapy. In addition, hyper-activity in striatal regions observed at baseline in OCD was significantly modulated by attentional load. Together, these findings suggest a possible therapeutic role for cognitive training in regulating brain circuits that underlie this common psychiatric disease.

NR1-22

EXERCISE TRAINING REDUCES ANXIETY SYMPTOMS AMONG PATIENTS WITH A CHRONIC MEDICAL ILLNESS

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SUMMARY:
Background: Anxiety often remains unrecognized or untreated among patients with a chronic medical illness. The influence of exercise training, an inexpensive, accessible adjuvant to therapy, on anxiety symptoms among these patients is poorly understood. Objectives: To estimate the population effect size for exercise training effects on anxiety symptoms and to learn whether selected variables of theoretical or practical importance moderate the estimated population effect. Methods: Articles published from January 1995 to August 10, 2007 were located using the Physical Activity Guidelines for Americans Scientific Database and supplemented by additional searches through December 2008 of the following databases: Google Scholar, MEDLINE, PsycInfo, PubMed, and Web of Science. Forty English-language articles in peer-reviewed scholarly journals involving sedentary adults with a chronic medical illness (including psychiatric illnesses) that incorporated both an anxiety outcome measured at baseline and after exercise training and random assignment to either an exercise intervention of =3 weeks or a comparison condition that lacked exercise training were selected. Two coauthors independently calculated Hedge's d effect sizes from studies of 2914 patients and extracted information regarding potential moderator variables. Random effects models used heterogeneity between-studies and sampling error to estimate population variance for the overall and moderator analyses. Results: Compared to no treatment comparison conditions, exercise training significantly reduced anxiety symptoms by a mean effect delta of 0.29 (95%CI, 0.23 to 0.36). Exercise training programs of =12 weeks, using session durations =30 minutes, and an anxiety recall time frame greater than the past week resulted in the largest anxiety improvements. Conclusion: Exercise training reduces anxiety symptoms among sedentary patients with a chronic medical illness.

NR1-23

COMPARISON OF THE INFLUENCE OF PSYCHOSOCIAL AND GENETIC FACTORS ON ADOLESCENT SUICIDAL IDEATION: A POPULATION-BASED STUDY

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SUMMARY:
Objective: Guidelines concerning the psychopathological aspects of suicide prevention are insufficient. Future interventions would benefit from information that is easier to evaluate. We aimed to determine the influence of parental suicidal ideation on adolescent suicidal ideation and compare it with other factors. Method: A population-based sample of 2,965 subjects between 15 and 18 years old and their parents was surveyed directly. Chi-square analysis, Student's t-test, binary logistic regression and path analysis was used to investigate the influence various factors have on adolescent suicidal ideation. Results: Among the subject variables, gender, satisfaction with one's health, insufficient sleep, having an illness, and satisfaction with family and parents were significantly different in adolescents who reported suicidal ideation in the past year compared to those who reported none. Among parental variables, fathers' satisfaction with health; mothers' insufficient sleep; a history of suicidal ideation; and parents' satisfaction with family, spouse, and offspring were significantly different. Odds ratios indicated that increased risk of adolescent suicidal ideation was associated with the subject factors female gender (OR: 1.475, p=0.004), insufficient sleep (OR: 1.431, p=0.009), dissatisfaction with one's health (OR: 2.264, p<0.001), dissatisfaction with family (OR: 5.051, p<0.001), and with maternal data showing insufficient sleep (OR: 1.417, p=0.02) and a positive history of suicidal impulse (OR: 1.951, p<0.001). A path analysis model (comparative fit index (CFI) = .907; root mean square error of approximation (RMSEA) = .047), indicated that psychosocial factors (ß=.139) had a greater influence on adolescent suicidal ideation than did genetic factors (ß=.062). Conclusion: These results show psychosocial factors have an almost two-fold greater influence on adolescent suicidal ideation than genetic factors. Assessment and modification of these factors would greatly assist future interventions.

NR1-24

THE PREVALENCE AND SEVERITY OF NEUROPSYCHIATRIC SYMPTOMS IN ALZHEIMER'S DISEASE AND SUBCORTICAL VASCULAR DEMENTIA: THE CREDOS STUDY

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SUMMARY:
Objective: Subcortical Vascular Dementia (SVD) is

relatively common, and due to its progressive, deteriorating nature, is often confused with Alzheimer's disease (AD). This study aimed to compare the prevalence and severity of clinically relevant neuropsychiatric symptoms between patients with AD and SVD. Method: The CREDOS study is a multicenter longitudinal cohort study that was organized to study the long-term outcome of dementia patients. A total of 3,080 subjects were enrolled in the study. From these subjects, we selected 1,390 AD subjects and 247 SVD subjects with very mild to moderate levels of dementia, and divided them into two groups according to type of dementia. The neuropsychiatric inventory (NPI) was used to assess neuropsychiatric symptoms. Clinically relevant symptoms are defined as symptoms with a NPI composite score equal to or above 4. The Clinical Dementia Rating Scale (CDR) was used to assess the severity of dementia, and subjects with CDR scores of 0.5, 1 and 2 were selected. Statistical analysis was done using Chi-square analysis, Student's t-test, binary logistic regression, and nonparametric analysis of covariates (ANCOVA). We used CDR sum of box scores to minimize loss of information, and analysis was based on clinically relevant symptoms only. Results: Apathy and agitation symptoms were more common in SVD subjects compared to AD subjects. After controlling for other factors, the association between SVD and the presence of apathy symptoms remained statistically significant (p=0.025). Subjects with SVD also tended to have higher composite scores in the apathy domain. This association also remained significant after controlling for other factors (F=7.88, p=0.01). The severity of dementia was strongly associated with the prevalence and severity of all neuropsychiatric symptoms. Conclusions: Future studies concerning clinically relevant neuropsychiatric symptoms in very mild to very severe dementia subjects would greatly help clarify the characteristics of neuropsychiatric symptoms. This study was supported by a grant of the Korean Health 21 R&D Project, Ministry of Health & Welfare, Republic of Korea (A050079).

NR1-25

DELIRIUM IN THE OLDEST-OLD: SOCIODEMOGRAPHIC AND EPIDEMIOLOGIC FEATURES AND RESPONSE TO TREATMENT

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SUMMARY:
Introduction: Delirium is a severe and prevalent disorder in inpatient settings and is associated with greater mortality, longer hospitalizations and higher hospitalization costs. The oldest-old (those aged 85 and over) is the fastest growing population group in several countries. They are specially prone to delirium when hospitalized for a medical disorder, but very few studies on delirium risk factors and treatment have been conducted in this population. Objective: To evaluate sociodemographic and epidemiologic features of delirium in the oldest-old (OO) and response to treatment with antipsychotics (haloperidol, risperidone, olanzapine or quetiapine). Method: a retrospective study was conducted (chart review of OO patients with delirium treated by consultation-liaison psychatry staff in a 250-bed private general hospital in a two-year period). Treatment was chosen according to the psychiatrist's decision. Sociodemographic (age, gender, ethnicity and marital status), epidemiologic (type of delirium and comorbidities classified according to ICD-10) and treatment-related data (medications, doses, duration of treatment and outcome evaluated by CGI-I scale) were analyzed using descriptive statistic methods. Results: 33 patients (13 males and 20 females) were included. Mean age was 88,94±3,10 years. A high ratio of comorbidities was found (3,27± 1,64/patient) – high systolic blood pressure (63,36%) and dementia (36,36%) were the most frequent. 69,70% of the patients treated with antipsychotics (32) presented favorable results (CGI-I 1 or 2). Conclusion: This study reveals a pattern of comorbidities which might identify which patients among the OO are more vulnerable to delirium. Early and systematic evaluations of OO hospitalized patients with dementia or high systolic blood pressure could identify delirium at an early stage, allowing early treatment, preventing the occurrence of severe delirium and reducing length of hospitalizations and incidence of complications.

NR1-26

COMPARISON ON THE EFFICACY OF RISPERIDONE VERSUS HALOPERIDOL IN THE TREATMENT OF DELIRIUM: PROSPECTIVE, RANDOMIZED, DOUBLE BLIND TRIAL

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SUMMARY:
Objectives: Haloperidol has been the medication of choice in most deliriums. But due to fewer side effects, atypical antipsychotics are becoming the first line drugs in various neuropsychiatric conditions, and also increasing in delirium treatment. The aim of this study was to compare the clinical efficacy of ridperidone with haloperidol in the treatment of delirium. Method: Sixty-seven subjects completed the study receiving a flexible-dose regimen of risperidone (n=25, mean dosage 0.88mg) or haloperidol (n=42, mean dosage 1.4mg). Delirium rating scale (DRS) was administered as a specific tool to rate the severity of delirium and Neurobehavioral rating scale (NRS) to rate psychiatric and behavioral symptoms and Mini mental state examination Korean version(MMSE-K) to access cognitive status, specifically. The symptoms were checked at baseline, on day 3 and day 7 of treatment and compared between the two groups. Results: In both risperidone and haloperidol groups, DRS and NRS scores improved significantly on day 3 and day 7 compared to baseline. In MMSE-K scores, compared to baseline, risperidone group improved significantly on day 3 and day 7, whereas haloperidol group showed no improvement on neither day 3 nor day 7.
Conclusion: This study demonstrated that risperidone is as efficacious as haloperidol in the treatment of delirium. In particular, cognitive impairments improved with risperidone and not haloperidol. Thus, it is possible that risperidone can be used as a first-line treatment in delirium. Further prospective studies are warranted.

NR1-27

AGE AT ONSET OF FIRST SUICIDE ATTEMPT IN MEN AND WOMEN: FURTHER EVIDENCE FOR TWO SUBGROUPS

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SUMMARY:
Background: Age at onset (AAO) has been useful to explore the heterogeneity of several psychiatric disorders such as schizophrenia. AAO may be a marker for different subtypes of suicide attempts (SA). The main aims of this study were to find the best fitting model for the AAO distribution in adult patients separated by gender and to evaluate sociodemographic and clinical differences between groups. Method: Participants were 229 suicide attempters (147 females; 82 males) admitted to a general hospital in Madrid, Spain. We used admixture analysis to determine the best-fitting model for the AAO of SA. We investigated whether the observed AAO distribution consisted of a mixture of Gaussian distributions. A set of logistic regression analyses yielded odds ratios (ORs) indicating measures of association between early- and late-onset suicide attempters and sociodemographic and clinical variables separated by gender.
Results: The best-fitted model for the observed AAO distribution was a mixture of two gaussian distributions (mean ± S.D.): (29.13 ± 6.87 years) and (51.44 ± 15.13 years), with a cutoff point at 42 years. The Gaussian distributions differed with regard to gender. Females showed a younger AAO in both Gaussian distributions (26.98 ± 5.69 and 47.98 ± 14.13) than males (32.77 ± 8.11 and 61.31 ± 14.61). Late-onset female attempters were less likely to be diagnosed with higher levels of impulsivity (OR=0.437; 95%CI=0.217-0.879), aggression (OR=0.440; 95%CI=0.221-0.877), and borderline (OR=0.93; 95%CI=0.02-0.41) and dependent personality disorders (OR=0.07; 95%CI=0.01-0.50). Late-onset male suicide attempters were less likely to show elevated aggression levels (OR=0.247; 95%CI=0.078-0.776). Conclusions: These results suggest that AAO of SA serves to characterize different subpopulations of suicide attempters. The existence of two subgroups in each gender was further confirmed by their differences in psychopathological profiles.

NR1-28

OLFACTORY REFERENCE SYNDROME: PART OF THE OCD SPECTRUM OR PSYCHOSIS? A DISCUSSION ILLUSTRATED WITH A CASE

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SUMMARY:
Objectives: Our aim was, from a case report, to make a brief review about the literature on ORS diagnostic criteria and treatment options, as well as to emphasize the use of atypical antipsychotics as a first option for this condition and to provoke discussion on the assumption that ORS should be classified in the OCD spectrum or not by comparing its phenomenology to that of OCD. Methods: Our main source of bibliography was obtained

from the MEDLINE database accessed on November 20, 2010 using the term "olfactory reference syndrome" as the key-word. There were 47 related articles, but only 20 fit the purposes of this present research. Additional data was later incorporated from the references cited in the previous material. Results: Pryse-Philips´ pioneer report of 36 patients with ORS found that 60% had lost insight of their disease while poor insight has been reported in only 15% to 36% of patients with OCD. SPECT findings in 2 cases of ORS differed partially from the classic findings of OCD. Additionally, some case reports show a nosological overlap of ORS with depression, bipolar affective disorder and schizophrenia which would corroborate with Luckhaus´ notion that ORS develops on the basis of various underlying psychiatric illnesses. Few cases of ORS have been described after 1971, and they all showed a varied response to antidepressants, typical and atypical antipsychotics. The secondary depressive symptoms responded better and faster than the psychotic features of ORS. Conclusions: There´s not enough evidence to classify ORS in the OCD spectrum. This diagnostic dilemma will probably remain until more research is done, however treatment with atypical antipsychotics should be considered.

NR1-29

DIFFERENTIATING PARANEOPLASTIC SYNDROMES FROM PSYCHOSIS OF A PSYCHIATRIC ETIOLOGY

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SUMMARY:

Background: Depression, and commonly, psychosis, often signs of recent-onset psychiatric disorders, can frequently be the presenting signs of a recently identified entity called anti-NMDAR encephalitis, and can sometimes be associated with limbic and brainstem involvement in classic paraneoplastic syndromes. The California Encephalitis Project has identified numerous cases of anti-NMDAR encephalitis and some associated with a classic paraneoplastic syndromes, and it seeks to elucidate the diagnosis and course of such entities so that they can be differentiated from psychosis of a psychiatric etiology. Methods: Using standardized reports and chart review to gather clinical data, twelve cases of anti-NMDAR encephalitis who received psychiatric intervention are examined, as are three cases of psychosis and severe depression associated with anti-Yo and anti-Hu antibodies. Results: Nearly 50% of those with anti-NMDAR encephalitis were hospitalized for psychiatric symptoms. Psychosis predominated on admission. The median age for anti-NMDAR patients was 20.5. All patients lacked a significant response to treatment, and those with anti-NMDAR encephalitis went on to decompensate rapidly, experiencing neurologic abnormalities and autonomic instability, while those with classic paraneoplastic syndromes had a more gradual decline marked by dementia and muscle weakness. Anti-NMDAR cases appeared to have a predictable course and normal CSF and MRI findings without the presence of tumor, while those with classic paraneoplastic syndromes had a more variable course and were associated with abnormalities on MRI, CSF pleocytosis, and the presence of tumor in all cases. Treatment with plasmapheresis, IVIG, and immunosupression was effective in all cases of anti-NMDAR encephalitis, while without tumor removal in the classic cases, there was continued progression. Conclusion: Paraneoplastic syndromes, particularly anti-NMDAR encephalitis because of its predominance in a younger population in whom new-onset psychosis if often suspected, should enter the differential diagnosis in all patients with sudden or recent-onset psychiatric illness. Diagnostic delays can diminish the potential for early and thus more efficacious treatment.

NR1-30

THE DIAGNOSTIC STABILITY OF BRIEF PSYCHOTIC DISORDER

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SUMMARY:

Introduction: The diagnostic stability of ATPD is known to be between 30 -60%. Although brief psychotic disorder (BPD) and acute transient psychotic disorder (ATPD) have similar concepts, BPD evolves more rapidly, has a shorter duration, and is expected to have a better prognosis, but evidence supporting this is scarce. The aim of this study was to investigate the diagnostic stability of BPD. Materials and Methods: This retrospective chart review was based

on all BPD patients who had a first-ever admission, and were readmitted at least once, to the psychiatric ward of the Asan Medical Center, from 1988 to 2009. All diagnoses were reviewed by an experienced research psychiatrist (Y. Hong). Results: Thirty-five subjects met our inclusion criteria. The mean age at first admission with BPD was 32.2 ± 9.3 (14-64) years and the majority (71.4%) of patients was female. At a median follow-up of 2782.5 ± 1838.8 (92-7140) days, 3.3 ± 1.6 (2-9) episodes developed so mean interepisode interval was 959.5 ± 679.5 (46-3570) days. The number of cases in the 'diagnostically stable' group was 11, with an overall stability rate of only 31.4%. The number of subjects whose diagnosis changed increased with each subsequent admission; the diagnosis of more than half was changed to bipolar I disorder (n=13), schizophrenia (n=5), schizophreniform disorder (n=2), or schizoaffective disorder (n=4). Except for just one episode, bipolar I disorder patients relapsed with a manic episode, with or without psychotic features. Almost no interepisode depressive features were observed. And a substantial proportion (63.6%) had maintained their jobs including subjects whose diagnosis was changed later to schizophrenia. This indicates patients with either schizophrenia or Bipolar disorders, with an onset as BPD may have a better prognosis compared to those who do not. Conclusion: BPD patients had a high possibility of conversion to schizophrenia or bipolar spectrum disorder. However, in those cases, they still showed prominently better outcomes compared to patients who were originally diagnosed with schizophrenia or bipolar disorder.

NR1-31

USE OF BODY IMAGE SOFTWARE TO EVALUATE BODY IMAGE DISTORTION IN PATIENTS WITH ANOREXIA NERVOSA

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SUMMARY:
Objective: Body image distortion is one of the core diagnostic criteria for Anorexia Nervosa (AN). However, methods for measuring body image have historically been highly subjective. The Body Image Software (BIS) program was developed to provide an objective measure of body image, including perception of current and desired body size. The purpose of this study was to evaluate the use of the BIS in subjects with AN. Methods: Informed consent was obtained from 67 female subjects with AN (mean age 16, range 12-21) and their parents (for those < age 18) for this IRB-approved study. The 3 BIS tasks utilize a digital image of the subject and take a total of 15-30 minutes to complete. There are 2 "Adjustment" tasks: "Current Image" and "Desired Image." The subject is presented a series of 10 images; each distorted wider or thinner than the actual photograph and adjusts the distorted images to their perceived "Current" size for the first set of 10 and to their "Desired" size for the second set. The Adjustment Probit Estimation (APE) task consists of 8 blocks of 40 images. The subject must identify each image as "wider" or "thinner" than her actual size. The BIS program adjusts the presented images until the subject reaches a "Point of Subjective Equality" (PSE), which is their perceived current size. Results: The mean % Ideal Body Weight (IBW) at the time of testing was 78.2% (SD = 5.1). The mean BIS Adjustment task for "Current" body size was 10.4% larger than their actual body size (SD = 13.4) and the mean BIS Adjustment task for "Desired" body size was 6.8% less than their actual size (SD = 11.2). On the APE task the PSE was 7.0% larger than actual body size (SD = 10.0). On average, AN subjects could reliably detect a 2.3% change in body size (SD = 0.8). The results of all three BIS tasks were highly correlated with other measures of body image, specifically the Color-A-Person Test and the Eating Disorder Inventory-2 subscales "drive for thinness" and "body dissatisfaction." Conclusion: These findings suggest that subjects with AN do have body image distortion, which can be measured with the BIS program. The finding that AN subjects are able to detect small changes in body size supports current thinking that sensory impairment is not responsible for body image distortion in AN patients. The BIS program is a unique and useful tool in the study of AN for objectively measuring body image distortion.

NR1-32

QUALITY OF LIFE IN INDIVIDUALS WITH TRICHOTILLOMANIA AND PATHOLOGICAL SKIN PICKING

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SUMMARY:
Objective: Trichotillomania (TTM) and Pathological Skin Picking (PSP) are disorders characterized by distress and impaired psychosocial functioning. Although these disorders are clinically similar, little is known about the quality of life of individuals with TTM or PSP. This study

sought to compare quality of life for individuals with TTM and PSP and its relationship to clinical severity and psychiatric comorbidity. Method: Demographic and clinical characteristic information were obtained in a treatment-seeking sample of subjects diagnosed with TTM or PSP, and 25 healthy controls. Subjects were either participants of pharmacotherapy studies conducted between 2004-2009 or outpatients of a large United States University psychiatry clinic. Healthy controls were obtained through local advertising. All subjects, including controls, were interviewed using the Structured Clinical Interview for Mental Disorders and completed the Quality of Life Inventory. Additional tests, including the Hamilton Depression and Anxiety Scales, Sheehan Disability Scale, and Clinical Global Impressions-Severity, were administered to TTM and PSP subjects. Results: 70 subjects meeting criteria for TTM (mean age 34.8±12.0; 88.6% female), 59 subjects meeting proposed criteria for PSP (mean age 33.4±12.8; 88.1% female), and 25 healthy control subjects (mean age 31.3±10.1; 80% female) were included in this sample. PSP subjects reported more psychosocial impairment compared to TTM subjects (p=0.013), however, quality of life scores were low for both groups. TTM and PSP subjects had significantly lower scores on quality of life measures compared to healthy controls. Conclusions: To our knowledge, this is the largest comparison of quality of life in a treatment-seeking sample of patients with TTM or PSP compared to a sample of healthy controls. Our results indicate that both TTM and PSP subjects suffer a significantly impaired perception of quality of life compared to those without psychiatric illness. Future research should address this perception in order to improve life satisfaction.

NR1-33

LATEST CLINICAL TRIALS FOR MAJOR DEPRESSIVE DISORDER: WHAT KINDS OF DRUGS AND WHAT KINDS OF TRIALS?

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SUMMARY:
Introduction: We aimed to describe potential treatments currently in clinical trials for major depressive disorder and characteristics of these trials. Methods: Registration of clinical trials is now mandatory, so we searched clinicaltrials.gov for ongoing treatment trials in MDD. Data was extracted and trials were classified based on predefined variables of interest. Results: 157 ongoing treatment trials were identified (sample sizes varying 5 to 1000). Of these trials, 17.8% are uncontrolled, 28.0% have an active comparator, and 54.1% are placebo-controlled. The trials are evaluating drugs (63.6%), psychotherapy (17.1%), or TMS (13.3%). In adults, 17.2% trials are evaluating psychotherapy vs. 53.8% in children/adolescents (Fisher's exact test p=.007). Primary treatment of MDD is the focus of 78.3% of trials, including with novel agents (eg, triple reuptake inhibitors, norepinephrine reuptake inhibitor, nicotinic receptor antagonist, CRF-1 antagonist, 5HT-7 antagonist, vilazodone, riluzole). Augmentation of antidepressants is being studied by 21.6% of trials, including with novel agents (eg, D-cycloserine, cysteamine, cimicoxib, creatine, aerobic exercise, and magnetic seizure therapy). Median planned sample size is greater for industry-funded trials (376) than for others (68; Mann Whitney U test p<.0001). Only 8.2% trials are in children/adolescents. However, median sample size for trials in children/adolescents (78) vs. in adults (100) is not statistically significantly different. Also, the proportion of trials in children/adolescents funded by industry was not statistically significantly different from that in adults (Fisher's exact test p=.488). Conclusion: A robust pipeline exists of drugs being evaluated for primary treatment or augmentation in MDD, including drugs with novel mechanisms. Psychotherapy trials and trials in children continue to be neglected. Trials not funded by industry have smaller sample sizes which may reduce their impact.

NR1-34

GENDER DIFFERENCES IN CLINICAL FEATURES AND PREDOMINANT POLARITY AMONGST BIPOLAR DISORDERS

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SUMMARY:
Introduction: Gender differences literature amongst bipolar patients are controversial. However, the most solid finding differentiating bipolar men and women has to do with the higher burden of depressive features in women, in terms of initial depressive episode, number of episodes, depressive predominant polarity (PP), depressive features during a manic episode, and the so called "mixed mania" (Sherazi 2006). To our knowledge, this is the first comprehensive study that specifically addresses the

issue of gender differences and predominant polarity in bipolar disorder in a longitudinal evaluation. Objective: To explore gender differences regarding clinical and socio-demographic characteristics amongst bipolar patients with particular attention to predominant polarity and depressive symptoms. Methods: Six-hundred and four (604) DSM-IV-tr Bipolar type I and II outpatients consecutively admitted to the Bipolar Disorders Program of the Hospital Clinic and University of Barcelona were enrolled, throughout a systematic prospective follow-up over at least 10 years (Colom et al., 2006, Daban et al., 2006). Clinical and socio-demographic variables were analyzed with Student's t-tests and ANOVA for continuous variables and Chi-square and Fisher's exact test for categorical (? value, two tailed). Significance was set at p<0.05 (two tailed). Power analyses indicated that with sample size we have sufficient power (>80%) to detect a statistically significant difference between genders in the range of 15-20%. Results: The sample was composed of 604 bipolar patients, 272 men (45%) and 332 women (55%). Bipolar men are more likely to have a manic/hypomanic PP (56.3% vs 45.1%, ?2=4.8, p=.029), a manic/hypomanic onset (?2 =4.79, p=.029), higher comorbidity with substance use disorders, both at time of evaluation (79.4% vs 64.5%, ?2 =16.3, p< .001) and at first episode (77.6% vs 60.8%; ?2 = 19.35, p<.001). Suicide attempts are more often violent amongst bipolar men (n=7, 58.3% in male; n=7, 23.3% in female; ?2 =4.72, p= .030). Female patients showed significantly more symptoms of psychotic depression (30.9% vs 21.8%; ?2 =4.38, p=.036), Axis II comorbidity (34.3% vs 26.8%, ?2 =3.93, p=.047), and higher numbers of depressive (8.06 ±10.92; Z=30706.5, p=.039, Mann-Whitney U Test) and mixed episodes (0.74±1.76; Z=27354.0, p=.041, Mann-Whitney U Test). Life events preceding illness onset were more likely to occur amongst women (54.4% vs 69.7%; ?2 =12.2, p<.001).

NR1-35

POST-PARTUM BIPOLAR EPISODES ARE NOT DISTINCT FROM SPONTANEOUS EPISODES: IMPLICATIONS FOR *DSM-V*

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SUMMARY:

Introduction: DSM course modifiers include a variety of distinctive symptomatic or temporal features which may help to refine the information on a certain patient on the basis of his/her expected outcome according to the existing knowledge on the course of the illness. Unfortunately, this is not always the case for course modifiers in bipolar disorders. The case of postpartum mood episode is a clear example of a course modifier with very poor evidence behind it. Its influence on the outcome of bipolar disorders remains unclear, as there is little data showing differences on illness outcome according to the lifetime history of postpartum onset. Hereby we present the first prospective clinical study comparing the outcome of female bipolar patients according to lifetime history of postpartum mood episode. Objective: To compare female bipolar patients with and without lifetime history of postpartum mood episode. Methods: Systematic prospective follow-up (12 years) of 200 female bipolar I or II patients with or without history of postpartum episodes was performed, amongst patients from the systematic follow-up of the Bipolar Disorders Program of the Hospital Clinic and University of Barcelona for at least ten years. Postpartum mood episode was defined according to DSM-IV. Patients with and without postpartum onset of a mood episode were compared regarding clinical and sociodemographic variables. Statistical methods consisted of chi-square statistic with Yates' correction or Fisher's exact test for the comparison of categorical data, and Student's t-test for dimensional variables normally distributed. All statistics were two-tailed, and significance was set at p less than 0.05. Results: Lifetime history of postpartum episode was present in 43 patients and absent in 137 patients. From the 43 patients having suffered from a postpartum-triggered episode, 32 (74.4%) presented a postpartum depressive episode, 9 (20.9%) a manic postpartum episode and one (2.3%) a mixed episode. One patient (2.3%) had a postpartum depressive episode after delivering her first child and a hypomanic episode after her second, four years later. The only significant difference found between PME and Non-PME patients concerned the duration of bipolar illness, with PME patients showing a longer duration of the illness. Conclusion: The role of postpartum onset as a DSM course modifier should be reconsidered, as it seems to have no impact on prognosis or functioning.

NR1-36

ABNORMALITIES DURING RESTING STATE FUNCTIONAL MAGNETIC RESONANCE IMAGING IN TREATMENT-NAIVE PATIENTS WITH MAJOR DEPRESSION DISORDER

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SUMMARY:
Objective: We explored differences of brain spontaneous activity in resting state between patients with major depressive disorder (MDD) and normal controls using function magnetic resonance imaging (fMRI) in order to find the base of neural activity associated with pathophysiological mechanism of depression. Methods: Forty-nine subjects with depression and 47 sex, age and education-matched controls underwent 3 min and 40 sec fMRI scans while in resting state. ReHo and ALFF analysis were used to detect neural spontaneous activity across the whole brain by the REST software. Two sample t-tests were performed to compare between groups (the threshold were set at p<0.001, uncorrected, 10 voxels) using the SPM5 software. Results: 1.) Demographic data: there were no significant differences among the patients with MDD and the control group in age, gender and education. 2.) fMRI results: (2.1) ReHo analysis: The ReHo of bilateral medial frontal gyrus were significantly decreased in the patient group when compared to the controls. (2.2) ALFF analysis: The ALFF of right medial frontal gyrus and right cingulate gyrus were significantly decreased in in the patient group when compared to the controls. Conclusion: 1.) Compared to the controls, the patients with MDD showed decreased ReHo in bilateral medial frontal gyrus, which indicated that the decreased regional homogeneity of these regions may be the neuropathotogical substrate in depression. 2.) Compared to the controls, the patients with MDD showed decreased ALFF in right medial frontal gyrus and right cingulate gyrus, which implicated the decreased amplitude of regional activity in these regions may be the neuropathotogical substrate in depression. 3.) Compared to the controls, the patients with MDD showed decreased ReHo and ALFF in right medial frontal gyrus, implicating that these regions may play an important role in mechanism of neuropathological in depression.

NR1-37

THE COMBINED EFFECTS OF THE BDNF AND GSK3B GENES MODULATE THE RELATIONSHIP BETWEEN NEGATIVE LIFE EVENTS AND MAJOR DEPRESSIVE DISORDER

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SUMMARY:
Objective: BDNF and GSK3B have been seen as the logical source of candidate genes for Major Depressive Disorder (MDD). The gene-environment interaction between BDNF polymorphism and negative life events had been found on MDD. Our previous study revealed that a gene-gene interaction among BDNF and GSK3B may confer the risk of MDD. Here, we hypothesized that there is a gene-environment interaction between the BDNF-GSK3B combination and negative life events on the risk of MDD. Method: To test this hypothesis, we conducted a case-controlled study with data from a northern Han Chinese population to analyze this combined effect on MDD. This study recruited a total of 404 patients with MDD and 388 age- and gender-matched control subjects. Negative life events and objective social supports were assessed using standard rating scales. Three polymorphisms of BDNF and GSK3B gene were identified by sequence. Gene-environment interaction analyses were performed by the Multifactor Dimensionality Reduction (MDR). Results: The dominant model analyses showed an association tendency between the GSK3B rs6782799 and MDD (P<0.1), while others were not. MDR analyses revealed a significant three-way interaction among BDNF rs7124442,GSK3B rs6782799 and negative life events(corrected P<0.001) with a CV consistency of 9 and PE of 0.3979. In addition,a two-way interaction between the BDNF rs7124442 and negative life events (corrected P value ranged from 0.020 to 0.021) also were found. Conclusions: To our knowledge, this is the first report showing the BDNF/GSK3B combination may modify the relationship between negative life events and MDD in the Chinese population. It gave further evidence to support the possibility that the BDNF /GSK3B combination is an important genetic factor in susceptibility to MDD. Key words: Major depressive disorder (MDD); Brain-derived neurotrophic factor (BDNF); glycogen synthase kinase-3B (GSK3B); negative life events; gene-environment interaction; genetic association.

NR1-38

CONTRASTING PATTERNS OF DEFICITS IN VISUOSPATIAL MEMORY AND EXECUTIVE FUNCTION IN PATIENTS WITH MAJOR DEPRESSION, WITH AND WITHOUT ECT REFERRAL

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SUMMARY:
Objectives: The issue of isolating distinct subtypes of major depression (MDD) carries significant experimental interest, as it may address the neurophysiological substrate of the disorder and its frequent resistance to pharmacotherapy. Patients referred for electroconvulsive treatment (ECTs) constitute a distinct MDD category characterised by the necessary, though perhaps not sufficient condition, of drug resistance. In this study we compared the neuropsychological profile of ECT candidates to that of MDD patients without ECT referral (NECTs). Method: 30 MDD patients, 15 with (ECTs), 15 without ECT (NECTs) referral at hospitalization, and 15 non-psychiatric controls (CONTs) were assessed with 5 tests of the Cambridge Neuropsychological Test Automated Battery (CANTAB). Patients also received the Hamilton Depression (HAM-D) and Mini Mental (MMSE) scales. Clinical and neuropsychological scores were analysed through one-way ANOVAs. Results: ECTs had higher HAM-D scores than NECTs, but not significantly so ($p=0.06$); however their MMSE scores were significantly lower ($p=0.01$). NECTs performed significantly lower than CONTs in Paired Associates Learning ($p=0.03$; CONT vs NECT $p<0.01$) and Spatial Recognition Memory ($p=0.05$; NECT vs CONT $p<0.05$); in both tests ECTs performed between CONT and NECT levels, not differing from either. In Intra/Extradimensional Shift ECTs but not NECTs performed significantly lower that CONTs ($p=0.01$; ECTvsCONT $p<0.01$). The ECTs' deficit was most pronounced in the ID-ED shift phases of IED, suggesting reduced attentional flexibility. In Stockings of Cambridge ECTs abandoned early more often than CONTs and NECTs (Kruskal-Wallis: $H=11$, $p<0.01$), but those patients who completed SOC performed as the other 2 groups. Conclusions: We noted a double dissociation in the cognitive profiles of MDD patients with and without ECT referral at intake. ECTs showed deficits in tests addressing executive function, particularly attentional flexibility, but performed normally in tests of visuospatial learning/memory. NECTs presented the opposite pattern. This may suggest a predominantly frontostriatal involvement in ECT vs temporal involvement in NECT depressives.

NR1-39

A CLINICAL COMPARISON BETWEEN EARLY (< 15 YEARS) AND LATE-ONSET BIPOLAR PATIENTS

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SUMMARY:
Objective: To contrast the clinical histories of early onset (15 and below) and late onset (16 and above) bipolar patients attending a University- sponsored psychiatric clinic. Method: All new outpatients administered a structured diagnostic interview before being seen by a physician (N=1458) were eligible for the study; most also completed a Psychosocial History and the SCL-90-R in order to obtain information about social demographic characteristics, family history of mental illness, ratings of early childhood, the amount and type of lifetime psychiatric comorbidity, current levels of symptomatic distress, and treatments received. Results: A total of 269 patients (18%) satisfied criteria for both mania and depression: Eighty-three or 31% of these reported an early onset of mania while 186 or 69% reported the onset of mania after the age of 15. Age at onset did not distinguish patients according to sex, education or employment status: early-onset patients were younger (31.8 vs 37.2 years). Early-onset patients reported more mania and phobia among their biological relatives and met criteria for more lifetime psychiatric syndromes for themselves. Alcohol Dependence, ASPD, Somatization Disorder, OCD and Phobia were more prevalent in early-onset patients. Early-onset patients reported greater unhappiness and more problems in childhood than late-onset patients and indicated greater symptomatic distress when first seen. However, no treatment differences were found between the two groups. Conclusion: Early-onset bipolar patients represent a particular challenge to the practitioner because their clinical histories suggest a more severe and virulent form of the illness.

NR1-40

DEPRESSIVE SYMPTOMS IN ANXIETY DISORDERS AND MAJOR DEPRESSIVE

DISORDER

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SUMMARY:
Objective: Depressive symptoms are often reported by individuals with anxiety disorders. High comorbidity with depressive disorder may explain this phenomenon; however, overlapping features of anxiety and depressive symptoms or lack of discriminant validity of instruments measuring depression may also contribute. Thus, to explore the associated factors with depressive symptoms in both disorders may shed light on what depressive symptoms in anxiety disorders actually are comprised of.
Methods: We surveyed a consecutive sample of 192 outpatients with DSM-IV anxiety disorders (acute stress disorder, posttraumatic stress disorder, panic disorder, generalized anxiety disorder, obsessive-compulsive disorder, social phobia, anxiety disorder not otherwise specified) at the psychiatric department of a university-affiliated hospital and compared with 119 patients with major depressive disorder. The questionnaire comprised of Symptom Checklist-90-Revised (SCL-90-R), Beck Depression Inventory (BDI), State and Trait Anxiety Inventory, and sociodemographic variables. Results: Patients with anxiety disorders show significantly fewer depressive symptoms, however, difference was confined to negative attitude subscale of BDI, not somatic symptoms and performance difficulty. Multiple regression showed general symptom severity, state anxiety, lower education and older age predicted depression in anxiety disorders, whereas only general symptom severity and trait anxiety in major depressive disorder. Conclusion: This cross-sectional study indicated that self-reported depression in anxiety disorder overlaps with anxiety symptoms and constructs more severe aspects of anxiety symptoms. Further studies are needed to disentangle the role of comorbidity from this finding.

NR1-41

A COMPARISON OF MEDICAL COMORBIDITIES IN ELDERLY VERSUS YOUNGER BIPOLAR PATIENTS

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SUMMARY:
Introduction: Currently, in individuals 65 years and older, prevalence rates of bipolar disorder range from 0.1% to 0.4%. It remains a chronic mental illness that leads to significant health care costs. Methods: We reviewed 133 patient charts with the diagnosis of bipolar disorder in an urban outpatient clinic setting from June 2006 to September 2007: 67 patients 55 and older, and 66 patients younger than 55. The average age of the Age > 55 group was 62.6 years. The average age of the Age < 55 group was 41.0 years. We compared the groups based on age, demographic variables, and frequency of co-morbid medical disease. Results: The prevalence of geriatric bipolar patients was 4.3% compared to 9.1% for the younger subset. Statistical significance was noted for the elderly group for cardiac (37.3%), dementia-related illness (6%), GU disease (6%), and musculoskeletal illness (16.4%). Discussion: Geriatric bipolar patients have more co-morbid medical illness, which can lead to higher rates of medical hospitalization and functional impairment. The management of bipolar disorder is complex and reflects the multiple co-morbid conditions associated with an aging population.

NR1-42

FEASIBILITY AND EFFECTIVENESS OF USING E-MAIL TO SCREEN COLLEGE STUDENTS FOR DEPRESSION

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SUMMARY:
Objective: To investigate the usefulness of e-mail to screen college students for depression and of online information resources to initiate help-seeking. Methods: Undergraduate and graduate students at six participating colleges were invited to complete a depression screening survey through e-mail lists provided by student groups on campus. The e-mail described the study's purpose and the chance for participants to win a $200 gift card. The survey included questions on demographic information, treatment history, and the Patient Health Questionnaire 9-Item (PHQ-9) for depression screening. Students with a PHQ-9 score>=10 were considered screened positive for major depressive disorder (MDD). They were informed of the results and offered links to online information on depression and local treatment resources. Students who screened positive

were followed-up 8 weeks later using the same survey, with added questions on their utilization and evaluation of the online information. Results: Six hundred thirty-one students consented to take the survey. Twenty-one point seven percent reported history of depression; 9.4% were receiving treatment for depression, including therapy (40%), medication (30%), and both (30%). Twelve point nine percent endorsed suicidal symptoms. Eighty-two students (14.5%) screened positive for MDD, and the prevalence is significantly greater than that reported in the national survey in the community (10.3%, p=0.002). Out of these 82 students, 46.3% completed the follow-up survey. Among them, 8 students had used the resources provided in the initial survey, depression information (n=7) and peer counseling groups on campus (n=1). Providing the resources did not increase help-seeking for depression (McNemar test, p>0.05). Conclusions: E-mail appears to be an effective and inexpensive method to screen college students for depression. The prevalence of MDD among college students was found to be high. Simply offering online information on depression and available treatment resources had limited effects on students' help-seeking behavior.

NR1-43

SEASONAL VARIATION OF MOOD AND BEHAVIOR IN BIPOLAR I AND BIPOLAR II DISORDERS

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SUMMARY:

Objective: Recurrence of mood episodes associated with specific seasons has been described in mood disorders. Seasonal changes in mood and behavior might also be observed in healthy individuals without any mood disorder. This study aimed to compare seasonal variations of mood and behavior among bipolar I, bipolar II patients and unaffected controls. Effects of gender and age on the seasonality were also evaluated. Methods: Subjects were ninety-four clinically stable patients with bipolar I (n=48) or bipolar II (n=46) disorder and 188 age and sex-matched healthy controls. Seasonality of mood and behavior was retrospectively assessed on lifetime trait basis using Seasonal Pattern Assessment Questionnaire (SPAQ). Results: Prevalence of seasonal affective disorder (SAD) based on the criteria adopted for the SPAQ was observed in 16.7%, 23.9%, and 2.7% of the bipolar I, bipolar II, and control groups, respectively. Two patient groups showed higher mean global seasonality scores compared to the control group ($F(2,279)=33.59$, $P<0.0001$). There were no significant differences in the prevalence of SAD and the global severity of seasonality between bipolar I patient group and bipolar II patient group. Significant gender or age effect was not observed in all of the groups. Conclusions: This study suggests that patients with bipolar disorder more frequently experience seasonal changes in mood and behavior compared to the healthy control. The difference of global severity of seasonality by bipolar subtype, gender, and age was not significantly observed.

NR1-44

COMORBID ANXIETY AND MOOD DISORDERS IN A TERTIARY CARE OUTPATIENT SETTING

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SUMMARY:

Background: Anxiety Disorders (ADs) have been found to be among the most prevalent psychiatric comorbidity in patients with Bipolar Disorder (BPD) and Major Depressive Disorder (MDD). The co-occurrence of ADs and mood disorders are associated with an intensification of symptoms, poor functional outcome and suicidality. Previous epidemiological reports have described the lifetime prevalence of ADs with mood disorders; however, these reports have been primarily derived from large randomized clinical trails and therefore may not be reflective of the degree of comorbidity seen in outpatient settings. The authors conducted an epidemiological investigation regarding the prevalence and extent of comorbidity of ADs in a cohort of individuals with a primary diagnosis of BPD or MDD seeking care in a tertiary care outpatient setting. Methods: A cross-sectional baseline analysis of 178 patients with a primary diagnosis of BPD or MDD enrolled in a larger naturalistic cohort study was performed. The MINI-STEP was utilized to systematically assess for Bipolar I Disorder (BPDI), Bipolar II Disorder (BPDII), MDD, Generalized Anxiety Disorder (GAD), Post Traumatic Stress Disorder (PTSD), Social Phobia (SP), and Panic Disorder (PD). Bivariate analysis utilizing Pearson's chi-square test was conducted to assess the strength of association between mood and anxiety disorders. Results: The prevalence of mood disorders evaluated among 178 patients was as

follows: MDD, 41.7% (N=80); BP1, 39.6%(N=76); BP2, 12.0% (N=23). OCD was found to be significantly associated with MDD (12.5%, p=0.041). Statistically significant associations were observed between BPDII and PD (60.9%; p=0.016), SP (78.3%, p=0.044), and GAD (60.9%, p=0.018). No statistically significant associations were observed between ADs and BPDI. Conclusions: Our analysis suggests a strong degree of overlap between ADs and BPDII in the setting of a tertiary care outpatient setting. The prevalence of ADs in BPDII in the current study was found to be greater than the prevalence of ADs in BPDII found in previous studies. Future studies utilizing larger cohorts are warranted.

NR1-45

DIAGNOSTIC STABILITY OF FIRST-EPISODE PSYCHOSES RETROSPECTIVELY ASSESSED AFTER RECURRENCE OF PSYCHOTIC EPISODES

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SUMMARY:

Objectives: It is well known that diagnostic change during follow-up is not uncommon in first-episode psychoses. Accurate diagnosis at the first episode is important for better treatment outcome and doctor-patient rapport which could influence patients' compliance to the treatment. Diagnostic stability and predictive factors associated with diagnostic changes for the first-episode psychoses could not be grasped enough in previous prospective studies with follow-up periods of a few years. Considering that diagnostic confirmation would be reliably made at the time of recurrence, and that time to recurrence is highly variable in patients with first-episode psychoses, retrospective evaluation of diagnostic stability after the recurrence is warranted. This study aims to evaluate the diagnostic stability of first-episode psychoses, and to identify clinical factors associated with diagnostic shifts at the second episode. Methods: The authors screened 155 patients with psychotic disorders who were admitted in the psychiatric ward of Samsung Medical Center from January 1990 to February 2009 for both of their first and second episodes of psychoses. DSM-IV based consensus diagnosis was made for each episode by the review of medical records. One hundred and eight patients diagnosed with non-affective psychosis (schizophrenia, schizophreniform disorder, or brief psychotic disorder) at their first episode were included in the analysis of factors associated with diagnostic shift. These patients were divided into two groups according to the diagnosis at second episode, i.e., 'diagnosis change' (shifting to affective psychosis at second episode) and 'diagnosis non-change' groups. Demographic and clinical characteristics of the first episode were compared between the two groups.

Results: In the comparison of diagnoses between the first episode and second episodes, 79.5% of the patients initially diagnosed with affective psychosis (depressive or manic episode with psychotic features) remained in the same diagnosis. Among the patients initially diagnosed with non-affective psychoses, 88.9% of the patients belong to the 'diagnosis non-change' group.

NR1-46

ATR AS A PREDICTOR OF RESPONSE TO REBOXETINE

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SUMMARY:

Objective: Major depressive disorder (MDD) is a common mental illness that leads to significant interpersonal disability and high associated disability costs. Predicting response to antidepressant therapy is a challenge for clinicians, who are limited to clinical depression scales of modest utility in predicting 8-week response to an antidepressant. Biomarkers of treatment response that would predict remitters early in the course of treatment are, therefore, eagerly sought after. In the BRITE-MD study (www.brite-md.com), we reported that response and remission to escitalopram and bupropion were predicted by the Antidepressant Treatment Response index (ATR), a frontal quantitative EEG biomarker based on brain functional data at baseline and after one week of medication [1,2]. Here, we examined the relationship of ATR to treatment outcome with reboxetine (REB), a noradrenergic reuptake inhibitor antidepressant. Methods: Twenty-five adults (age 23-60, mean 43.07 (11.73 s.d.), 14F:9M) with non-psychotic unipolar MDD were studied in an 8-week single-blind outpatient trial at an academic medical center. Mean Hamilton Depression Rating Scale (HAMD-17) scores at study entry were 22.46 (3.1 s.d.), range 17 to 30. Subjects received REB 10 mg/d. ATR values were calculated using EEG data from pre-treatment baseline and after one week of REB treatment, from electrodes at FPz, FT8, FT9, A1, and A2 locations, using

the algorithm previously described for BRITE-MD [1,2]. Primary outcomes of interest were response (>= 50% improvement in HAMD-17), remission (HAMD-17 <7), and change in HAMD-17 score. Results: ATR in the first week of treatment was significantly predictive of change in HAMD-17 at the end of the 8-week trial (r=-0.485 p=0.014). ATR predicted response with 64.7% sensitivity and 75% specificity, and remission with 54.5% sensitivity and 71.4% specificity, using a cutpoint value of 52.1; this was derived from ROC analysis of this data set and differed from the cutpoint (56.8) calculated for SSRI outcome prediction in the BRITE-MD trial. Conclusions: The ATR index was significantly associated with clinical outcome with reboxetine treatment. As the first report examining ATR in a noradrenergic reuptake inhibitor antidepressant, these results expand the findings of the BRITE-MD trial with an SSRI (escitalopram) and a mixed dopaminergic-noradrenergic agent (bupropion).

NR1-47

GENETIC ASSOCIATION OF THE INTERACTION BETWEEN THE BDNF AND GSK3B GENES AND MAJOR DEPRESSIVE DISORDER IN A CHINESE POPULATION

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SUMMARY:

Objective: Alterations in brain-derived neurotrophic factor (BDNF)-signaling pathways may play an important role in the pathophysiology of major depressive disorder (MDD). Several lines of evidence have suggested that gene-gene interactions may confer susceptibility to MDD. The aim of this study was to analyze the single and combined effects of genes in the BDNF signal-transduction pathway on MDD in a Chinese population. Method: We recruited 447 patients with MDD and 432 age- and gender-matched control subjects. Five SNPs in three BDNF signal-transduction pathway genes (BDNF, GSK3B and AKT1) were used in association analyses. Results: An allelic association between the GSK3B SNP rs6782799 and MDD was found in our sample (allelic: ?2 = 5.24, P = 0.022, corrected P = 0.107; genotypic: ?2 = 5.55, P = 0.062) with an odds ratio (OR) of 1.25 (95 % confidence interval (CI), 1.03–1.52). Further gene-gene interaction analyses showed a significant effect of a two-locus BDNF/GSK3B interaction with MDD (GSK3B rs6782799 and BDNF rs7124442) (corrected P = 0.011), and also for a three-locus interaction (GSK3B rs6782799, BDNF rs6265 and BDNF rs7124442) (corrected P = 0.019). Individuals carrying the combination of two risk alleles showed an OR value of 4.00 (95 % CI, 2.05–7.79), while those with the combination of three risk alleles gave the largest OR value of 4.46 (95 % CI, 2.15–9.24). Conclusions: Taken together, these findings support the assertion that the GSK3B gene is an important susceptibility factor for MDD in a Han Chinese population. Keywords: major depressive disorder (MDD); brain-derived neurotrophic factor (BDNF); glycogen synthase kinase 3 beta (GSK3B); genetic association; gene-gene interaction.

NR1-48

HOW TO USE ADVERSE EVENTS LISTED IN THE PDR FOR ANTIDEPRESSANTS?

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SUMMARY:

Introduction: Side effects (SEs) are central to choosing an antidepressant (AD). Adverse Events (AEs) are undesirable events during clinical trials but may not be SEs of medication. Large numbers of AEs are listed in the Physicians' Drug Reference (PDR) and relationship to medication is unclear. Methods: AEs of ADs were extracted systematically from pdr.net. Different cutoffs for frequency of AEs and for difference between AD and placebo (PL) were explored. Results: Median 2.5 (range 0-11) AEs led to discontinuation in at least 1% and at least 100% more than on PL; most common were nausea, somnolence, and dizziness. Median of 7.5 (range 1-15) AEs occurred in 5% or more on AD and at least 100% more than on PL. Keeping at least 100% more than on PL, but lowering cutoff to 1% or more added another 2-20 AEs (median 11) which significantly increases the number of AEs considered SEs. However, of AEs occurring in 5% or more on AD, lowering cutoff for AD-PL difference to at least 50% more than on PL added only another 0-8 (median 3) AEs. Also, for AEs occurring in 5% or more on AD, most AD-PL differences were statistically significant (Fisher's exact test) not only if the AE occurred at least 100% more than on PL, but also if it occurred 50-99% more than on PL (though not if this was only

1-49% more than on PL). Most AD-PL differences were not statistically significant for AEs occurring in < 5% on AD unless they both occurred in at least 3% on AD and at least 100% more than on PL. Some AEs occurring only slightly more often than on PL are listed as SEs in textbooks (eg, headaches with bupropion though 26% vs. 23% on PL). Conclusions: The limited number of SEs leading to discontinuation should be specifically targeted. Based on their number (practicality) and statistical testing, AEs occurring in 5% or more on AD should be considered SEs even if occurring only 50-99% more than on PL, otherwise common SEs may be missed. Validity of SEs listed in textbooks needs critical assessment.

NR1-49

ACTIVATION/INHIBITION RESPONSE, EFFICACY, SAFETY OF OLANZAPINE IN ACUTE BIPOLAR PATIENTS: SECONDARY OUTCOMES OF A 24-WEEKS OPEN-LABEL SINGLE-ARM TRIAL

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SUMMARY:

Objective: To assess the response in the activation/inhibition dimension as well as the efficacy and safety of olanzapine in 4 groups of acute bipolar patients following DSM-IV criteria: manic, hypomanic, mixed or depressive. Methods: The MAThyS (Multidimensional Assessment of Thymic State) study is a phase IIIb, open-label, olanzapine (dose 5 to 20 mg/day), single-arm clinical trial in which primary outcome was the validation of the MAThyS scale, which assesses activation/inhibition process in the four bipolar groups. Efficacy and safety secondary outcomes are presented here: (a) Change from baseline to endpoints of HAMD-17, YMRS, HAM-A and MAThyS scales from baseline to 6 weeks (acute treatment phase or period II) and to 24 weeks (maintenance phase or period III); (b) Time to response in the total population and in each subgroup, from baseline to 6 weeks (period II) and to 24 weeks (period III). Results: One hundred forty-one patients were included (36 manic states, 31 hypomanic states, 26 mixed states and 48 depressive states). Fifty-six point seven percent were female, with a mean age of 45.6 (±12.9) years and a mean duration of illness of 16.9 (±13.9) years. More than 90% of manic and hypomanic patients and ¾ of mixed states were considered as hyper reactive whereas more than half of depressive patients were considered as hyporeactive. MAThyS score improved in all groups with most of the improvement occurring during the acute treatment phase. Similarly, all groups improved statistically and clinically their scores in the HAMD-17, YMRS, HAM-A at 6 and 24 weeks. Safety analyses were consistent with known olanzapine metabolic side effects. Conclusion: All groups improved both their thymic and activation/inhibition scores through the 24 weeks. Activation/inhibition process as a marker of response should be studied more specifically. Although olanzapine monotherapy seemed efficient and safe in depressed patients in this one-arm study, it has not been confirmed in double-blind randomized trials and is not indicated for these patients.

NR1-50

RESTING-STATE SPONTANEOUS NEURAL ACTIVITIES IN PATIENTS WITH A FIRST-EPISODE OF MAJOR DEPRESSIVE DISORDER AND THEIR FIRST-DEGREE RELATIVES

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SUMMARY:

Objective: Major depressive disorder (MDD) is known to be relevant to genetic deficits and brain dysfunction. In the present stuty, we explored the characteristics of resting-state spontaneous brain activities in patients with a first episode of MDD and their first-degree relatives using function magnetic resonance imaging (fMRI). Methods: The subjects included: 1) medication-naive patients with a first episode of MDD; 2) first-degree relatives of the patients; 3) healthy controls. There were 27 participants in each group. Images were acquired using a Siemens Trio 3-Tesla scanner during resting state. The amplitude of low-frequency fluctuation (ALFF) was calculated to measure spontaneous neural activities. Demographic data were analyzed using the SPSS 11.0 software. The preprocessing of imaging data was done using the SPM5 software, then individual ALFF maps were generated using the REST software. Finally, two-sample t-tests were performed to compare the differences in ALFF between every two groups. Voxels with a P value < 0.001 (uncorrected) and cluster size > 135 mm3 (5 voxels) were considered to show significant difference. Results: There were no differences

between the three groups in sex, age and years of education. When compared with the controls, the patient group exhibited increased ALFF in left posterior cingulate cortex, left superior temporal gyrus, right parahippocampal gyrus, left medial/superior frontal gyrus and left cerebellum, and decreased ALFF in left superior parietal lobule and right occipital lobe. When compared with the controls, the first-degree relative group showed increased ALFF in left uncus/parahippocampal gyrus and left medial frotal gyrus, and decreased ALFF in bilateral inferior parietal lobule, bilateral middle frontal gyrus and sensorimotor area (left paracentral lobule and right precentral gyrus). When compared with the first-degree relative group, the patients showed increased ALFF in left medial frontal gyrus and decreased ALFF in left occipital lobe and left thalamus. Conclusions: The patients with MDD and their first-degree relatives all exhibited increased spontaneous neural activities in medial frontal cortex and the limbic areas, and decreased spontaneous activities in the parietal lobe, suggesting dysfunction in the frontal-limbic system and parietal cortex may be trait markers in MDD.

NR1-51

DECREASED REGIONAL HOMOGENEITY IN INSULA AND CEREBELLUM: A RESTING-STATE FMRI STUDY IN PATIENTS WITH DEPRESSION AND SUBJECTS AT RISK FOR DEPRESSION

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SUMMARY:
Objective: Functional disconnectivity during the resting state has been observed in subjects with major depression disorder (MDD), and in subjects at high genetic risk for major depression during task performance. It is hypothesized that functional impairments in certain brain areas are present in patients with MDD and in their first-degree relatives. Method: To test this hypothesis, an analysis of regional homogeneity (ReHo) of the whole brain was performed on 45 subjects.
Results: Compared with the control group, subjects with MDD and those at high risk for MDD exhibited significantly decreased ReHo in the right insula and in the left cerebellum. Conclusions: These abnormalities may play an important role in the pathophysiology of depression.

NR1-52

DOES GENDER IMPACT THE RELATIONSHIP BETWEEN PARENTAL MALTREATMENT AND PERSONALITY PATHOLOGY IN ADULTHOOD?

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SUMMARY:
Objective: It is of interest to question whether there is an effect of gender on the relationship between parental maltreatment and personality pathology in adulthood. In this study, we investigated the relationship between maternal and paternal maltreatment in both male and female subjects. Methods: The sample consisted of 156 adults from the Beth Israel Medical Center psychiatric department. Exclusion criteria included: psychotic disorder, mania, dementia, +65 age, organic brain impairment, cognitive deficits, mental retardation and inability to read English. Adult personality pathology, the dependent variable, was assessed using the Personality Diagnostic Questionnaire which includes adaptations from the diagnostic criteria for personality disorders of the DSM-IV. PDQ-4 questions are scored to highlight personality pathology within nine subscales. Parental maltreatment was assessed using the Conflict in Tactics Scale Parent-Child version (CTSPC-CA). Each question was asked independently for the mother and the father. Scores highlighted parental maltreatment in three subscales: psychological aggression, physical assault and neglect. Results: Bivariate logistic regression analysis of each CTSPC-CA scale onto the PDQ-4 total score of personality pathology were statistically insignificant when performed for males only. However, repeat analysis for females only indicated maternal physical abuse and neglect and paternal neglect to be significantly associated with level of total personality pathology (OR's 2.7, 4.4 and 3.0 respectively). Conclusion: In this clinical population, data suggests that there is a strong correlation between female personality pathology and maternal physical abuse and neglect and paternal neglect. Men and women may differ as to the actual effect of parental maltreatment on personality pathology or as to the propensity to report such an effect.

NR1-53

RISK FACTORS FOR OBESITY IN PATIENTS WITH BORDERLINE PERSONALITY DISORDER OVER 10 YEARS OF PROSPECTIVE FOLLOW-UP

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SUMMARY:
Objective: The purpose of this study was to identify risk factors for obesity in female patients with borderline personality disorder (BPD). Methods: Two hundred and thirteen female borderline patients who met DIB-R and DSM-III-R criteria for BPD were interviewed concerning their symptomatic and psychosocial functioning as well as medical history at six, eight, and ten years after their index admission. Their BMI at baseline was calculated using their measured height and weight. It was assessed at each follow-up period using subject self-report. Family history of obesity, psychiatric medication, and meeting criteria for binge eating disorder (BED) were considered as predictors of obesity. We conducted a longitudinal analysis of obesity based on a generalized estimating equations (GEE) approach that accounted for the correlation among the repeated measures of obesity. These analyses modeled the log prevalence of obesity, yielding an odds ratio (OR), and 95% confidence interval (95%CI), for each of the predictors. Results: Over ten years of follow-up, a family history of obesity, taking atypical antipsychotics, and a diagnosis of BED were significant predictors of obesity. More specifically, those women with a family history of obesity have 53% (OR: 1.527, 95%CI: 1.070, 2.178) greater odds of becoming obese, those reporting taking atypical antipsychotics have 79% (OR: 1.787, 95%CI: 1.247, 2.561) greater odds, and those with a diagnosis of BED have 85% (OR: 1.848, 95%CI: 1.216, 2.809) greater odds of obesity. Conclusion: These results suggest that the risk factors for obesity in women with BPD are complex, including aspects of family history, concurrent treatment, and disordered eating.

NR1-54

PREVALENCE OF PERSONALITY DISORDERS IN ADULT GAY, LESBIAN, BISEXUAL, AND TRANSGENDER PATIENTS IN AN INPATIENT CHEMICAL DEPENDENCY TREATMENT PROGRAM

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SUMMARY:
Background: Several studies have been conducted looking at the prevalence of personality disorders in the chemically dependent population. Previous research has found that there is a high prevalence of personality disorders among individuals with substance use disorders, and that personality disorders may contribute to treatment noncompliance, relapse, medical problems, legal difficulties, and increased suicide risk. To our knowledge, however, there are no studies which have examined personality disorders and their related clinical variables in a sample of gay and lesbian individuals with substance use disorders. Methods: Study participants are members of the gay, lesbian, bisexual, and transgender (GLBT) population who were actively enrolled in an inpatient chemical dependency treatment program. Participants volunteered to undergo the SCID II diagnostic evaluation for personality disorders. For each participant, consent was obtained for a formal chart review to obtain pertinent demographic, medical, and psychiatric information. Study enrollment was initiated in May 2009 and is ongoing. The estimated total number of participants by study end will be approximately 200. Results: As of November 2009, a total of 53 patients have been enrolled in the study. Forty-two are male, 6 female, and 5 transgender. A total of 48 (90.5%) had at least one personality disorder. The most common personality disorders were obsessive-compulsive personality disorder (54.7%; n=29), borderline personality disorder (50.9%; n=27), and avoidant personality disorder (45.3%; n=24). The mean number of personality disorders was 4.25 ± 2.2 for subjects with two or more personality disorders. Data is still being collected with a projected end date of March 2010. Conclusion: Preliminary data suggests there is a high prevalence of personality disorders in the GLBT population undergoing chemical dependency treatment. Proper identification and management of these disorders in this population may improve long-term abstinence from substances.

NR1-55

REDUCTION OF TYPICAL GENDER DIFFERENCES AMONG PSYCHIATRIC OUTPATIENTS WITH ASPD

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SUMMARY:

Objective: To examine gender effects on the clinical characteristics of psychiatric outpatients who satisfied criteria for Antisocial Personality Disorder (ASPD). Method: During a five-year period, all new patients (N=1458) admitted to a University-sponsored psychiatric outpatient clinic were given a structured diagnostic interview, a written psychosocial history and the Symptom Checklist-90-R (SCL-90): 9 percent (N=127) met criteria for ASPD. Results: ASPD patients were younger, more likely to be male and less well educated. In the non-ASPD comparison group (N=1331), female patients were more likely than males to suffer from Major Depression, Panic Attacks, Phobic Disorder and Somatization Disorder while males were more likely to endorse Alcohol and Drug Dependence. In the ASPD group, no gender differences were found for Major Depression, Alcohol Dependence, or Drug Dependence. ASPD females had more Anxiety Disorder and Somatization Disorder than ASPD males. Females in the non-ASPD group reported more psychiatric comorbidity than males. No gender difference was found in the amount of comorbidity in the ASPD group. On the SCL-90, gender differences were striking for the non-ASPD patients with females showing higher distress levels on all scales. No significant gender differences were found on the SCL-90 scales in the ASPD group. Conclusion: Almost one in 10 outpatients met criteria for ASPD. Overall, ASPD patients reported greater psychiatric comorbidity and a greater amount of emotional suffering than non-ASPD patients. However, gender differences were reduced in the ASPD group where males and females were equally likely to suffer from Depression, Alcohol Dependence and Drug Dependence and were also equally likely to report high levels of symptomatic distress. Providers should be sensitive to the possible unrecognized gender effects of ASPD in their patients.

NR1-56

WITHDRAWN

NR1-57

QUALITY OF CARE AND CRIME RATES AMONG PATIENTS WITH SCHIZOPHRENIA: A NATIONWIDE POPULATION-BASED FOLLOW-UP STUDY

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SUMMARY:

Introduction: Crime rates are higher among patients with schizophrenia than in the general population. Denmark has seen a substantial increase in the number of forensic patients since 1980 with annual growth rates reaching 7%. In the same period, the population of forensic patients with schizophrenia has increased from 50% to 75%. Evidence-based care for patients with schizophrenia is well-established in international and national guidelines. However, a possible association between quality of care and risk of crime among patients with schizophrenia has not previously been studied. Aim: To study the association between quality of care and risk of crime among patients with schizophrenia. Methods: This nationwide population-based follow-up study is based on the Danish National Indictor Project (DNIP), a national clinical database for patients with schizophrenia, and the Danish Crime Register, a national register of criminal offences. We include all incident and prevalent patients diagnosed with schizophrenia (ICD-10: F20.00-F20.99), who are Danish citizens and older than 18 years. All patients have been admitted as inpatients at a psychiatric ward in the period 1 January 2004 to 31 December 2007 (approx 20,000 patients). In DNIP quality of care is assessed as fulfilment of a set of quality of care criteria related to the diagnostic process, contact with the health care system, use of antipsychotic medication, evaluation of side effects, family intervention, psycho education, planned outpatient treatment by discharge and suicide prevention. All patients will be followed up for one year after discharge. We identified all convictions for both violent and property crimes in the population. Separate analyses will be made for subtypes of crimes. The association between quality of care and risk of crime will be analysed using Cox proportional hazards regression with adjustment for a wide range of possible confounding factors. Results: The study is in progress and will be completed and published in 2010.

NR1-58

THE EFFICACY OF LOW-FREQUENCY REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION TREATMENT FOR AUDITORY VERBAL HALLUCINATIONS MAY BE LOW

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SUMMARY:

Auditory Verbal Hallucinations (AVH) are resistant

to antipsychotic medication in 25% of patients with schizophrenia. Several studies have applied low-frequency repetitive Transcranial Magnetic Stimulation (rTMS) directed at the left temporo-parietal area (TP) for the treatment of AVH, with inconsistent results. Furthermore, a large recent fMRI study indicated that the left TP is not a general focus of activation during the experience of AVH. To test efficacy of rTMS for AVH, rTMS was contrasted to sham in a double blind randomized study. Sixty-two patients were randomized over 3 conditions: 1.) rTMS targeted at the area of maximal halucinatory activity as demonstrated with individual fMRI scans; 2.) rTMS directed at the left TP and 3.) sham treatment. Repetitive TMS was applied during 15 sessions of 20 minutes each, at 1 Hertz and 90% of the individual motor threshold. The severity of AVH and other psychotic symptoms were monitored during treatment and 3 months follow-up, using the Auditory Hallucination Rating Scale (AHRS) and the positive items of the Positive and Negative Syndrome Scale (PANSS). Mean decrease in AVH severity did not differ significantly between the 3 groups ($F = 0.619$, $p = 0.54$), nor did decrease in severity of psychosis ($F = 1.640$, $p = 0.21$). Even when guided and non-guided rTMS were combined and compared to sham treatment, no significant differences in efficacy were observed (sum of the AHRS, $F = 1.172$, $p = 0.29$). Low-frequency rTMS directed at the area of maximal hallucinatory activity and rTMS directed at the left TP are not superior to sham treatment for medication-resistant AVH.

NR1-59

METABOLIC AND CARDIOVASCULAR RISK IN PSYCHOTIC PATIENTS TREATED WITH ATYPICAL ANTIPSYCHOTICS

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SUMMARY:
Because of the bigger interest in recent times about the need to monitor the physical health of patients with mental illness, as well as potential side effects of antipsychotics and other psychoactive drugs, this study was designed to analyze, in a sample of patients with schizophrenia and other psychotic disorders, the possible occurrence of metabolic disorders, their relationship with treatment and the interventions needed in this regard. Methodology: A prospective study with patients followed up in the Day Hospital of Psychiatry, Hospital Clínico Universitario de Valladolid, and who continued treatment with an atypical antipsychotic. Results: The results describe a young population with a mean age of 36.77 years, 59% male and 41% female. Regarding their dietary habits, most patients did not follow any type of diet at baseline (63.9%). The activity level was, in the most cases, between light activity (47.5%) and median (32.8%) which may be related to the presence of negative symptoms of the disease that involve lack of initiative and motivation and a sedentary lifestyle in these patients. With regard to weight, the sample observed in most patients at baseline showed different degrees of overweight and obesity, with only 26.2% of the sample at normal weight. On the other hand the presence of metabolic syndrome was proportionately somewhat greater in the group of patients treated with olanzapine, because 21.7% of those treated with the drug had an altered but not statistically significant relationship, and in 33% of those treated with risperidone long-acting injectable, which were the largest group included. In the sample has been found the influence of certain doses of these antipsychotics and their influence on weight, but has only been significantly correlated with ziprasidone. Of note is the decrease in weight with olanzapine, usually associated with antipsychotic drug weight gain, while this study gives an opposite result which may be related to psycho-educational interventions on healthy lifestyles and the consequent change in the behavior in this regard. The alteration of prolactin widely studied as a side effect of certain antipsychotics also becomes apparent here in the studied patients especially with risperidone oral and injectable risperidone long-term, being in both cases a statistically significant correlation.

NR1-60

"HOW LONG SHOULD I TAKE THIS MEDICINE?": A LITERATURE REVIEW OF THE DURATION OF MAINTENANCE TREATMENT IN SCHIZOPHRENIA

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SUMMARY:
A 40 year old male with Schizophrenia is seen every six months in the Clozapine clinic. For the last 10 years, he has been compliant with clozapine and has not experienced

any psychotic symptoms. He works and has excellent family support. On a clinic visit, he questions the need for ongoing antipsychotic medication, which made us examine the literature on the topic. A literature search using PubMed on discontinuation of antipsychotics in patients with schizophrenia remission recovered limited data. The two main articles listed included a 2007 naturalistic study and a review article published in 1997. The APA practice guidelines for treatment of schizophrenia are based on data prior to 1997. All of these articles highlight the lack of well designed studies and the need to collaborate with patients and their families using a case by case approach regarding the duration and dose of antipsychotics needed. The APA Practice Guidelines recommend maintenance treatment with antipsychotic medication for up to one year following one episode of psychosis. Life-long maintenance treatment is recommended for patients who have had more than two episodes in five years or with history of multiple episodes. If a decision is made to taper the antipsychotic, then the dose should be cut by 10% every month with close monitoring. Several interesting issues related to the duration of antipsychotic maintenance in schizophrenia were reported in the literature. There is a proportion of the schizophrenic population who will remit completely and have no further relapses. If a decision is made to stop antipsychotics it is important to do a gradual taper since sudden discontinuation can lead to rapid-onset/super sensitivity psychosis. This is characterized by auditory hallucinations and persecutory delusions which may be similar in pattern to previous psychotic episodes but is readily abolished by reintroduction of medication or resolves spontaneously within 4-6 weeks. Clinicians may aim to prescribe a minimal effective dose to provide symptomatic control and yet limit side effects. Conclusion: A proportion of schizophrenia patients have complete remission and may not need indefinite treatment with antipsychotics. This is especially significant given the adverse effects associated with long term antipsychotic use. Further research is needed to identify such patients which would provide better insight into optimal treatment of schizophrenia.

NR1-61

BEYOND SMOKING CESSATION: VARENICLINE IN SCHIZOPHRENIA?

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SUMMARY:

Smoking in patients with schizophrenia is highly prevalent and ranges from 50-80%. Available literature indicates that these high rates of nicotine dependence may be related to decreased activity at a7 nACh receptor, which also seems to be linked to P50 auditory evoked potential and smooth pursuit and anti-saccadic eye movements. Nicotinic receptor stimulation from smoking is also hypothesized to improve the tolerance of antipsychotic medications. There have been a number of research trials using modulators of nACh receptors for management of negative symptoms and cognitive deficits seen in schizophrenia although none have been marketed yet. Varenicline acts on nicotinic cholinergic receptors (nACh) and was approved for smoking cessation in 2006. It is a partial agonist of a4 ß2 nACh receptor that promotes dopamine release in nucleus accumbens and thus decreases the craving for nicotine. Varenicline is also a full agonist at a7 nACh receptor. As a result, it has been hypothesized that varenicline could help not only with smoking cessation but could also enhance cognitive functioning in schizophrenia. It is interesting to note that patients with schizophrenia were excluded from premarketing analysis. On the contrary, recent warnings for aggression, anxiety, and suicidal ideation, and emergence of manic and psychotic symptoms impede varenicline use in this population. Furthermore, through its action on a4 ß2 receptors, it also increases dopamine and promotes the emergence of psychiatric symptoms. This poster discusses these conflictual reports and reviews the literature on the topic in an evidence-based manner. A Pubmed search using "varenicline, psychosis, schizophrenia" yields only a few articles, mainly case reports with a spectrum of results. The way to move forward on this issue is by conducting well-designed randomized control studies, with extended periods of varenicline use and close monitoring in patients with schizophrenia. Conclusion: Varenicline is the only approved nACh receptor agent in market and is approved for smoking cessation. There have been conflicting reports about its use in schizophrenia and it deserves a well-designed study to elicit any benefits on the cognitive and negative symptom domains which are not really addressed by the available antipsychotics.

NR1-62

FACIAL EMOTION RECOGNITION IN CHINESE WITH FIRST-EPISODE SCHIZOPHRENIA: EMOTION SPECIFIC DEFICIT AND ERROR PATTERN

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SUMMARY:
Background: In recent years, studying facial emotion recognition emerges as a new line of research in understanding the social deficit in patients with schizophrenia. While impaired facial emotion recognition in schizophrenia has been demonstrated in the Western population, Chinese data is relatively lacking. In view of the cultural variations in shaping accuracy of recognition, it would be interesting to examine if deficits can be found in Chinese with schizophrenia, particularly those with first-episode of illness where the influence of potential confounders associated with disease chronicity can be minimized. Objective: This study was designed to 1) examine the performance of facial emotion recognition in local Chinese with first-episode schizophrenia, 2) investigate the pattern of identification in specific facial emotions, and 3) explore pattern of error in misidentified emotions. Methods: Fifty stabilized outpatients with first-episode schizophrenia and 26 healthy controls matched in age and sex were recruited. Their level of nonverbal intelligence was tested and diagnostic examination conducted. The ability to recognize the six universal facial emotions was examined using locally validated colored photographs from the Japanese and Caucasian Facial Expressions of Emotion. The illness severity and mood status were assessed with standardized instruments. Results: Chinese patients with first-episode schizophrenia performed significantly worse than their control counterparts on overall facial emotion recognition ($p<0.001$). The diagnostic effect remained significant after statistical control of potential confounding variables using analyses of covariance. Among six universal facial emotions, specific impairment in identifying surprise, fear and disgust was identified. In comparing pattern of errors, patients and controls differed only in the misidentification of angry faces. Conclusion: Impaired facial emotion recognition was demonstrated in Chinese with first-episode schizophrenia, supporting it as a trait deficit of the illness. The emotion-specific deficit and error may have implications for understanding the behavior and difficulties in schizophrenia.

NR1-63

PREVIOUS OFFENDING AMONG FIRST-EPISODE PSYCHOSIS PATIENTS: PREVALENCE AND CLINICAL CORRELATES

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SUMMARY:
Introduction: The relationship between criminality and psychosis has not been thoroughly explored. The aim of the study was to examine the prevalence and clinical correlates of previous offending in first episode psychosis. Method: Fifty-one patients aged 16 to 45 years with newly diagnosed schizophreniform disorder, schizoaffective disorder or schizophrenia were recruited from a geographically defined catchment area of Cape Town, South Africa. Psychopathology was assessed with the Positive and Negative Syndrome Scale (PANSS), Calgary Depression Rating Scale (CDSS) and the Clinical Global Impression Scale (CGI-S). A history of criminality and illicit substance use was established on the basis of respondents' self-report and collateral informant interviews. Results: Nineteen (37%) of the 51 subjects had a history of police contact. Twenty percent of subjects had previously been incarcerated, 29% had a previous charge laid against them and for 15% the police had been called without a charge being laid. The strongest predictors of previous offending were male gender ($p=0.00061$) and a history of illicit substance use ($p=0.00024$). Subjects with a history of criminal behaviour were more likely to have a higher baseline CDSS score ($p=0.03$), positive ($p=0.001$), general ($p=0.01$), and total ($p=0.01$) PANSS score. Previous criminal behavior was not significantly differentiated on the basis of CGI-S scores and socio-demographic variables. Conclusions: This study suggests an association between first episode psychosis and previous offending. This relationship is strongly associated with substance abuse comorbidity. The clinical and management implications of these findings will be discussed with attention paid to key factors associated with first episode psychosis.

NR1-64

ANTIPSYCHOTICS AND LONG-TERM OUTCOME IN SCHIZOPHRENIA: MILAN-STANFORD COLLABORATIVE PROJECT

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SUMMARY:
Objective: The treatment of schizophrenia is aimed not

only to the remission of the acute episode, but, most of all, to the prevention of relapses (1). The aim of this naturalistic study was to evaluate the effectiveness in prevention of recurrences and the tolerability of haloperidol versus atypical antipsychotics (risperidone, olanzapine, clozapine and aripiprazole) in patients with schizophrenia. Method: Fifty-four schizophrenic outpatients were divided into two groups according to the prescribed single oral antipsychotic: haloperidol (n=16) and atypical antipsychotics (n=38; risperidone=16, olanzapine=19, aripiprazole=1 and clozapine=2). A survival analysis (Kaplan-Meier) of the follow-up period (4 years) was performed considering as death events the change of treatment due to side effects, relapses and hospitalizations. A further Kaplan-Meier was performed to compare antipsychotic treatments. Results: Mean duration of illness was 12 years for the whole sample. The two groups were not different with respect to demographic and clinical variables. Kaplan-Meier survival analysis showed a superiority for atypical antipsychotics (Log Rank: chi-square=6.861, p=0.009; Breslow: chi-square=6.894, p=0.009) compared to haloperidol. With respect to specific antipsychotics, olanzapine showed a superiority in terms of survival compared to haloperidol (Log Rank: chi-square=7.339, p=0.007; Breslow: chi-square=7.592, p=0.006). Moreover, side effects, in particular extrapyramidal side effects (EPS), were more frequent in the group treated with haloperidol compared to the group treated with atypical antipsychotics (chi-square=8.588, df=4, p=0.04). Of note, 31.4 % of patients treated with atypical antipsychotics were fully employed compared to 18.7% of patients treated with haloperidol (chi-square=2.099, df=2, p=0.33, Phi=0.2), indicating a possible difference in overall functioning and quality of life between the two treatment groups. Conclusions: These preliminary data seem to show differences in terms of reduced recurrences between haloperidol and atypical antipsychotics (2), indicating, moreover, for the former the presence of more frequent side effects, in particular extrapyramidal ones (EPS). These naturalistic observations need to be confirmed by studies with larger samples and a prospective design.

NR1-65

EXACERBATION OF PSYCHOSIS IN RELATION TO MENSTRUAL CYCLE IN WOMEN: ROLE OF ESTROGEN

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SUMMARY:

The first observation of a possible connection between menstruation and psychological disorder appeared in the 18th century, where premenstrual psychosis was described by Amard in 1807 and by Boismont in 1842. During premenstruation, it had been discovered that psychotic symptoms were exacerbated. Furthermore, studies indicate that symptoms tend to worsen after childbirth and menopause when estrogen levels are lower and ease during menstruation and pregnancy when hormone levels are higher. In 2008, Australian researchers reported that 56 schizophrenic women who were given an estrogen patch, in addition to their standard psychiatric medications, experienced fewer psychotic symptoms, including hallucinations, delusions and movement disorders as compared to 46 women who were given placebo patch. Methods: This retrospective study included female patients of reproductive age who were evaluated in the emergency room and admitted to Bergen Regional medical center with a preexisting formal diagnosis or new diagnosis of schizophrenia, schizoaffective disorder or psychotic disorder not otherwise specified. Information was collected from chart review regarding the date of onset of menstrual cycle, reproductive history, psychiatric diagnosis and psychiatric medications. Subjects with an abnormal or irregular menstrual cycle due to a pathological reason (e.g. polycystic ovarian syndrome) or with amenorrhea were excluded from the study. Subjects with a recent severe stressor were excluded, as this may have been a confounding variable for the exacerbation of psychotic episode. Furthermore, subjects with a general medical condition, as indicated on Axis III, were excluded. The data was collected and compared by using biostatistical analysis.

Result: Out of 105 charts reviewed, 44 patients with psychotic episode, who were admitted to the hospital, were in the premenstrual phase of their menstrual cycle i.e. within a 7-day period preceding their date of onset of menstruation. Conclusion: We concluded that there is a significant relationship between exacerbation of psychotic symptoms and the premenstrual phase as evidenced by 42% of hospitalizations falling in that period of menstrual cycle which in turn supports the research that estrogen may be a potential therapy for severe mental illness in such patients.

NR1-66

DELUSIONS, DELUSIONAL CONVICTION AND METACOGNITIVE IMPAIRMENTS IN PATIENTS

WITH SCHIZOPHRENIA

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SUMMARY:
While diverse in range, delusions share two main characteristics central to their definition as delusions: they are highly resistant to change and they are accompanied by a strong feeling of subjective conviction. The factors underlying these central characteristics remain ill-understood. The present study is motivated by the need to explore the nature of these factors. It aims at testing the hypothesis that metacognitive deficits may play an important role in accounting for the persistence of delusional beliefs and thus constitute plausible candidates for the putative factors. It is also unclear what factors trigger or exacerbate metacognitive dysfunction, yielding extreme metacognitive responses. One possibility is that emotionally salient material or content may be one such factor. A secondary aim of our study was to test this hypothesis. Fourteen actively delusional patients with schizophrenia (D), 14 non-delusional patients (ND) and 14 healthy controls (C) were administered an emotional metacognitive version of the WCST adapted from Koren et al. The two groups of patients also completed the Beck Cognitive Insight Scale. There was a significant difference ($p<0.001$) between D and ND subjects for the Self-Certainty component, higher in the delusional group, but not for the Self-Reflectiveness component. Relative to both controls and ND patients, delusional participants were specifically impaired on metacognitive measures of free choice improvement ($p=0.0388$) and global monitoring ($p=0.0390$). This was correlated with high Self-Certainty for D patients relative to ND patients. We found no effects of the emotional valence or intensity of words on either the cognitive or metacognitive measures. Our results regarding high Self-Certainty on the BCIS in deluded patients are consistent with the findings of prior studies that have reported an association between active delusions and increased Self-Certainty. Our results support the idea that, although all schizophrenic patients present with metacognitive impairments, patients with delusions are more seriously impaired in particular on the control dimension of metacognition. It remains unclear whether emotions favour this metacognitive disruption and need to be tested further. Utimately, this study supports the fundamental idea that metacognitive remediation could be a first-rate candidate among the psychotherapeutic resources available to relieve schizophrenic patients from their delusional symptoms.

NR1-67

PREDICTORS OF FUNCTIONAL DISABILITY AND NUMBER OF HOSPITALIZATIONS IN SCHIZOPHRENIA: RELATIONS WITH NEUROCOGNITION, SYMPTOMS AND PREMORBID ADJUSTMENT

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SUMMARY:
Cognition in schizophrenia has received significant attention because of its robust prediction of functional outcome. Negative symptoms and premorbid adjustment have also been related to the longitudinal course of the illness. However, the high degree of intercorrelation among all of these variables leaves unclear whether neurocognitive deficits have a direct effect on functional outcome and clinical improvement or whether that relationship is mediated by additional variables in the illness. Purpose: To analyse the specific contribution of each variable to the resulting level of functional disability and number of hospitalisations. Method: We examined 95 patients with chronic schizophrenia (DSM-IV criteria). PANSS ratings were used to evaluate clinical symptoms, while illness duration and number of hospitalisations were obtained from digital medical records. The cognitive battery included tests for verbal and working memory, executive functioning and processing speed. Functional disability was assessed six months after the recruitment with the Disability Assessment Schedule (DAS-WHO). Results: Although negative symptoms were found to be significantly related to functional disability ($p< 0.01$), positive symptoms were not. Cognitive deficits were significantly related to functional disability ($p< 0.01$), illness duration ($p< 0.01$) and number of hospitalisations ($p< 0.01$). However, these correlations were mediated by processing speed, so that once the effect of processing speed is controlled, the magnitude of the relationship among other cognitive variables and outcome significantly decreases. Additionally, after controlling processing speed, negative symptoms and premorbid adjustment maintain a significant level of prediction on functional disability. Importance/Relevance: A better understanding of the complex interactions among the studied variables will allow the clinician to reach more accurate decisions about

treatment priorities to improve functional disability in schizophrenia.

NR1-68

COMPARATIVE ANALYSIS OF INVOLUNTARY ADMISSION AND VOLUNTARY ADMISSION IN SCHIZOPHRENIA: A THREE-YEAR FOLLOW UP

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SUMMARY:
Objectives: The purpose of this study was to investigate differences between the involuntary hospitalized patients and voluntary hospitalized patients in schizophrenia. Methods: Patients experiencing hospitalization between 2001 and 2005 with a diagnosis of DSM-IV schizophrenia were included. The subjects were grouped by whether their participation was voluntary or involuntary in the aspects of admission. The data were collected through inpatient medical records. The two groups were compared regarding demographic variables and clinical features, and we examined number of rehospitalizations, duration of follow-up, follow-up retention rate and second admission pattern for three years after discharge. Results: One hundred eighty-one subjects were classified as involuntary group, and 69 subjects as voluntary group. There were more female patients, more past admissions and longer duration of illness in involuntary group. The patients in involuntary group had more problematic behaviors and complained chiefly of delusions. The follow-up retention rate was lower (44.8% vs. 59.4%) and the rate of the second involuntary admission was higher in the involuntary group. Conclusion: The results of this study suggest that the involuntary hospitalized patients are more vulnerable to the follow-up loss. Involuntary hospitalization may be an important variable as a predictor for treatment maintenance in patients with schizophrenia.

NR1-69

CARBON DIOXIDE-INDUCED PANIC IN SCHIZOPHRENIA WITH AUDITORY HALLUCINATIONS

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SUMMARY:
Background: Panic disorder has been seen as unimportant and uncommon in patients with the severe diagnosis of schizophrenia. Recent observations raise the possibility that panic (and other anxiety disorders) may be an important part of schizophrenic psychopathology. Panic may emerge prodromally; contribute to acute distress, disability, and specific psychotic symptoms; and predict medication side effects, regimen and response. It may predict significant benefit from adjunctive clonazepam. However, panic is easily missed in schizophrenia, due to limited clinician awareness, agitation, impaired cognition, and psychotic symptom overlap. It is vital to improve diagnostic methods. Methods: Seven schizophrenic inpatients with auditory hallucinations (despite current antipsychotic medication) underwent a structured Panic and Schizophrenia Interview (PASI; which assessed panic symptoms concurrent with voices), followed by a carbon dioxide challenge test for panic (30 seconds of 35% carbon dioxide/65% oxygen). Results: All subjects screened positive for concurrent panic and voices on the PASI. All subjects experienced acute panic anxiety to carbon dioxide, but none to placebo. There were no unexpected adverse consequences. One subject had acute voices concurrent with induced panic (the only subject not on any antipanic medication). Clonazepam q12h was then openly added to her anti-psychotic, and dose was gradually raised until voices ceased clinically. Carbon dioxide rechallenge then produced neither panic nor voices. Conclusions: This first systematic examination of panic induction in schizophrenia suggests that carbon dioxide challenge is safe and effective, that panic is prevalent in schizophrenia with voices, and that panic may sometimes be linked to voices. Further investigation is warranted.

NR1-70

THREE-DIMENSIONAL ELECTROENCEPHALOGRAPHIC MAPPING WITH ELORETA DURING SLEEP ONSET PERIOD

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SUMMARY:
Objective: We analyzed the changes of EEG power spectra three-dimensionally using eLORETA (exact low resolution brain electromagnetic tomography) during the transition from wakefulness to sleep to localize the brain regions

associated with sleep onset process.
Methods: Thirty channel EEG was recorded in 61 healthy subjects (male: female = 34:27, age = 27.2 ± 3.0 years). EEG power spectra were computed in seven frequency bands (delta, theta, alpha-1,alpha-2, beta-1, beta-2 and beta-3) and compared between four kinds of thirty-second wakefulness-sleep states such as wakefulness (WAKE), transitional sleep onset period (TSOP), early sleep onset period (ESOP), and late sleep onset period (LSOP).
Results: 1.) The TSOP compared to the WAKE showed increased delta power in the occipital lobe, and increased theta power in the occipital lobe, the parietal lobe, the precentral gyrus and the superior temporal gyrus. The alpha-1 power was decreased in the occipital lobe and the precuneus. 2.) The ESOP compared to the TSOP was characterized mainly by the global decrease of alpha-1 and alpha-2 powers, and increased theta power in the posterior cingulate gyrus, the occipital lobe, the parietal lobe and the superior temporal gyrus. 3.) The LSOP compared to the ESOP showed further decrease of alpha-1 power in the parahippocampal gyrus, the cingulate gyrus, the inferior parietal lobule and the superior temporal gyrus, and decrease of alpha-2 power in the precentral gyrus, the cingulate gyrus, the postcentral gyrus, the inferior parietal lobule and the precuneus. 4.) The LSOP was also characterized by decreased powers of beta-2 and beta-3 bands in the fronal lobe and some parts of the parietal lobe. Conclusions: The characteristic findings in the very transitional sleep onset period were changes in the occipital lobe such as increased delta and theta power and the decrease of alpha-1 power including decreased theta power in the parietal lobe. Thereafter the global decrease of alpha-1 and alpha-2 powers and further increase of theta power in the occipital and the parietal lobes occurred. As sleep went deeper in stage 1, beta-2 and beta-3 powers showed decrease mainly in the frontal lobe and in some other areas. Thease results suggest that the sleep onset process includes at least three steps in sequencial manner such as theta increase in the posterior part of the cerebral cortex, the global decrease of alpha, and the decrease of beta in the frontal lobe.

NR1-71

STUDY COMPARING PSG DATA IN INSOMNIA PATIENTS WITH HIV VERSUS MATCHED CONTROLS WITH INSOMNIA

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SUMMARY:
Introduction: Insomnia is estimated to affect up to 70% of those infected with HIV. However, limited data are available on the nature of the sleep difficulties in this population. Alterations in the distribution of REM and slow-wave sleep over the night have been reported and hypothesized to be due to co-morbid mood disturbances in this population, however, this has yet to be established. The purpose of this study was to test the hypothesis that there would be differences in self-reported and polysomnographic (PSG) sleep in HIV infected individuals with insomnia and matched insomnia controls not accounted for by medical or psychiatric disorders. Methods: We selected 14 HIV+ subjects and matched them to controls based on age, sex, psychiatric disorders, substance abuse, medical disorders and ethnicity. Diagnosis of insomnia was based on the consensus of 6 clinician interviews. SCID was used to determine psychiatric diagnoses. Sleep data derived from average of 2 nights of PSG data and average of up to 2 weeks of daily sleep diaries. Results: Multivariate analysis revealed an overall significant difference between HIV and control subjects as well a significant group by gender interaction among the PSG sleep variables ($p < 0.05$). Post-hoc analyses identified that the HIV group had longer self-reported ($p<0.01$) and PSG ($p<0.10$) sleep onset latency, and less self-reported sleep efficiency ($p<0.05$), while HIV+ women had a greater percentage Stage 1 sleep ($p<0.02$). Conclusion: This study provides preliminary evidence that HIV+ individuals with insomnia have significantly worse sleep than matched insomnia controls which is not due to greater medical or psychiatric disorder burden. The cause of this difference in sleep disturbance is unclear. Possibilities include the effects of HIV-related medications, psychosocial effects of being diagnosed with HIV, and neuropsychiatric effects of the virus.

NR1-72

DECREASES IN SOLUBLE CD40 LIGAND ARE ASSOCIATED WITH IMPROVEMENTS IN SEVERITY OF INSOMNIA IN HIV-INFECTED PATIENTS: A PILOT STUDY

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SUMMARY:

Previous studies have shown that soluble CD40 ligand (sCD40L) is elevated in HIV patients and it is negatively correlated with CD4 count. Soluble CD40L is also elevated in patients with obstructive sleep apnea with treatment with continuous positive airway pressure (cPAP) associated with reductions in sCD40L. The current study examined whether improvements in severity of insomnia, fatigue and distress and CD4 predict decreases in sCD40L in 14 asymptomatic subjects with human immunodeficiency virus (HIV) receiving highly active antiretroviral treatment (HAART). Inclusion criteria included scores above 5 on the Insomnia Severity Index (ISI) and HAART. Subjects were randomized to either doxepin 10 mg, temazepam 15 mg or placebo for 3 months. Insomnia, fatigue and distress were assessed at entry and at 6- and 12-weeks. CD4 count and serum levels of sCD40L were assessed at entry and at 12-weeks. To control for potential baseline differences, analyses were conducted on percent change scores. Significant reductions were observed for ISI (mean D = -60%), fatigue (mean D = -35%) and distress (mean D = -20%) with no significant treatment group differences (p's > .5). No treatment group differences were observed for changes in CD4 and sCD40L (p's > .3). Regression analyses revealed that decreases in sCD40L over the 12-week follow-up period were associated with decreases in ISI (beta = 2.10, p = .03) but not fatigue (beta = -0.66), distress (beta = -0.75) and CD4 (beta = .05). These preliminary findings suggest that, in patients with HIV infection, decreases in sCD40L reflect improvements in insomnia.

NR1-73

PERCEIVED STRESS AND PSYCHOPATHOLOGY IN SCHIZOPHRENIA

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SUMMARY:
Objective: Prolonged psychological stress is a precipitating factor for the development of psychosis and has neurobiological effects of relevance to the pathophysiology of schizophrenia (1). The Perceived Stress Scale, 10-item (PSS) is a self-report questionnaire assessing the severity of perceived stress during the last 4 weeks (2). The scale consists of ten simple questions addressing aspects of stress, which is given a score of 0-4. It has primarily been used in public health studies and in studies of affective disorders. To our knowledge, it has never been validated in a schizophrenia population. Methods: Twenty patients with an ICD-10 diagnosis of schizophrenia and 30 healthy, age-matched controls filled out the PSS. We limited the time period to two weeks due to the frequent acute onset of psychotic exacerbations. Patients were all on medication, had a median duration of illness of 82 months, no drug or alcohol abuse and were somatically healthy. For the assesment of psychopathology, patients were rated with the Positive And Negative Syndrome Scale (PANSS). All participants had blood drawn in the fasting state between 9 and 10 AM for the measurement of plasma cortisol concentration. Results: Patients had substantially higher PSS score than controls (mean 13.2 points, independent samples t-test, 95% confidence interval 10.0-16.4, p<0.0001). There was a borderline significant positive correlation between the PSS and the PANSS score (Spearmans correlation coefficient 0.35, p=0.138). There was no difference in the AM plasma cortisol concentration between patients and controls and no significant correlation between cortisol and PSS score in either group. Conclusion: In patients with schizophrenia who are able to give an informed consent, the PSS is an applicable and valid measure of subjective stress. The elevated subjective stress either does not result in an elevated plasma cortisol concentration, or, more likely, a single AM plasma cortisol measurement is not a good estimate of the glucocorticoid reaction to stress.

NR2-01

EXPLORING THE RELATIONSHIP BETWEEN SLEEP AND AN ANXIETY-RELATED ENDOPHENOTYPE: ACTIVE AVOIDANCE LEARNING INCREASES REM SLEEP

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SUMMARY:
Research strongly suggests that affective memory consolidation depends on post-training rapid eye movement (REM) sleep. Many of these findings have come from animal literature employing the emotional learning paradigm, active avoidance. Human studies involving fear conditioning and sleep have yet to be accomplished. In this experiment, a computer adaptation of the shuttle-box task was created and piloted for effectiveness. Baseline and post-training polysomnographic recordings were done for each participant. In accordance with findings in animals, human participants who learned the shuttle-box analog had a higher percentage of REM sleep compared to

baseline. Performance in the task also positively correlated with the amount of REM sleep increase. These findings are consistent with findings in animals, and strengthen the notion that REM sleep is critical for the consolidation of memory.

NR2-02

THE SECOND DIGIT TO THE FOURTH DIGIT LENGTH RATIO AND ITS PERSONALITY AND TEMPERAMENT CHARACTERISTIC

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SUMMARY:

Backgrounds: Recently, many studies regarding the second digit to the fourth digit ratio (2D: 4D) are carrying out as a expectation digit to express the level of intermediation characteristics of both sexual dimorphism and sex hormone. The 2D to 4D ratio expresses the exposure level to the testosterone and estrogen of the embryo period and it is known that it is fixed after being influenced until 14 weeks since pregnancy. Generally, woman shows the higher 2D to 4D ratio than man and the precedent studies show that the 2D to 4D ratio is related to a psychological characteristic and behavioral traits as well as a physical characteristic. The 2D to 4D ratio reflects the exposure and sensitivity of the prenatal sex hormone and it is considered to be the most convenient and useful way to know the level of sex hormone in the human behavioral traits. Focusing on the general adults in Korea, this Study was carried out to know the correlation between the 2D to 4D ratio and the temperament characteristic. Methods: Focusing on the adults over 19 years, this Study surveyed 72 university students (M 57 and F 15 persons, the average age: 24.2), sought the 2D to 4D ratio after measuring the length of 2D to 4D with the photo copy measure and conducted the temperament examination (Humor theory-sanguine, phlegmatic, choleric, melancholic) and the temperament and character inventory (TCI) about the same person. Results: TCI item explaining the personality characteristic didn't show a significant correlation with the 2D to 4D ratio. The item of temperament examination and TCI item explaining the temperament charecteristic showed a significant correlation with the 2D to 4D ratio. In the event of examining the total of woman and man, the 2D to 4D ratio showed a significant minus-correlation (r=-0.283, p=0.036) in a sub-item [the shyness with stranger] of harm avoidance items in TCI. In the event of analyzing only men, the 2D to 4D ratio showed a significant plus-correlation (r=0.354, p=0.019) with a sanguine temperament item of the temperament examination and a significant minus-correlation (r=-0.317, p=0.083) with melancholic temperament item of the temperament examination. In the event of analyzing of only women, the 2D to 4D ratio showed a significant minus-correlation in two sub-items [the fear to uncertainty (r=-0.660, p=0.0190)] and [the shyness to stranger (r=-0.712, p=0.009)] of harm avoidance items in TCI.

NR2-03

LOSS OF HEART RATE COMPLEXITY IN MEN WITH DEPRESSION

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SUMMARY:

Introduction: Major depression is highly prevalent and affects multiple physiologic functions, including neuroautonomic regulation of heart rate. Accruing evidence supports the concept that healthy heart rate variability is highly complex and that dynamical complexity decreases with aging and disease. Hypothesis: We tested the hypothesis that in non-medicated, young to middle-aged males (n=24; age: median [min-max]: 39 [19-55] years) during an acute depressive episode, heart rate dynamics would exhibit lower complexity compared with healthy counterparts (n=19; age: median [min-max] : 36 [27-52] years). Methods: To minimize the effects of physical activity, we analyzed cardiac interbeat interval time series during sleep and its sub-phases. As a measure of complexity, we employed the multiscale entropy (MSE) method. Results: Our results showed a significant reduction (p< :0.03) in heart rate MSE in depressed versus non-depressed subjects during the whole night and during the different sleep sub-phases. Further, the MSE profiles of depressed patients resembled those of healthy, older adults. Conclusion: These findings support putative mechanistic links between aging and depression, and the possibility of developing an objective, inexpensive, biomarker of major depression.

NR2-04

NEUROBIOLOGIC CORRELATES OF LOW PLAN/IMPULSIVE SUICIDE ATTEMPT: A REVIEW

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SUMMARY:
We reviewed the research on neurobiologic correlates of low plan/impulsive suicide attempt (LPISA) such as biomarkers, genetics, and brain structure and function. Investigation of neurobiologic characteristics associated with LPISA could both inform clinical decision-making and a diathesis-stress model of suicidal behavior. Seven relevant articles were found from a search of PsycINFO, PubMed, and Medline and supplemented with articles found in reference sections of relevant articles. Inclusion criteria were that articles relate to neurobiologic characteristics and a history of LPISA. Current research provides preliminary evidence that LPISA may be associated with: 1.) reduced levels of 5-hydroxyindoleacetic acid (5-HIAA) in cerebral spinal fluid, 2.) reduced platelet monoamine oxidase (MAO) activity, 3.) the rs6311: C polymorphism of the serotonin 2A (5-HT-2A) receptor gene, and 4.) electroencephalographic (EEG) abnormalities localized to the temporal lobes. Current research also provides preliminary evidence that LPISA is not correlated with: 1.) variations in the estrogen receptor gene 1, or 2.) the -1438A polymorphism of the 5-HT-2A receptor gene. Thus, monoamine function and temporal lobe activity may be abnormal in those with LPISA. Further investigation is required to confirm and specify these abnormalities, and to determine their theoretical significance and clinical utility.

NR2-05

UP-REGULATION IN SERUM TROPOMYOSIN-RELATED KINASE B PROTEIN LEVEL IN ACUTE STAGE OF MAJOR DEPRESSION

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SUMMARY:
Objective: Accumulating evidences suggest brain-derived neurotrophic factor (BDNF) and its receptor tropomyosin-related kinase B (TrkB) are involved in the pathophysiology of major depressive disorder and response of antidepressants. Methods: To examine both BDNF and TrkB protein levels and their relationship with psychopathology in patients with major depressive disorder, 55 physically healthy patients with major depressive disorder were compared with 53 healthy controls in a tertiary medical center in Kaohsiung, Taiwan. The severity of major depression was assessed by the 17-item Hamilton Depression Rating Scale (HDRS). Serum BDNF and TrkB protein levels were measured with ELISA kits. Results: After using ANCOVA with age adjustment, the results showed that BDNF presented no significant change but TrkB protein level was significantly higher in female patients in acute stage of depression than in healthy control subjects. A significant negative correlation between TrkB protein levels and duration of illness in females was also found under Pearson's product moment correlation coefficients. Conclusion: These findings suggest that TrkB protein level present up-regulation during acute stage of depression in female. However, the real role of TrkB protein in the psychopathology of major depression remains to be elucidated in future.

NR2-06

ASSOCIATION STUDY OF PERSONALITY AND BRAIN EVOKED POTENTIALS IN HEALTHY CHINESE

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SUMMARY:
Objective: To investigate the relationship between personality traits and the brain evoked potentials in healthy Chinese. Methods: We collected 180 healthy Chinese, and all subjects gave informed consent. The Eysenck Personality Questionnaire (EPQ) was used to measure personality, measuring internal and external to the personality (E), neuroticism (N), psychoticism (P), calculating the dimensions of standard scores (T), and dividing them into two grades. The Nicolet Bravo EEG was used to examine event-related potentials (P300). We compared the difference of brain evoked potentials during different personalities groups, analyzing the relevance of evoked potentials of various indicators and personality. Results: 1.) In introversion personality, P300 P2-N2 latency shortened (P =0.005). 2.) In non-neurotic

personality, P300 P1 latency was extended (P = 0.013), P300 N2 latency was extended(P = 0.002). 3.) Correlation analysis: The internal and external personality and P300 P2-N2 latency were positively correlated (r = 0.187, P = 0.018); neurotic personality and P300 P3b latency were negatively correlated (r = -0.152, P = 0.044).
Conclusions: Different personality traits have different characteristics of evoked potentials, internal personality showed P300 P2-N2 latency decreased, non-neurotic personality showed P300 P1 and N2 latency extented. There is a certain correlation between the P300 and personality.

NR2-07

STRUCTURAL VOLUMES OF THE CEREBELLAR VERMIS IN A PEDIATRIC BIPOLAR POPULATION WITH COMORBID ADHD

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SUMMARY:
The cerebellum, while primarily involved with motor function, also has projections to limbic brain regions which may indicate that it modulates mood. Previous neuroimaging studies have shown cerebellar abnormalities in patients with bipolar disorder (BPD) and attention deficit hyperactivity disorder (ADHD) alike. However, it is unclear to what extent these abnormalities develop independently within each patient group. This project will examine cerebellar structural volumes in pediatric BPD with and without comorbid ADHD. We predict that patients with comorbid ADHD and BPD will have the greatest structural abnormalities of cerebellar vermis when examined with structural MRI. Additionally, we expect that vermal volumes with be related to mood symptoms due to interconnections between the cerebellum and limbic system. Pediatric bipolar patients with (n = 11) and without comorbid ADHD (n =16) will be compared with a demographically matched control group (n = 19) on the volume of vermal subregions 1, 2, and 3. These patients will meet the DSM-IV criteria for BPD. They will be administered symptom rating scales and a Continuous Performance Task (CPT) for clinical correlation with vermal volumes. The inclusion and exclusion criteria for these participants have been previous published. MRI scans were previously obtained. Scans were performed with a 3.0 Tesla Bruker Biospec scanner. A high resolution T1-weighted three dimensional brain scan was obtained using a modified driven equilibrium Fourier transform (MDEFT) protocol (time to inversion (TI) = 550 ms; time to repetition (TR) =16.5; time to echo (TE) = 4.3ms; field of view (FOV) 25.6 x 19.2 x 14.4, 256 x 128 x 96; flip angle = 20°). The volume of subregions 1, 2, and 3 were manually traced by a trained, blinded rater (kappa = 0.96, 0.94, 0.90). It is hypothesized that comorbid ADHD will result in greater abnormalities with the vermal subregions and affective instability. Statistical analysis will be performed on the three study groups to examine mean differences in the structural volume of the cerebellum. These data will be correlated with the patient's scores on various rating scales. Additional tests may be conducted to assess the variables which might predict diagnostic group membership. DelBello K-Award# K23MH63373, NARSAD 2006 Independent Investigator Award.

NR2-08

NEURAL REPRESENTATION OF VISUAL PROCESSING OF ATTACHMENT FIGURES IN YOUNG ADULT WOMEN USING FMRI

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SUMMARY:
Objective: To determine neural correlates of the visual processing of attachment figures and the relationship of attachment styles to the observed neural activation. Introduction: Attachment style -- the ability to adaptively reflect upon the thoughts, feelings or memories associated with attachment relationships -- has been shown to influence the efficacy of individual psychotherapy in depression (McBride et al, 2006). The neurobiological mechanisms subsuming this influence and their relationship to depression are unknown. To this end we employed functional magnetic resonance imaging (fMRI) to study neural representation of attachment in depressed and healthy young females. Method: Twenty to thirty year-old female subjects with no psychopathology (healthy controls) completed a battery of assessments including the Relationship Style Questionnaire (RSQ). The BDI, BAI, MDQ and WHO MINI Plus, as well as a detailed clinical history were taken to rule out axis I pathology. The secure and preoccupied attachment subtypes were used for analysis. Subjects viewed photos of their mother, a close female friend and age matched strangers (old and

young). Images were acquired using a Siemens 3T scanner (TR=2s, slice thickness=3mm) and analyzed using SPM8. Results: For the mother vs. others condition significant activation was seen in the medial frontal gyrus, superior temporal gyrus, orbital gyrus and Brodmann areas 19, 31, 41, 47 Deactivation was seen in the insula and precentral gyrus. For the mother vs. friend, activation was seen in the insula. Preoccupied attachment style was related to activation in the orbitofrontal cortex, fusiform area, superior temporal gyrus, cuneus and brodmann areas 19, 37, 4, 6. Secure attachment was related to activation in the thalamus. Conclusion: Brain regions uniquely associated with viewing of the mother compared to others can be identified and are consistent with previous research on face processing, attachment and related topics. The insula appears to be related to differential activation for the mother when compared to others and another familiar person (friend), indicating this might be an important area in visual processing of attachment figures. Additionally, secure and preoccupied attachment styles are associated with unique patterns of neural activation.

NR2-09

A COMPARISON STUDY BETWEEN VISUAL INTERPRETATION AND STATISTICAL PARAMETRIC MAPPING (SPM) ANALYSIS OF SPECT IMAGES IN PATIENTS WITH TRAUMATIC BRAIN INJURY

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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 ± 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.

NR2-10

RELATIONSHIP BETWEEN RCBF AND NEUROPSYCHIATRIC SYMPTOMS IN TRAUMATIC BRAIN INJURY AT THE CHRONIC STAGE: A SPECT STUDY WITH SPM ANALYSIS

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SUMMARY:
Purpose: Although neuropsychiatric symptoms of traumatic brain injury (TBI) patients become relatively stable at the chronic stage, physicians would face difficulties when trying to establish an association between their patient's symptom and the extent of brain injury. This study investigated regional cerebral blood flow (rCBF) in chronic TBI patients using statistical parametric mapping (SPM) to detect hypoperfusion and find correlation between rCBF and neuropsychiatric sequelae on SPECT scans. Method: SPECT images from 14 chronic TBI patients and 14 control subjects were analyzed by SPM2. The Korean-Wechsler Adult Intelligence Scale (K-WAIS) and Symptoms Checklist-90-R (SCL-90-R) were used to evaluate cognitive function and emotional symptoms of the patient group. Results: Relative to control group, the hypoperfused regions in the patient group were in the cingulate gyrus, caudate nucleus, midbrain, thalamus, insula and prefrontal cortex. There was no significant relationship between rCBF and a full scale intelligence quotient of the K-WAIS in the patient group. However, a significant correlation was found between several emotional symptoms scores on the SCL-90-R and rCBF in specific brain regions interconnected with the limbic system. Conclusion: The prefrontal and limbic hypoperfusion may play a significant role in the neuropsychiatric symptoms of chronic TBI patients.

NR2-11

THE LINK BETWEEN TOURETTE'S SYNDROME AND BIPOLAR DISORDER: A CLOSER LOOK

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SUMMARY:
A 20-year-old male was brought to the psychiatric Emergency Room after making a suicidal statement to a friend. The patient had a history of ADHD diagnosed at age 6 and Tourette's syndrome diagnosed at age 12. The patient denied substance abuse and was compliant with treatment. The patient was later diagnosed with Bipolar disorder at the age of 18 after having a manic episode in which the patient had a decreased need for sleep, decrease in concentration, increase in goal-directed activity, increased self esteem and engaging in unrestrained buying sprees. In 1995, a study was published that examined if Bipolar disorder could be associated with Tourette's syndrome. The study looked at randomly sampled patients with Tourette's syndrome and calculated the risk ratios for patients with comorbid Tourette's syndrome and Bipolar disorder. Results from the study indicated that the estimated risk of acquiring Bipolar disorder among the patient with Tourette's disorder was four times greater than the level expected by chance alone. This finding, however, was unable to reach statistical significance. Another study examined the clinical features found in 30 patients with comorbid Bipolar Disorder and TS. This second study revealed that patients with comorbid Bipolar Disorder and TS could present with the full spectrum for Bipolar Disorder, which includes Bipolar I, Bipolar II, Schizoaffective Disorder Bipolar type, and Cyclothymic Disorder. Results of this study also showed that Bipolar Disorder mainly occurred in late adolescence or early adulthood and was associated with mild motor and/or phonic tics. Thirdly, it was found that in the sample of TS patients, Bipolar Disorder was associated with high lifetime prevalence rates of other psychiatric disorders which included GAD, OCD, ADHD, phobias, and panic attacks. The patient we present shares similar features to the participants mentioned in the literature as evidenced by having a diagnosis of Tourette's syndrome and Bipolar disorder with mild motor tics and a concurrent diagnosis of ADHD. The topic of co-morbidity between Tourette's syndrome and Bipolar Disorder needs more research. However, the few studies that have been published do show some statistical evidence that can refute the idea of comorbid TS and BPD being due to just chance alone.

NR2-12

IMPROVEMENT IN MULTIPLE SYMPTOM DOMAINS IN YOUTH FOLLOWING 12 WEEKS OF ATYPICAL ANTIPSYCHOTIC TREATMENT FOR IRRITABILITY AND AGGRESSION

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SUMMARY:
Background: Atypical antipsychotics are demonstrated to be effective in the treatment of irritability and aggression in specific childhood disorders (e.g., autism), but are increasingly prescribed off-label for similar symptoms in children with a variety of other psychiatric diagnoses. It remains less clear what effect antipsychotic treatment has on other symptom domains. This analysis aims to characterize the overall pattern of symptom response in a diagnostically heterogeneous population of children presenting for treatment of irritability and aggression, antipsychotic naïve at baseline. Methods: Treatment data was obtained from the ongoing MEAC (Metabolic Effects of Antipsychotics in Children) study, which measures metabolic and clinical effects of a 12-week initial trial of antipsychotic treatment. Symptom domains were evaluated using a validated and reliable clinical and research instrument, the Child-Behavior Checklist (CBCL). CBCL profiles were obtained at baseline and endpoint. Results: Improvements in all symptom subscale scores of the CBCL were observed after 12 weeks of antipsychotic treatment (mean change in total CBCL score -23.5 +/- 23.6). The largest improvement occurred in the aggressive symptom subscale both in the pooled group (-6.7 +/- 6.3) and in groups divided by diagnosis. All other mean subscale changes were statistically significant. In the pooled group (n=85), decreases in thought problems (-2.9 +/- 3.9), attention problems (-3.3 +/- 3.5), and rule-breaking behavior (-2.7 +/- 3.4) were in a range associated with clinical significance, while anxious/depressed (-2.0 +/- 3.7), withdrawn/depressed (-1.7 +/- 2.9), social problems (-1.9 +/- 3.0), somatic symptoms (-0.7 +/- 2.9) and miscellaneous problems (-1.6 +/- 3.1) subscales demonstrated smaller improvements. The majority of subscale score changes were not correlated, and no subscale change was significantly correlated with change in aggression subscale scores. Conclusions: The results of this analysis demonstrate broad improvement across all CBCL subscales in addition to substantial improvement in aggressive symptoms in a heterogeneous, real-world population undergoing an initial course of antipsychotic treatment.

NR2-13

ZIPRASIDONE-INDUCED GALACTORRHEA IN

AN ADOLESCENT FEMALE: A CASE REPORT

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SUMMARY:

Prolactin is a lactogenic harmone and its release is tonically inhibited by hypothalamic dopamine. D2 receptors blockage in the tuberoinfundibular pathway releases prolactin. Second generation neuroleptics (SGA) are not particularly associated with hyperprolactenaemia, with the exception of risperdal; it is assumed that heperprolectenemia with (SGA) is rare and transient. The rise in serum prolactin is directly associated with the degree of dopamine receptor blockage . Ziprasidone is considered to be a weak blocker of D2 receptor. Significant prolactin elevation was not reportedly being associated with Ziprasidone. Chronic elevation in prolactin in female can lead to loss of libido, galactorrhea, gynaecomastia, amenorrhea, oligomenorrhea, hirsutism, disturbance of normal ovarian cycle or increased chronic risk of osteoporosis. Case report: Our patient is a 16 year-old African-American female with a history of sexual trauma and multiple losses. She presented with multidimensional symptomatology which includes ADHD-like symptoms (hyperactivity, impulsivity and inattention), PTSD-like symptoms (nightmares, flashbacks, numbing, avoidance and sexually acting out behavior), psychotic symptoms (auditory hallucinations, e.g. "voices asking me to do bad stuff," paranoia i.e. "people are gossiping about me"), bipolar spectrum symptoms e.g. rapid mood swings, anger control issues, impulsivity, decreased sleep and oppositional defiant behavior. There was no past history of illicit substance abuse or alcohol drinking. She has a longstanding history of self-mutilating behavior by cutting her wrists and overdosing on pills, which requires multiple psychiatric hospitalizations including long-term placement in residential treatment programs. Prior to current hospitalization, she had been treated with divalproex, quetiapine and fluoxetine. During the hospitalization, she was started on Ziprasidone 80 mg bid. and divalproex was continued. Two weeks after Ziprasidone treatment, she developed galactorrhea and her prolactin level was 68.6 ng/ml (laboratory reference value, 1.40-24.20). The Ziprasidone was discontinued and aripiprazol 2 mg per day was started. Three weeks later, Galactorrhea had stopped and her serum prolactin level was within normal range. Conclusion: Physicians should routinely inquire about symptoms of hyperprolactenaemia. If not treated, these symptoms could lead to noncompliance. Prolactin levels can be elevated even in the absence of galactorrhea.

NR2-14

INTELLIGENCE AND NEUROCOGNITIVE FUNCTIONING BY KPI-C PROFILE TYPE IN CHILDREN WITH ADHD

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SUMMARY:

This study investigated characteristics of intelligence and neurocognitive functions in children with ADHD. This was based on their performance in Korean Personality Inventory for Children(KPI-C), which is one of the widely used extensive behavioral symptom scales both for normal children and ones with ADHD. The children with ADHD between 7 and 12 years old were selected as the subjects of this study, intellectual evaluation was conducted by K-ABC abd WISC-?, and the neurocognitive functioning test was carried out by using Computerized Neurocognitive Test(ver.4.0). The subjects were 213 male children (87.7%) and 30 female children (12.3%), and their average age was 9.18 years old (standard deviation was 1.78). In subtypes of ADHD, the combined types were 191, and attention-deficit dominant? types were 52 (21.4%). We conducted the cluster analysis, based on KPI-C scores, and the result shows that the cluster 1 performed lower than others in language and movement development, and it was high in depression, anxiety, and autism scales. The cluster 2 was higher in hyper-activity scales than other scales, and the cluster 3 was in average range in almost every scale. Compared to each cluster, there were group differences in most of the sub-measurement indices, except for overall intelligence level, digit span and visual span digits forward and digits backward, auditory verbal learning test, most sub-measurement index, spending time and errors of trail making test type B, number of categones achieved in Wisconsin card sorting test. The intelligence level was lowest in the cluster 1, and cluster 2 and 3 had no difference. Additionally, in the cognitive intelligence functions which showed difference, the cluster 1 performed mostly low, whose language and movement development, and the possibilities of the other coexisted disorders were high. Therefore, in the case that shows increased language and movement development, as well as depression and anxiety scales, and autism scales, it means low intelligence and

neurocogntive functions. Moreover, the cluster 2 showed relative increase in hyper-activity scales, and performed similar to the cluster 3. Consequently, this study shows that intelligence level, as well as neurocognitive function level in children with ADHD can be judged by KPI-C.

NR2-15

CHRONIC DEPRESSION IN AN 11-YEAR-OLD ASTHMATIC MALE: A CASE REPORT AND LITERATURE REVIEW

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SUMMARY:

Objectives: We present a case of chronic depression in an 11-year-old boy improved after discontinuing montelukast. He presented for evaluation of depression and was taking sertraline. He had asthma and seasonal allergies treated with montelukast and budesonide. Montelukast was discontinued and at subsequent visits he improved with a comparable dose change from sertraline and fluoxetine. After seven months, he showed significant improvement in subjective mood, depressive symptoms, suicidal thoughts, functioning, and affect. Methods: A literature search using PubMed on 11/10/09 using "childhood depression", "montelukast", and "suicide" in various combinations yielded no publications encompassing these topics. Although no definitive reports exist that link montelukast with depression or suicide in children, these searches revealed a potential interaction between montelukast and mood, behavior, suicidality, and suicide. Results: Some medical disorders and medications have been shown to induce symptoms of depression; therefore, a thorough medical investigation must be part of the initial psychiatric evaluation. In March 2008, the United States Food and Drug Administration released an early communication regarding a possible association between the use of montelukast and behavioral/mood changes, suicidality, and suicide. Merck & Co, Inc. has since updated the prescribing information to include these post-marketing adverse events: agitation including aggressive behavior, anxiousness, dream abnormalities and hallucinations, depression, insomnia, irritability, restlessness, suicidal thoughts and actions, and tremor. Conclusions: After discontinuing montelukast, the patient's depression was improved with his current medication regimen. Our case illustrates that a close review of the patient's medical problems and medications should be undertaken and, if able, medications that may contribute to the patient's complaints and symptoms should be reconsidered.

NR2-16

WELL-BEING AND PSYCHIATRIC STATUS OF PARENTS OF CHILDREN WITH MENTAL RETARDATION IN PAKISTAN

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SUMMARY:

Background: Studies have shown an association between parental distress 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 assess the level of distress and risk for psychopathology among parents of children with Mental Retardation (MR). Methods: This was a prospective study conducted at a tertiary care hospital in Pakistan. Participants were 200 parents (100 fathers/100 mothers) of 100 children with the diagnosis of MR. Parents were administered Self Report Questionnaire 20 (SRQ 20) and the Quality of Life BREF (QOL BREF). 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. Nineteen percent 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. 89% of the families lived in urban areas and 11% in rural areas. Comorbid diagnosis included: cerebral palsy 22%, epilepsy 34%, and autistic disorder 11%. Eighty-two percent of the cases of MR were congenital. Seventy-nine percent of the children have various behavioral difficulties, including aggression. On SRQ 20, 25% of the mothers and 43% of fathers scored above the cut off indicating possible psychiatric disorder. Mean QOL domain scores were for mothers (M) and fathers (F): M 13.2/ F 13.9 for physical health; M13.1 / F 13.7 for psychological health; M 13.9 / F 13.9 for social relationships and M 13.4 / F 14.8 for environment. Conclusions: 1.) Parents of children with MR are at

higher risk for psychopathology, needing mental health assessment. 2.) Fathers' scores on the SRQ reflect more distress and psychiatric symptoms than mothers SRQ scores while raising children with MR. 3.) Limitations include lack of comparison group and small sample size.

NR2-17

REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION AND OLANZAPINE VERSUS OLANZAPINE ALONE IN THE TREATMENT OF ADOLESCENTS WITH BIPOLAR MANIA

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SUMMARY:

Objective: The purpose of this study was to evaluate the efficacy of repetitive transcranial magnetic stimulation combined with Olanzapine versus Olanzapine alone for the treatment of acute manic or mixed episodes associated with bipolar disorder in adolescents. Method: A 3-week open label trial was conducted at one site in India. The participants were outpatient and inpatient male and female adolescents 13–17 years of age with an acute manic or mixed episode. Subjects received either a combination of Olanzapine (10-20 mg/day) and daily treatments of 10-Hz rTMS at 80% motor threshold over the right dorsolateral prefrontal cortex [N=10]) or Olanzapine 10-20mg/day (N=08). The mean change from baseline to endpoint in the Young Mania Rating Scale total score was the primary outcome measure. Results: The mean baseline-to-endpoint change in the Young Mania Rating Scale total score was significantly greater for patients receiving Olanzapine and right DLPFC rTMS relative to patients receiving only Olanzapine, and a greater proportion of combination-treated patients met response and remission criteria (70% versus 37.5% and 50% versus 20%, respectively). Patients receiving rTMS required lower dose of Olanzapine (mean dose 12.25mg/day) and hence the mean baseline-to-endpoint changes in weight, prolactin, fasting glucose, fasting total cholesterol, uric acid, and the hepatic enzymes aspartate transaminase and alanine transaminase were significantly greater in patients treated with Olanzapine alone (mean dose 16.87 mg/day) relative to patients receiving placebo. Conclusions: Right DLPFC rTMS when combined with Olanzapine is superior to Olanzapine alone in the treatment of bipolar mania in adolescent patients.

NR2-18

NEUROFEEDBACK: AN EFFECTIVE AND SAFE TREATMENT OPTION FOR CHRONIC TENSION TYPE HEADACHES

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SUMMARY:

Introduction: Chronic Tension Type Headache (TTH) is a prevalent condition associated with impaired functioning. Amitriptyline along with behavioural treatments has long been used for chronic Tension Type Headache. Neurofeedback uses operant conditioning as to reinforce desirable self regulated changes in EEG rhythms, changes that are believed to correspond to reorganization in neural networks, particularly in thalamocortical and corticothalamic circuits. Sensori-motor rhythm (SMR) reinforcement has been effective in facilitating recovery in patients with traumatic brain injury, stroke, seizures and certain sleep disorders. This study aims to determine the utility of neurofeedback when used alone or with amitriptyline. Objective: To compare the effectiveness of Neurofeedback (QEEG based biofeedback) therapy, amitriptyline and combination of amitriptyline & neurofeedback therapy for chronic tension-type headache. Methods: Single site, randomized & controlled trial using three parallel groups. The study consisted of a 6-week treatment period and a 4-week post treatment follow-up period. From an Outpatient clinic setting, 150 patients between the ages of 18 and 65 with a diagnosis of tension-type headaches of at least 6 months' duration at a frequency of at least once per week were enrolled. They were randomly divided into three treatment groups; each group consisted of 50 patients. Treatment group I was given 6 weeks of 3 per week Neurofeedback therapy, treatment group II was given 6 weeks of amitryptiline treatment, dose depending upon tolerability and treatment group III received the combination of neurofeedback therapy and amitriptyline. Change in patient-reported daily headache intensity, weekly headache frequency, over-the-counter medication usage and functional health status (SF-36) were used as main outcome measures. Results: A total of 180 patients were screened from outpatients over the period of 6 months, 150 were enrolled for the study. Of the 150 patients who were enrolled in the study, 26 (17.3%) dropped out. During the treatment period, group III showed improvement at much faster rates in all primary outcomes. In relation to baseline values at 6 weeks after onset of treatment, the reduction of headache intensity for

treatment groups I, II & III were 39%, 37% and 62% respectively. The treatment group III showed a significantly greater reduction of headache frequency, over-the-counter medication usage and a greater improvement in functional health status.

NR2-19

PREVALENCE OF MENTAL ILLNESS AND SUBSTANCE ABUSE AMONG CHILD AND ADOLESCENT SUICIDE VICTIMS

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SUMMARY:

Objective: The objective of this study is to explore how mental illness (MI) and substance abuse (SA) vary and covary among children and adolescents who commit suicide. Suicide is the third leading cause of mortality for children under 18 after unintentional injury and homicide. (1) There is a significant relationship between MI and suicide, and depression has been the main predictor of suicidal ideation. (2) SA increases the risk of suicide as well, especially when it co-occurs with mood and disruptive behavior disorders. This study examines the prevalence and relationships of MI and SA histories among child and adolescent suicide victims, and their relationship to suicide methods used in North Carolina. Method: Medical investigation records of 234 suicide victims, between 6 to 17 years old, were obtained from the NC Coroners Office for the years 1999-2008. National rates were obtained from the CDC. Descriptive statistics and logistic regression analyses were performed using SPSS 16.0. Results: Of 234 victims, 120 (51.3%) had a history of MI and/or SA, 10 victims (4.3 %) had comorbid of MI and SA, 95 (40.6%) had only MI history and 15 (6.4%) had only SA history. 27 (11.5%) were intoxicated and 17 (7.3%) victims were positive only for alcohol at the time of suicide. Depression (DEP) was the leading MI among victims with 68 (29%) cases followed by disruptive behavior disorder (DBD) with 25 (10.6%) victims. There were gender and racial differences in DEP history. It was 44% more prevalent for females than males (p=0.01) and 43% more for Caucasians (CA) than African-Americans (AA) (p=0.04). The DEP history rate was 11% higher for AA females than AA males (p=0.01). There were no gender differences among CAs. Of victims with only SA history (n=15), 13 (86.7%) were CA and 14 (93.3%) were male. In NC, firearms (FAs) were the leading method of suicide, followed by hanging (HNG) and overdose (OD). Males are 1.8 times more likely to use FAs. Among DEP, FAs were the most common method (50%) followed by HNG (35.3%) and OD (12%). Among DBD, HNG was the most common method (62.5%) followed by FA (25%) and OD (8.3%). There were higher rates of suicides with FAs and lower rates of HNG in NC than in US. Conclusion: Diagnosis of MI and SA, especially DEP, is present in more than 50% of child/adolescent suicides, an important risk factor for suicide in child and adolescent populations for all races and both genders. FAs continue to be the leading method of suicide.

NR2-20

THE JOKER: A DARK NIGHT FOR DEPICTIONS OF MENTAL ILLNESS

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SUMMARY:

It has been argued that media portrayals of mental illness are grounded in lay understandings of madness and images of the mad man or woman (1-4). This hypothesis may be unfamiliar but is consistent with analyses of mass media depictions of persons with a mental illness most of which emphasize crime and violence (5-7), unpredictability (8-10) and social incompetence (2, 11). Film is the great story-telling medium, yet few have studied how madness is depicted in film (4). Extant studies merely described aspects of the content (8, 12). To facilitate effective destigmatization, studies need to show how a portrayal was assembled (13) and placed it in its institutional and cultural-historical context (3, 4). Recent analyses of media show that depicting someone as mad positions them as 'other than human' (14-16). 'Othering', is done using language and images familiar from use in previous depictions of mad men and women creating intertextual echoes in the present image (4, 17). For example, the sheer consistency of media depictions has established 'mad' as a 'membership categorization device' (18, 19); those categorized as mad are expected to be violent, unpredictable or antisocial. If, or when they act in those ways, the categorization appears to be confirmed as valid and explanatory. Such resources are tremendously useful for media personnel and journalists. In this poster we report our analysis of the construction of a significant movie character, the Joker in "The Dark Knight" (20). At the time of writing The Dark Knight is the fourth highest grossing movie of all time. Oscar winner Heath Ledger, who played the Joker, described him

as "a psychopathic, mass-murdering, schizophrenic clown with zero empathy" (21). The president and publisher of DC Comics said "I keep coming back to the way he (the Joker) physically incarnates madness" (22). We analyzed the portrayal identifying technical, semiotic (signs, codes and the meanings they convey) and discursive resources (words, images and brief narratives through which meanings are made) that helped construct his madness for viewers. Our primary goal in showing how the Joker's madness was constructed is to create an understanding that could inform destigmatization efforts. For that reason we highlight processes, cultural resources, and images that need to be addressed to alter the depictions and related stigma.

NR2-21

MIGRATION PSYCHIATRIC DISORDERS AT AN ACUTE PSYCHIATRIC UNIT

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SUMMARY:
Introduction: Migration has a great impact in social, economic, cultural and health aspects. It is also associated with a higher risk of developing mental disorders. The aim of this study is to analyze clinical and demographical characteristics of the immigrant patients at a Psychiatric Unit. Methods: The sample was comprised of 138 inpatients admitted to an Acute Psychiatry Unit at a general hospital in Madrid, Spain, between January 2006 and June 2009. A retrospective case-series study has been done, analyzing data with SPSS PC. Gender, age, marital status, diagnosis in axes I and II (according to the APA Diagnostic Classification DMS-IV TR), type of admission, reason for admission, treatment and prior existence of psychiatric disorder have been the analyzed variables. Results: Immigrant population represented 9% of our inpatients, mainly from Latin-American (56%), Maghrebian (18.8%), Eastern European (13.7%) and Western European (10.8%) countries. The immigrant patient profile is a man in his thirties, with an axis I Psychotic disorder diagnosis (from 30.8% in Latin-American inpatients to 80.8% in Maghrebian) and under involuntary admission. Some differences were found according to nationalities: Maghrebian patients were more likely to be women (76.9%) and Western Europeans were in their forties. Mood Disorders were reported in 26.9% of Latin Americans and in 10.5% of Eastern Europeans. Substance Abuse Disorder was reported in 20.5% of Latin Americans. Discussion: Broad cultural issues may affect to diagnosis and understanding of immigrant population. In our sample, psychosis was the most frequent diagnosis, which could add higher communication difficulties. More investigation about this population may provide a better management of immigrant inpatients.

NR2-22

IS SHE BIPOLAR? CONSIDERING CONTRIBUTIONS OF A CULTURAL BACKGROUND FROM A SPANISH-SPEAKING PATIENT AND BILINGUAL MENTAL HEALTH TREATMENT TEAM

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SUMMARY:
Objectives: To provide a case example of how ethnicity and language influence affect presentation and ultimately diagnosis. Method: Case report. Results: A sixty-one year-old Columbian monolingual Spanish-speaking female with a history of bipolar disorder presented to an emergency department after becoming distraught over military medical benefits. She was admitted for inpatient psychiatric treatment and was found to have varying affective presentations based on the provider's Spanish-speaking ability. English-speaking providers felt her proper diagnosis was Bipolar disorder whereas Spanish speaking providers felt her proper diagnoses were an adjustment disorder with a depressed and anxious mood and an acculturation problem. Conclusions: Patient's and provider's cultural beliefs and choice of language used during sessions influence patient diagnoses and outcomes. Immigrant patient's choice and/or rigidity in their use of their primary or secondary language can both facilitate affect and/or serve as a form of resistance. The mental health provider must be cognizant of these effects during mental health evaluations. Applying the DSM-IV-TR Cultural Formulation may aid in understanding the patent's case thus rendering a greater likelihood of an accurate diagnosis and positive treatment outcome.

NR2-23

THE IMPACT OF RACE, ETHNICITY, AND

CULTURE ON THE DIAGNOSIS OF BIPOLAR DISORDER: A REVIEW

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SUMMARY:
Over several decades, a wide range of research studies in the US and the UK have reported that Caucasian individuals are more likely to be diagnosed with bipolar and affective disorders, whereas individuals of African origin appear to be at higher risk for diagnoses within the schizophrenia spectrum. Despite the pressing need for strategies aimed at eliminating racial, ethnic and cultural disparities in diagnosis and treatment of bipolar disorder, there has not, to date, been any systematic review of the existing literature in this area. The current investigation draws together the disparate strands of information in an up to date, comprehensive and digestible overview of the wide-ranging research base in this critical area. Methods: Electronic searches of articles in the Medline and PsychINFO databases were conducted in October 2009. The search terms "bipolar" and "mania" were each used in combination with the terms "race," "ethnicity," "culture," "diagnosis," "African," "African-American" and "Black". The literature search was then supplemented with a review of references of the articles identified in the initial search. Fifty-six articles were included in this qualitative review of the literature. Results: In the US, African-Americans have been found to be over four times more likely than Caucasians to be diagnosed with schizophrenia rather than with bipolar disorder. Factors involved in misdiagnosis include: clinical presentation and expression of symptoms (14% of papers), access to care and help-seeking behaviors (34% of papers), and cultural background and clinical judgment (21% of papers). In order to refine comparison of symptom presentation and local norms, clinicians must cultivate understanding of the various cultural contexts pertinent to their patient populations, such as ethnicity, religiosity and culture-specific idioms of distress (1). Providers should acknowledge sociocultural perspectives, such as the desire for autonomy versus familial inclusion, emphasis on religiosity and spirituality, and stigma associated with illness and its treatment in order to provide appropriate and effective care for culturally diverse populations (2). Conclusion: Despite efforts to curtail the phenomenon, racial disparities in diagnosis of bipolar disorder persist. Further research should focus on context-based understanding of the reasons for this diagnostic instability across racial and ethnic minorities and strategies to mitigate it.

NR2-24

CLINICAL AND DEMOGRAPHICAL CHARACTERISTICS AMONG PSYCHIATRIC PATIENTS IN AN EMERGENCY SERVICE

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SUMMARY:
Introduction: Psychiatric Emergency Services are frequently used by outpatients in crisis. Adequate interventions in those situations can prevent psychiatric admissions and their impact over the patient and his family. The aim of this study is to analyze clinical and demographical characteristics of psychiatric patients in an Emergency setting. Methods: The sample comprises 4,235 patients at an Emergency Service of a general hospital in Madrid, Spain, between January 2008 and November 2009. A retrospective case-series study has been done, analyzing data with SPSS PC. Age, gender, nationality, history of psychiatric illness, alcohol or substance consumption, reason for consultation in Emergency Service, family support availability, necessity of hospital stay and type of hospital admission have been the analyzed variables. Results: Suicide attempts were the most frequent reason to visit Psychiatric Emergency Service in our hospital (22.4%). Acute psychiatric descompensation of prior diagnosis (16.3%), substance-related disorders (11.3%) and anxiety disorders (16.3%) were also common causes. Female patients had significantly more emergency visits than male patients (57.8% versus 42.2%; $p<0.05$) with a higher proportion of suicide attempt (15.4% vs 7%) and anxiety disorders (10.9% vs 5.4%). Most patients with acute psychiatric descompensation or first psychotic or manic episode needed to be admitted to the hospital (66.1%, 75% and 64%). In other cases, like anxiety disorders, substance-related disorders, suicide attempts and behavior disorders were mainly discharged from hospital after crisis management (81.6%; 79.8%; 74% and 60.5%). Involuntary admission was more frequent than voluntary (69.3% vs 30.7%). No differences had been found between immigrants and Spanish patients according to the reason for consultation. Nevertheless, there were significantly more immigrants with involuntary admission

(86.6% versus 66.5%). Family support availability was absent in 21.4% of immigrant patients and in 10.8% of Spanish, and this difference was statistically significant ($p<0.05$). Discussion: Suicide attempts represented one of the most frequent reasons for consultation in an Emergency Psychiatric Service. However, the principal cause for hospital admission is acute descompensation or first psychotic or manic episode. It is important to be aware of the existence of clinical and demographical differences among psychiatric patients in Emergency Services in order to improve their treatment.

NR2-25

FAMILIAL RELATION OF OBSESSIVE-COMPULSIVE AND SCHIZOID/SCHIZOTYPAL TRAITS TO AUTISM TRAITS IN PEDIATRIC OCD

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SUMMARY:
Background: Multiple studies report that relatives of children with autism have lack of emotional responsiveness, lack of empathy, mild social deficits as well as depressive disorders and obsessive-compulsive disorder (OCD) as part of the broad autism phenotype. Conversely, relatives of children with OCD with high autistic traits may also have personality characteristics associated with the broad autism phenotype, but this association has not been previously explored. Methods: One hundred sixty-seven adult relatives belonging to 38 families of pediatric OCD probands were examined with semi-structured psychiatric interviews (SID-P for personality traits; SCID for psychiatric disorders). The Social Responsiveness Scale (SRS) was used to measure autistic traits in child probands. Families were divided by median SRS scores for all probands, males and females separately. There were 20 high SRS child OCD probands (76 "high SRS relatives") and 18 low SRS child OCD probands (91 "low SRS relatives"). These two relative groups were compared for OCPD scores, Schizoid/Schizotypal (SCZ) Scores and Social Phobia frequencies. Results: High SRS relatives had higher OCPD traits than low SRS relatives (12.2 + 0.8 vs. 8.8 + 0.6; $p = 0.001$). Also, high SRS relatives had higher SCZ traits than the low SRS relatives (3.3 + 0.4 vs. 1.9 + 0.3; $p = 0.001$). For social phobia, 54% of relatives of the high SRS probands were affected compared to 46% in the low SRS group (NS). Conclusions: While it is recognized that the broad autism phenotype may include OCD, the reverse relationship has not been explored. From the current data, it is evident that OCPD and SCZ traits in relatives may be phenotypic correlates of--or be genetically related to--autism traits in probands. This characterization may aid in refining the phenotype for discovery of autism and OCD genes in future studies.

NR2-26

OUTPATIENT PSYCHOTHERAPY USE PREVALENCE, CORRELATES AND EXPENDITURES: A SYSTEMATIC REVIEW

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SUMMARY:
Introduction: Psychotherapy is a treatment which has been used for a long time, especially by those with troubled emotional lives, general health problems, personality or psychiatric disorders such as depression and anxiety. Controlled studies, meta-analysis and guidelines have confirmed the efficacy of psychotherapy, whether as a first choice or as a combined therapy, along with medication. However, its use is controversial since users, professionals, researchers and public health authorities do not agree on who should receive psychotherapy, who should pay for it and under which circumstances. Presently, little is known about psychotherapy's prevalence, its expenditures and its users' demographic and health characteristics. Objective: This study aims to describe a systematic review of original papers to determine outpatient psychotherapy use prevalence, correlates and expenditures. Methods: Search was conducted in three databases – Medline (January 1980 to December 2008), PsycInfo (January 1970 to December 2007) and Embase (January 1980 to December 2007). Search strategies varied slightly according to each database's characteristics and MeSH terms were "psychotherapy," "use" or "utilization," and "survey." Inclusion criteria were: 1) original study published in English, Spanish, French or Portuguese; 2) cross-sectional design; 3) population-based sample; and 4) adult subjects aged 16 years or more. Results: A total of 2240 papers were identified. After detailed evaluation of titles and abstracts, 21 papers were pre-selected; then, full-text evaluations were conducted and 6 papers were finally selected (Olfson and Pincus, 1994a,b; Olfson and Pincus, 2002; Brugha et al., 2004; Kovess et al., 2007; and Briffault et al., 2008). All evaluations were conducted by one of the authors (PFRS), with a following

separate evaluation by a different author (SLB) whenever necessary. Quality assessment of the selected papers was performed according to 1991 Fowkes and Fulton's guideline and checklist for the critical appraisal of medical articles and did not show major methodological problems in any of them. Samples varied from 6.500 to 38.446 individuals. Psychotherapy definition also varied, but was described in all six papers. Prevalence of outpatient psychotherapy use ranged from 1.07 to 1.90% at the moment; 3.06 to 3.60% within 12 months; and 5.19 to 11.50% in lifetime. Demographic characteristics of users were associated with outpatient psychotherapy use, such as gender (female) and age (middle age).

NR2-27

CAN ECONOMIC CRISES TURN DEADLY? MENTAL HEALTH EMERGENCIES IN TIMES OF ECONOMIC CRISIS IN A GENERAL HOSPITAL IN MADRID

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SUMMARY:
Introduction: There is evidence that worldwide economic crises have detrimental effects on mental health and well-being. During 2008 in Spain, a lot of companies became bankrupt, and many people lost their jobs and savings. As a consequence, people went to the emergency rooms to get medical care about psychiatric issues such as insomnia, mood disorders, or suicidal behavior. The aim of this study is to analyze the chief complaint and the number of psychiatric emergency room visits at our hospital from 2007 to 2009, and study the influence of the financial crisis on them. Material and methods: The sample was comprised of 5784 patients admitted to the emergency department in a general hospital in Madrid, Spain, between January 2007 and November 2009. A retrospective case-series study has been done, analyzing data with SPSS PC. Results: During 2008, 2525 people required a psichiatric evaluation in the emergency department of our hospital, an increase of almost 49% over the same period in 2007, and 23% over the first eleven months of 2009. Suicidal behavior (22%) and anxiety (14%) were the chief complaints, along with alcohol and sustance abuse (9%). The months between March and June of 2008 were those when more people came to our psychiatric emergency department, complaining about unemployment, inability to pay their creditors, and the lost of social status. Discussion: The Spanish financial crisis is part of the world crisis, but our long-term mortages and the building market crash which included the bankruptcy of major companies have created a very difficult economic environment. In times like these, it is easy to believe that there is no exit, because money is needed to pay for food, for a house or for raising children. The increase in psychiatric emergencies during 2008, as well as the suicidal behavior and anxiety, may indicate that financial crisis has a great impact in mental health. Further investigation may be useful and could provide an adequate diagnosis and treatment in these situations.

NR2-28

MENTAL HEALTH CHANGE IN FLOODED DISTRICT CITIZEN: TWO YEARS FOLLOW-UP

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SUMMARY:
Objective: On July 15, 2006, in Kangwon Province Inje district Garisanri, a flood left seven of the town's one hundred citizens missing or dead. A second batch of surveys was executed in January 2008, 18 months after the flood, which comparatively studied the change in mental health status before and after the flood. The author carried out a third batch of surveys in July 2008 to examine the result of a long term follow-up observation. Method: Kangwon Province Inje district Garisanri was chosen as the cohort for the survey of agricultural work safety control status, and the draft study about the actual physical and mental health conditions of the citizens was done from April 2006 to seven months just before the flood. The subjects who responded to both the second and third batch studies after the flood were comprised of 25 males (age 51.24.±15.4) and 32 females (age53.6±13.5). The second and third batches additionally studied Beck depression index, SF-36, MMPI-PTSD, PWI(Psychosocial Well-being Index), etc. Results: SF-36-K follow-up study, men above the age of 65 and men with high compensation satisfaction rate showed meaningful changes, and repetitive study variance analysis of SF-36-K subscale based on compensation satisfaction rate showed meaningful difference in the Physical component, Mental component, General health, Vitality, and Role limitation-Emotion (SF-36 subscale). Conclusions: This study was initiated to investigate the change in mental health status after a flood disaster and the difference in mental health status depending on the

extent of compensation satisfaction. The result of the study is that the disaster affects long-term victims of above two years, and although some symptoms improve, others continue, and there are differences in the mental health status depending on the compensation satisfaction. Additional studies are needed concerning studies about predictors and inducers of these results in the future, and change in symptom due to additional time lapse among survey subjects or effects from new natural disasters (like new flood disasters repeated annually).

NR2-29

TOO MANY DUTIES, TOO FEW RIGHTS: ETHICAL DILEMMAS IN PSYCHIATRISTS' RIGHTS VIS-À-VIS PATIENTS RIGHTS: PROPOSAL FOR AN INTERNATIONAL CONSENSUS

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SUMMARY:

To date, no compilation of psychiatrists' rights has been attempted in spite of the growing challenges that may create vulnerable aspects of service delivery. A tilt toward patient rights, stemming from an inaccurate assumption that patients are the only vulnerable party in the relation, calls upon an explicit recognition of the need for a consensus. Four target areas were identified as a potential medium for challenge that may undermine the integrity of the profession: balanced doctor-patient relation, professional discourse with the media, an untarnished neutral relationship with the industry and the necessity for identifying situations that warrant whistleblowing. This is a report on a workshop that was conducted in the context of the Annual International Psychiatry Conference of Kasr Al Ainy Faculty of Medicine. Thirty-six attendees at different stages of experience and working in different settings (university hospital, private practice and general hospital) participated. In light of the six identified tenets of professional ethical psychiatric practice (beneficence, nonmaleficence, confidentiality, autonomy, veracity and justice), six analogue tenets were proposed in order to ensure a balance between the demand imposed on psychiatrists, whether from insurance agencies, patients, their families, the media and the industry on one side, and the psychiatrists' rights on the other. The attendees were more likely to agree on the necessity of having these rights emphasised, highlighting three main areas: monetary aspects, safety and autonomy. Vigilance while delivering service is emphasised when confronting such areas that may challenge the integrity of ethical practice. An international consensus to include the proposed rights as an integral part of training is invited. The six proposed new tenets will be elaborated for discussion and refinement.

NR2-30

FREQUENCY OF THIRD PARTY NOTIFICATION FOLLOWING A THREAT IN AN INPATIENT STATE PSYCHIATRIC HOSPITAL POPULATION

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SUMMARY:

Introduction: Client-therapist confidentiality is one of the cornerstones of mental health care. Within its confines an individual feels safe to share his or her innermost thoughts, fears, and fantasies. As such, the breech of this confidentiality is undertaken only in the most serious, life-threatening cases. One such case is that of the need to protect others from foreseeable harm at the hands of a psychiatric patient. Methods: A retrospective chart review was performed of patients discharged from a state run psychiatric hospital who had been identified by a treatment team member as making a threat to harm a person or structure. Six months' worth of data was evaluated. Results: Seventy-three individuals were identified by their treatment teams as making a threat against an individual or structure. The mean age was 36 years. Seventy percent (51) were men. Twenty-three percent (17) of these threats were deemed credible by the treatment team. Only 9 (12%) of the individuals who were first identified as making a threat were believed to meet the duty to protect threshold and notification of a third party. The group that met the duty to protect threshold had a mean age of 34 years, was 89% male (8 of 9) and had a median length of stay of 31 (mean on 33). Conclusions: While there is an understandable amount of concern within the mental health community about sharing of patient information in duty to protect cases, this data shows that the threats that are made are rarely deemed credible by the treatment team, and even among those deemed credible and imminent, rarely necessitate notification of third parties.

NR2-31

NEUROCHEMICAL CHARACTERISTICS CO-VARY WITH PERSONALITY TRAITS: FORENSIC PSYCHIATRIC FINDINGS REPLICATED IN THE

GENERAL POPULATION

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SUMMARY:
Neurobiological markers in the cerebrospinal fluid (CSF), previously found to co-vary with destructive personality traits in violent offenders, were explored in a general population sample. In 24 patients undergoing knee surgery, results on the Karolinska Scales of Personality and the Temperament and Character Inventory were compared to CSF/serum albumin ratios and serum concentrations of beta trace protein (ßTP) (as markers for blood brain barrier (BBB) permeability), CSF ratios between dopamine and serotonin metabolites (HVA/5-HIAA), and CSF and serum concentrations of activated thyroid hormone (T3) and its precursor form (T4). Serum ßTP concentrations significantly correlated with CSF/serum albumin ratios and were used as an additional marker of BBB integrity. The following variables were significantly correlated: Serum ßTP with Monotony Avoidance and Impulsiveness, CSF HVA/5-HIAA ratios with Irritability and Low Inhibited Aggression and tended to correlate with low Cooperativeness. Analyses of thyroid hormones and personality traits were negative in whole study group, however there were some gender specific correlations that correspond to well-known symptoms of sub-clinical hyperthyroidism, such as irritability. Aggressive and unempathic personality traits seem to be associated with an increased dopaminergic in relation to serotonergic activity and impulsivity to increased BBB permeability also in the general population as well as among patients. The ßTP is a useful serum marker for BBB permeability that does not necessitate a lumbar puncture. Key words: Beta trace protein (ßTP); Blood brain barrier; Monoamine metabolites; Dopamine; Serotonin; Thyroid hormones; Personality.

NR2-32

T3111C CLOCK SNP AND MOOD DISORDERS: A SYSTEMATIC REVIEW

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SUMMARY:
Introduction: It has been hypothesized that abnormalities in the molecular clock underlie the development of mood disorders, in the direction of more prevalence in individuals that were born with an inability to adapt to important regulations of mood in response to changes in seasons, stress levels, sleep schedules and time zones. In particular, a T/C change (rs1801260) at the 3111 position of the circadian locomotor output cycles kaput (CLOCK) gene has been explored in psychiatry disorders. This systematic review was undertaken to determine the association of rs1801260 with mood disorders (v.g. unipolar depression, bipolar disorder) and with severity of depression. Methods: PubMed database was searched for studies relating to rs1801260 and mood disorders spectrum. Data were extracted by two reviewers and included publication year, location, reported ethnicity, diagnostic status, whether genotype frequencies were reported to be consistent with Hardy-Weinberg equilibrium, sample size and mean and standard deviation of the Hamilton Rating Scale for Depression (HRSD) total score. Both articles' description and Newcastle-Ottawa Scale assessed quality. Ascertainment bias was assessed by funnel plot and Egger's test. Results: We found no association between CLOCK genotype and mood disorders (OR 0.98, 95% CI 0.75 to 1.28, Z= 0.16, p= 0.87), even when we investigated ethnical homogeneous (OR 0.86, 95% CI 0.72 to 1.02, Z= 1.72, p= 0.08), bipolar (OR 0.86, 95% CI 0.67 to 1.09, Z= 1.23, p= 0.22) or unipolar disorders (OR 0.88, 95% CI 0.67 to 1.17, Z= 0.88, p= 0.38). Neither an association was found with severity of depression (OR -0.46, 95% CI -1.98 to 1.06, Z= 0.60, p= 0.55). Conclusion. Our meta-analysis shows that there is no association between rs1801260 and mood disorders (as a complete phenotype) or severity of depression and point out the necessity of further research in order to better understand the underlying biological machinery of circadian dysfunction in subjects affected by mood disorders.

NR2-33

NEUROPSYCHOLOGICAL AND PSYCHIATRIC ALTERATIONS CAUSED BY MUTATIONS OF THE MITOCHONDRIAL DNA

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SUMMARY:
Objective: Assessment of cognitive functions and psychiatric symptoms in patients with known mitochondrial DNA (mtDNA) mutations. Methods: Fifteen patients (mean age 31.5 years) with mitochondrial encephalomyopathy from 10 families have been investigated. Pathogenic mtDNA mutations have been detected in all patients. Complex neuropsychological test battery was used to assess the cognitive functions. Psychiatric examination used the Hungarian validated version of the Beck Depression Inventory, the Symptom Checklist-90-Revised and the SCID I and II diagnostic interviews. As control, 10 patients with hereditary sensomotor neuropathy, harboring the PMP22 mutation have been investigated. Results: Clinical profile was mainly dominated by depression and anxiety. These symptoms were present even in some genetically affected family members without neurological symptoms. Results of the questionnaire SCL-90-R and the SCID-II interview showed a large variety. Neuropsychological examination revealed cognitive deficit in all patients. The mean value of the WAIS-III score was 88 (lowest: 55, highest: 114, SD: 20.9) in patients with mitochondrial disorders. Their verbal perfomance was significantly better than the perfomational one (VQ mean: 94, SD: 15.9, PQ mean: 83, SD: 26.6). In some patients the follow-up examination showed severe progression over a six-month period. Conclusion: Mutations of the mtDNA can cause a variety of central nervous system symptoms because of the high energy demand of the brain. These include neurological, psychiatric and neuropsychological alterations. The relatively high prevalence of these mutations (1:5000) and their association with psychiatric symptoms indicates that psychiatrists must take mitochondrial encephalomyopathy into consideration when investigating patients with multisystemic disorders.

NR2-34

DENTAL CARE AND ASSOCIATED FACTORS AMONG OLDER ADULTS WITH SCHIZOPHRENIA

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SUMMARY:
Methods: The sample consisted of 198 community-dwelling persons aged >55 with schizophrenia and a matched group of 113 persons in the community. Subjects received a 2 ½ hour interview that included various instruments assessing psychiatric, physical, cognitive, social, and functional status. We used an adaptation of Krause's Model of Illness Behavior in Later Life as the basis to select 18 predictor variables. Results: There were no differences between the schizophrenia and community comparison groups in the percentage with at least one dental visit annually (48% and 54%, respectively). However, there were significant differences in the percentage of persons who stated that they had problems with their teeth/dentures (41% and 23%, respectively). When separately examining the schizophrenia group, we found that 8 variables were significant in bivariate analysis. However, only 4 variables--financial well-being (OR=1.12), better executive cognitive functioning (OR=1.11), fewer perceived problems with teeth/dentures (OR=0.33), and fewer oral dyskinesia (OR=0.86)--significantly associated with dental visits at least once annually. Conclusions: Older adults with schizophrenia do not receive the recommended level of dental care, although they are no worse than their age peers; however, they report more problems with their teeth/dentures. Further exploration is needed as to why the latter group is not seeking care. Also, identifying persons with more cognitive difficulties may increase dental visits.

NR2-35

BARRIERS IN METABOLIC SCREENING FOR PEOPLE WITH SEVERE MENTAL ILLNESSES IN COMMUNITY BEHAVIORAL HEALTH CLINICS IN SAN FRANCISCO AND NEW YORK CITY

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SUMMARY:
Background: People with severe mental illnesses (SMI) have high rates of, and are undertreated for, chronic health problems such as the metabolic syndrome, which can increase cardiovascular risk. Antipsychotic medications used to treat these patients can also cause metabolic side effects. Despite endeavors to encourage psychiatrists to begin metabolic screening, monitoring and treatment,

screening rates remain low, for unclear reasons. Objectives: (1) To determine psychiatrists' beliefs about the barriers to screening and monitoring for patients taking medications raising metabolic risk. (2) To determine differences in these barriers between psychiatrists working in public urban community mental health clinics in San Francisco and New York. Methods: Descriptive study of community psychiatrists working with people with SMI in New York and San Francisco. An anonymous 20-item survey, based on previously validated surveys, was distributed to two cohorts of psychiatrists to assess barriers to metabolic screening, affiliated with the New York State Psychiatric Institute and the SF County Community Behavioral Health Service (to be collected 12/2009). Most data will be presented as descriptive statistics. Responses from the two sites will be compared using t-tests and chi-square tests. Common trends will be identified in psychiatrists' beliefs about their roles in, and barriers to, screening and monitoring of patients. Results: Forty-nine percent (18/37) of eligible New York psychiatrists completed the survey when distributed in person, and 9% (19/215) completed the survey via e-mail. In preliminary review, primary barriers included challenges associated with referral to primary care, limited staff time, and severity of mental illness. Conclusions: Preliminary results suggest that primary care access and limited staff time are among the barriers for metabolic screening for people with SMI. [Data from both NY and SF will be presented.]

NR2-36

IMPROVING FOLLOW-UP AFTER INPATIENT CARE: STAFF PERSPECTIVES

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SUMMARY:
Objectives: As the duration of inpatient psychiatric hospitalizations has decreased, engagement in services after hospital discharge has become increasingly important (Hudson, 2004). Yet many patients discharged from psychiatric inpatient settings do not receive timely follow-up care (Stein et al, 2007). Although many inpatient facilities work toward improved rates of follow-up, challenges exist when hospitals and systems attempt to implement interventions. As part of a broader effort to collaboratively develop, implement, and evaluate feasible and effective approaches to improving follow-up care, we conducted a series of focus groups with inpatient mental health staff regarding current and optimal discharge activities intended to increase rates of follow-up care. Methods: Provider focus groups (n=4) with a total of 43 inpatient staff were held in 2008 to elicit inpatient staff input on practices around discharge planning. Participants included frontline staff from care management, nursing, social work, and inpatient administration. Focus group discussions were approximately two hours in duration and content was transcribed and analyzed for key themes and content. Results: Several key themes emerged across the focus groups about discharge activities designed to improve post-discharge follow-up care. These include: 1) Engagement of consumers and consumers' support networks in the discharge process, 2) Consumer expectations around mental health treatment, and 3) Consumers' knowledge regarding treatment options and recommendations. Within each theme, staff shared what is currently being done as well as ideas for improvements along with challenges that are experienced or anticipated. Conclusion: Community-academic partnerships such as this, in which empirically supported discharge-related activities are identified, and additional ideas for enhancing routine practices are generated, can inform research efforts to improve care in community settings. Engaging and supporting providers in reviewing and improving upon their own practices, using empirically supported approaches, offers an important opportunity to improve the quality as well as continuity of care. Support for this study was provided by Ortho-McNeil Janssen Scientific Affairs.

NR2-37

PILOT OF MEASUREMENT-BASED CARE FOR DEPRESSION IN AN HIV OUTPATIENT CLINIC

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SUMMARY:
Depression occurs up to twice as frequently in HIV-infected individuals as in those not infected. It can lead to decreased adherence to antiretroviral therapy (ART), greater viral loads, lower CD4 counts, faster HIV disease progression, and increased mortality. Treatment with selective serotonin reuptake inhibitors (SSRIs) increases adherence to ART, increases CD4 counts, and decreases viral loads. Successful treatment requires access to knowledgeable providers, often hampered by lack of insurance or paucity of mental

health specialists. Measurement-based care (MBC) is a health service model that trains non-physician, depression care managers to detect likely depression in patients, utilize a decision-support tool to recommend treatment to prescribers, and monitor response prospectively while making treatment adjustments as outlined by the decision-support tool, all under the supervision of a psychiatrist. The authors conducted a single-condition, 12-week, prospective pilot study of MBVC for depression in a university-based infectious diseases clinic. A decision support tool was developed with specific attention paid to potential drug interactions between ART and antidepressant medication (AD). A licensed clinical social worker functioned as the depression care manager. Participants were enrolled if they scored 10 or greater on the Patient Health Questionnaire-9 item (PHQ-9) and diagnosis of depression was confirmed by a psychiatrist. The depression care manager met with participants at baseline and monthly for three months to measure depression symptom severity and review ART use. The care manager then applied this information to the decision support tool and conveyed recommendations to participants' prescribers. Of 183 patients screened between May and August 2008, 53 (29%) scored 10 or higher on the PHQ-9 indicating likely major depression. Fifteen patients were excluded as they were already in depression care and fifteen were screened on a day when the care manager was not available to consent them. A total of 13 were enrolled for the three-month intervention. Participants were mostly men (69%), single (62%), employed (54%), and had attained at least a high school education (77%). All participants had a concurrent anxiety disorder and three had a substance use disorder. PHQ-9 scores dropped from a mean of 17 (n=13) to 11 (n=9) with three remissions (PHQ of 5 or less) by study end.

NR2-38

TRIAGING PSYCHIATRIC PATIENTS IN THE EMERGENCY DEPARTMENT: EFFECTIVENESS OF A BRIEF SCREENING TOOL

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SUMMARY:
Objective: Recommendations for the clearance of psychiatric patients range from a chief complaint-driven screen proposed in the Emergency Medicine literature to an evaluation that includes diagnostic testing, a physical examination and a mental status examination. We wanted to determine the effectiveness of the brief screening tool used at our facility, which is consistent with the recommendations of the Emergency Medicine literature. Method: We performed a retrospective chart review of 9805 patients evaluated in an urban Psychiatric Emergency Service (PES) over a one-year period. At our facility, all patients are initially screened for medical problems by the ED prior to evaluation in the PES. Patients were divided into 2 groups: patients who received a medical workup in the ED prior to transfer to the PES were compared to those who were briefly screened in the ED and triaged to the PES but were transferred back to the ED later for either missed or evolving medical complaints. Demographics, initial presentations, diagnostic work-ups, diagnoses, dispositions and outcomes were compared. Results: Of the cases we reviewed, 1.1% of patients who were briefly screened by the ED were subsequently referred back to the ED because of missed or evolving medical problems. In comparison, 7.3% were referred for medical evaluation in the ED prior to transfer to the PES. There were no differences between these two groups for demographic characteristics of age, race, sex or homeless status. Of the patients evaluated in the ED, irrespective of sequence, only 0.2% were admitted to a medical unit. Conclusion: The simple screening tool used at our facility is effective in ensuring that medically ill psychiatric patients are appropriately treated prior to transfer to a psychiatric facility. Of the total 9805 patients seen in a one-year period, only 1.1% of patients were missed by this brief screening tool.

NR2-39

THE CHRONIC PAIN PATIENT IN 5D: BETTER CARE THROUGH UNDERSTANDING OF 5 CORE COMPLICATING ISSUES IN THE TREATMENT OF CHRONIC PAIN PATIENTS

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SUMMARY:
Chronic pain patients are frequently described in training, practice, and in the literature, as "difficult" patients. We suggest the difficulty involved in caring for these patients derives from 5 core issues affecting physician and patient, which we present as the "5 Ds" for ease of recall and application in delivery of care for chronic pain.
1.) Diversity: While similarities present among chronic pain patients, critical individual differences inform care. These include original pain generators and pathophysiology,

traits, illness narrative, and context. Generalizations about "typical chronic pain patients" are often unhelpful.
2.) Dissention: Despite advances in neuroscience, expert opinion exceeds adequate data on central diagnostic and treatment issues. Resulting controversies create confusion for patients and clinicians.
3.) Disordered Rhythms: Chronic pain patients suffer circadian pain cycles in pain symptoms (e.g., neuropathic pains worsening at night, RA worst in AM) and sleep problems placing them out of synch with family, friends, coworkers and physicians.
4.) Doubt: Stigma surrounding legitimacy of chronic pain as disease deserving treatment leads patients, families, and physicians to question symptom validity and treatment appropriateness. Societal concern about diversion and misuse of controlled substances introduces reciprocal suspicion into treatment.
5.) Demoralization: Cynicism, pessimism, and nihlisim regarding prognosis and value of treatments can overwhelm patients and clinicians.
We developed the 5 Ds caring for patients in our multi-clinician tertiary pain practice, dialogue with colleagues, and review of the literature. We offer case vignettes that demonstrate the clarity the 5 D approach can bring to treatment of chronic pain.

NR2-40

VARIATIONS IN CANCER CARE AND OUTCOMES IN OLDER ADULTS WITH MENTAL ILLNESS: RESULTS FROM THE HEALTH AND RETIREMENT STUDY

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SUMMARY:
Introduction: It has been shown that adults with mental illness have lower rates of health care utilization including routine primary care, care for chronic conditions and receipt of some surgical interventions. The objective of this research is to determine whether cancer screening and treatment varies for persons with prior mental illness, and if mortality after a cancer diagnosis differs in this population. Methods: Data from the year 2000 wave of the Health and Retirement Study (HRS), a nationally representative longitudinal study sponsored by the National Institute on Aging and conducted by the University of Michigan, were used. Designed to assess mental health, financial status, family support, and retirement planning of aging Americans, the study surveys individuals born in 1947 or earlier. Results: Both men and women with a history of mental illness were as likely to receive clinical cancer screening as the general population. Models were constructed adjusting for age, race, sex, education, insurance type, marital status, past and current smoking, and problem drinking. Respondents with mental illness who had a recent cancer diagnosis had lower odds of receiving chemotherapy for their cancer (OR 0.33, 95% CI 0.15-0.71). There were no significant differences in receipt of radiation, surgery, biopsy. The odds of receiving medication for symptoms were somewhat greater for those with mental illness but not significantly so. Mortality: Men with a history of mental illness who had had cancer had significantly greater odds of dying than men without a history of mental illness (OR 2.91, 95% CI 1.49-5.68). Women with a history of mental illness who had had a cancer diagnosis had a significantly lower risk of mortality within two years than women without a history of mental illness (OR 0.36, 95% CI 0.15-0.86). Conclusions: Important and intruiging variations exist in cancer treatment for older adults with mental illness. If diagnosed with cancer, older adults with a history of mental illness were significantly less likely to receive chemotherapy than older adults without a history of mental illness. Men with mental illness history had greater odds of dying after cancer diagnosis, while women with mental illness history had significantly lower odds of dying after cancer diagnosis than women in the general population. Disparities in cancer treatment for persons with mental illness remain largely unexplored.

NR2-41

LANGUAGE, COMMUNICATION AND PSYCHIATRIC DISORDERS: A CASE FOR PSYCHOLINGUISTICS

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SUMMARY:
Introduction: Psycholinguistics has been defined as the study of the psychological and neurological factors that enable humans to acquire, use and understand language. It is concerned with the ways in which people use linguistic competency to generate and understand language. The aim of this paper is to review the literature on the application of psycholinguistics in psychiatric disorders. Methodology: Literature searches from Medline and PubMed were used

followed by manual searches of cross references. Results: We organized the reviewed literature according to the form, content and use of language in various psychiatric disorders including schizophrenia, affective disorders and language disorders in children including autism. We found that earlier research in schizophrenia focused on the semantic and syntactic speech abnormalities and that there was a trend towards studying the pragmatics of language in schizophrenia. Language dysfunction in schizophrenia had distinct clinical correlates, neurophysiological correlates and was also valuable as a trait indicator in normal relatives of patients with schizophrenia. As per some studies of language dysfunction in children, it was found that problems in language were most common issue in the clinical presentation of children aged three to sixteen and that children with speech and language disorders were at increased risk for psychiatric disorders. The psychiatric disorders observed in children who presented with language problems varied from attention deficit hyperactivity disorder to autism. Several reviews on the language deficits in autism concluded that the development of formal and semantic aspects was relatively spared and that pragmatic skills were specifically impaired. Discussion and conclusions: Language characteristics reflect specific aspects of psychiatric disorders and the importance of language does not preclude emotional, neurobiological, or other causes. Rather, some of these causes are evident in the language used. The extent to which psychiatric disorders are related to language processing problems is not clear but many disorders are recognized and defined through language use. Specifying the linguistic characteristics of psychiatric disorders leads to a clearer recognition of the phenomena of the disorders and thereby forms a step toward hypotheses for the disorder's causes. More work remains to map the details of language onto the details of psychiatric disorders.

NR2-42

COMBATING STIGMA IN MENTAL HEALTH: THE EFFECTS OF ETHNICITY AND EDUCATION ON MENTAL HEALTH LITERACY

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SUMMARY:
Objectives: Mental health literacy is neglected in developed and undeveloped nations. This is problematic because beliefs about mental illness can influence help-seeking behaviors among those in need. Little is known about how best to measure mental health literacy and differences that exist in literacy between ethnic and educational groups. The goals of this study were to determine the effects of ethnicity and education on mental health literacy and to evaluate mental health literacy in an urban population. Method: A mental health literacy survey containing 13 true and false questions and two opinion questions was used. Questions assessed performance across 1) factual information about mental illness, 2) stigma and stereotypes, and 3) spiritual and religious beliefs about mental illness. Two-hundred seventeen inner-city adults from Newark, New Jersey completed the questionnaires. Results: Preliminary findings suggest that the questionnaire has satisfactory reliability and validity. There was no significant effect for ethnicity on performance for factual information, but the more educated performed better across all areas. African-Americans and Latinos performed significantly worse than Caucasians on both the stereotype and the spirituality domains. Conclusion: Ethnicity and education level appear to be important factors associated with differences in mental health literacy. Non-Caucasians were more likely to have negative stigma and stereotypes toward the mentally ill and a greater belief in religion as a cure for mental illness. Higher education is associated with better mental health literacy. Specifically tailoring mental health education to diverse cultural backgrounds and needs may be a way to improve mental health literacy.

NR2-43

META-ANALYSIS OF 123I-MIBG CARDIAC SCINTIGRAPHY FOR THE DIAGNOSIS OF A-SYNUCLEINOPATHIES

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SUMMARY:
Background: Patients with Parkinson's disease (PD) and dementia with Lewy Bodies (DLB) have a diminished uptake of 123I-metaiodobenzylguanidine (123I-MIBG) on cardiac scintigraphy, which indicates a reduction in cardiac sympathetic innervation. In 2005, the DLB Consortium labeled 123I-MIBG cardiac scintigraphy as a "supportive" diagnostic feature, based on the then limited evidence available to support its utility. Since then, a growing number of studies have confirmed changes in cardiac 123I-MIBG uptake in DLB and related conditions. We report a meta-analysis of these studies, and assess 123I-MIBG's utility in making the diagnosis of DLB. Methods: We performed a literature search of Scopus,

Medline, and Psych Info databases from 1950 to January 2009. One thousand four hundred sixty-six abstracts were reviewed. Forty-six studies were included in the analysis, with data from 2680 patients. The samples were organized by diagnosis. A mixed effects regression model was used to analyze the mean heart to mediastinum (H/M) ratios of 123I-MIBG uptake. Receiver operating characteristic (ROC) analysis determined sensitivity and specificity to differentiate between two internally homogenous clusters. Results: 123I-MIBG cardiac scintigraphy has the potential to sensitively detect and specifically distinguish certain a-synucleinopathies from related conditions. Two clusters were identified by our mixed effects model (1) DLB, PD and rapid eye movement (REM) sleep behavior disorder (RBD) and (2) normal controls and patients with Alzheimer's disease (AD), multiple system atrophy (MSA), progressive supranuclear palsy (PSP), vascular dementia (VaD), and frontotemporal dementia (FTD). ROC analysis was 0.987 at a cluster discriminatory H/M ratio threshold of 1.77. Conclusions: Our findings confirm that 123I-MIBG cardiac scintigraphy is able to effectively distinguish between the two most common causes of dementia, AD and DLB, and between PD and MSA. RBD has a mean H/M ratio that is comparable to those of PD and DLB. These results suggest that a low H/M ratio should be considered a "core" feature of DLB.

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Escamilla-Sevilla F, Perez-Navarro MJ, Munoz-Pasadas M, et al. [Diagnostic value of cardiac 123

NR2-44

FIRST-ONSET PSYCHOTIC DISORDER CONCURRENT WITH A FIRST-ONSET SEIZURE DISORDER: A CASE REPORT

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SUMMARY:

This case presentation involves a 19 year-old female who developed psychotic symptoms co-existing with first-onset seizure disorder. The patient's presentation on admission included a four-week history of both new-onset seizure disorder and new-onset psychotic symptoms. The patient was diagnosed with Seizure Disorder, Tonic-Clonic Type via clinical presentation as her EEG exam was unremarkable. The patient was started on several medications including levetiracetam and risperidone. Regardless of several medication adjustments and changes, the patient continued to have disorganized behavior, unmanageable physical aggression and anger outbursts. It was the addition of Valproic acid to patient's treatment regimen (initiated at 250 mg PO TID and 500 mg PO QHS) that produced a substantial improvement in patient's physical aggression and assaultive behavior. However, her psychotic symptoms, which include disorganized behavior such as incoherent speech, internal preoccupation, and blank stare, have persisted for five months to date. The presentation of concurrent first-time onset of both Psychosis and Seizure Disorder suggests the diagnosis of Schizophrenia-like Psychosis of Epilepsy. This type of Psychosis takes a paranoid-hallucinatory form and can also have an unusual frequency of mood swings, mystical states, visual hallucinations, and catatonic features in epileptic schizophrenia-like states. The indicated diagnosis is therefore psychotic disorder due to seizure disorder with hallucinations or rather psychotic disorder due to general medical condition. There is a long-standing belief that a connection exists between epilepsy and psychotic disorders. When psychosis occurs in epilepsy, it appears to be particularly associated with temporal lobe epilepsy. To detect seizure activity in the temporal lobe one would perform an electroencephalogram test on the patient. An EEG is used to rule out seizure disorders, however, a negative EEG does not rule out seizure disorder according to the phenomenon termed "forced normalization" wherein after an epileptic episode, patients can have a negative EEG and also show no clinical evidence of clouding of consciousness. If the EEG is repeated, it will not reveal slowed activity or worsening of epileptic discharges. The patient's presentation and resistance to treatment proposes the cause of the psychiatric manifestations to be seizure disorder, Tonic-Clonic type.

NR2-45

PHANTOM LIMB AND PHANTOM PAIN SYNDROME IN COLOMBIAN MILITARY PERSONNEL AMPUTATED BY LANDMINES

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SUMMARY:

The phenomenology of diseases for military populations has always differed from that one of civil populations,

especially in the neuropsychiatric field. The phantom limb syndrome is not excluded from this differentiation. According to the office of the Colombian Presidency, in the year 2008, 197 soldiers were injured by landmines; of these, 146 survived and 51 died. Many of the survivors lost their feet, hands or fingers, and as expected presented phantom sensations. The objective of this research work was to describe these phantom sensations and the phantom pain in this specific population. We did a cross-sectional study with sixteen soldiers who had phantom limb sensations; the information was obtained by a single interview and physical examination. We inquired about the duration of the phantom sensation, its sharpness, and the awareness of it by the subject, as well as the phantom and stump pain. We found that the phenomenology of the disease differed significantly among patients in most of the cases, with some interesting similarities found in some of them. Some patients were also diagnosed with post traumatic stress disorder, and some others met criteria for it. The relation between this disorder and phantom limb syndrome is still a subject that requires further research. The presented work has allowed us to evaluate the comorbidity between the phantom limb and phantom pain, with the clinical psychopathology, as well to increase the available information on this subject, leading to extend the knowledge of the phantom limb syndrome in the military population. We will present a description and data analysis of the phantom limb syndrome and phantom pain in this subgroup of 16 soldiers from Colombia.

NR2-46

FIREARMS USE, PSYCHIATRIC ILLNESS, AND NEUROPSYCHOLOGICAL FUNCTION

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SUMMARY:
Military regulations, police hiring policies, and individual laws sometimes restrict an individual's ability to use firearms based on a psychiatric diagnosis. Psychiatrists may also be asked to comment regarding an individual's suitability to carry a firearm as part of his or her job. Little has been published, however, addressing exactly how psychiatric diagnosis or neuropsychological function relates to the proper use of a firearm. Objective: To establish a preliminary method by which established measures of neuropsychological function can be related to accuracy of firearms use. Methods: Volunteers at a military hospital, including both psychiatric patients and general volunteers, were administered a traditional, computerized test of neuropsychological function and asked to participate in a firearms simulation that involved using a light gun to "shoot" stationary targets and to "shoot" at hostile enemies while avoiding civilian casualties. They also completed self report measures for symptoms of depression, anxiety, and posttraumatic stress disorder (PTSD.) The Automated Neuropsychological Assessment Metric or ANAM was used as the traditional measure. The video game "Lethal Enforcers" was used as the firearms simulation. A research assistant monitored performance in the simulator to determine target scores, in addition to correct and incorrect hits in the simulated combat portion. Twenty volunteers participated, although not all participants completed all measures. Correlations were examined between traditional measures and firearms performance. Results: Target shooting accuracy was significantly ($R = 0.547$, $p < 0.05$) correlated with spatial processing. Accuracy of fire in combat simulation was significantly negatively correlated with reaction time go/no-go testing ($R = -0.774$, $p < 0.05$). Both depression ($R = 0.708$) and anxiety ($R = 0.710$) scores were significantly ($p < 0.001$) correlated with incorrect hits in the combat simulation. Conclusions: The ability to accurately use firearms may be reflected in traditional measures of anxiety, depression, and neuropsychological function. Additional testing is needed to refine methods and to establish normative scores.

NR2-47

RELATIONSHIPS BETWEEN MULTIPLE SCLEROSIS AND DEPRESSION

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SUMMARY:
Objective: Major depressive disorder (MDD) commonly occurs in persons with multiple sclerosis (MS) and rates of MDD are two times more prevalent in patients with MS when compared with other chronic illnesses. MDD may also occur before the development of neurological symptoms in MS. Thus, we examined the prevalence of MDD in MS, whether MDD occurs as a prodrome to MS and whether there is a correlation between severity of depression and brain lesions on MRI.
Methods: A study was conducted in 29 MS patients with clinically definite MS. Subjects were assessed with

a psychiatric battery including the Structured Clinical Interview for DSM-IV-TR (SCID), Beck Depression Inventory (BDI), Fatigue Severity Scale (FSS), Short Form Health Survey (SF-36)] and Multiple Sclerosis Impact Scale (MSIS-29). Results: A lifetime prevalence of MDD was found in 17 of 29 (59%) MS subjects. Four of 29 (14%) subjects reported a Major Depressive Episode (MDE) occurring as a prodrome to MS and 3 of 29 (10%) subjects in which MDE occurred as a prodrome reported a mean of 1.2 year delay in MS diagnosis. As severity of depression increased the severity of atrophy on brain MRI also increased. The number of gadolinium-enhancing lesions and T1WI hypointense lesions did not reveal a significant correlation with depression symptom severity. Severity of depression (BDI) correlated significantly with several quality of life measures. Discussion: Our findings suggest that MDD occurs as a prodrome to MS, may delay diagnosis of MS and may have a different etiology than in other psychiatric illnesses.

NR2-48

THE RETROSPECTIVE STUDY OF THE EFFECT OF EEG BIOFEEDBACK IN CHILD AND ADOLESCENT PATIENTS WITH PSYCHIATRIC DISORDERS

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SUMMARY:

Objectives: The purpose of this study was to evaluate the characteristics and the effects of EEG biofeedback for child & adolescent patients with psychiatric disorders in a naturalistic setting. Methods: One hundred-four (104) patients with psychiatric disorders who were applied EEG biofeedback in university hospital, Korea from July 2005 to July 2009 participated in this study. The demographic data (age, sex, etc), characteristics of psychiatric disorders (diagnosis, duration of illness, etc), and states of EEG biofeedback (total frequency, protocol) were analyzed. The effects of EEG biofeedback were also evaluated before & after training using CGI and subjective self rating scale (provided by EEG Spectrum International, Inc.). Results: Seventy-eight patients were males (75.0%). ADHD was the most common psychiatric disorder among those who were applied EEG biofeedback (52 patients, 50.0%). Seventy-five patients(72.1%) were taking medicines, and duration of medication below one year was forty-two patients(40.4%). The average frequency of EEG biofeedback was 33.49±22.23, and ninety-three patients (89.4%) were applied more than ten times. Forty-three patients (41.3%) were applied both ß/SMR & a/? training. The discontinuation rate was 20.2%(21 patients). Significant change of CGI before and after training was noticed using covariance with frequency (<.001), and self rating scale also showed significant changes in inattention, hyperactivity, impulsivity, and hostility (<.001). There were no significant differences of the CGI results between the groups with medications (75 patients) and without medications (29 patients)(>.05). Conclusion: This is the naturalistic study in a clinical setting, so there are several limitations such as absence of control group and validity of self rating scale, etc. But this study demonstrates the significant effects of EEG Biofeedback in objective & subjective rating scales for child & adolescent patients with certain psychiatric disorders. Prospective controlled studies are needed in the future.

NR2-49

EARLY FAMILY FACTORS AND RISK OF ATTEMPTED SUICIDES OR SUICIDES IN OFFSPRING: THE NORTHERN FINLAND 1966 BIRTH COHORT STUDY

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SUMMARY:

Objective: To investigate early family factors preceding suicide attempts and suicides, which have so far not been studied intensively. Method: Examination of the Northern Finland 1966 Birth Cohort (n=10,742), originally based on antenatal questionnaire data and now followed up from mid-pregnancy to age 39, to ascertain psychiatric disorders in the parents and offspring and suicides or attempted suicides in the offspring using nationwide registers. Results: A total of 121 suicide attempts (57 males) and 69 suicides (56 males) had occurred. Previously unstudied antenatal factors (maternal depressed mood and smoking, unwanted pregnancy) were not related to these after adjustment. Psychiatric disorders in the parents and offspring were risk factors in both genders. When adjusted for these, the statistically significant risk factors among males were a single-parent family for suicide attempts (OR 3.71, 95% CI 1.62-8.50) and grand multiparity for suicides (OR 2.67, 95% CI 1.15-6.18).

Conclusions: Early family structure was associated with suicide attempts and suicides even after taking mental disorders in the parents and offspring into account.

NR2-50

THE SUICIDE TRIGGER SCALE (STS-3): PRELIMINARY RESULTS FROM A PROSPECTIVE STUDY OF SUICIDAL PATIENTS IN THE ER

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SUMMARY:

Objective: Though many chronic factors placing an individual at increased risk for suicide are well established, the acute factors that lead a person to make a suicide attempt (SA) are not well understood, and at present, no instruments are well established for the prediction of imminent SA. Moreover, current measures of suicidality rely heavily on self-report of overt suicidal thoughts and plans. However, acutely suicidal individuals may not acknowledge suicidal intent, and the absence of a suicide plan is not protective, as many or most attempters report only fleeting ideation and no premeditated plan. Understanding which suicide ideators are at increased risk for attempt and which distressed patients who deny ideation may nonetheless make a suicide attempt is of crucial importance in the emergency room setting where such patients are often first encountered. In the present study we will examine the efficacy of the STS-3 in differentiating suicide ideators who go on to make an attempt in the following year from those who do not. Here we present preliminary findings on the demographic characteristics of the suicidal patients in phase one of this study. Methods: Patients presenting with suicidality were recruited from the Emergency Department of the Beth Israel Medical Center, an urban hospital in New York City. Inclusion criteria were: 21 to 65 years of age and ability to understand the informed consent. Exclusion criteria were: cognitive impairment that precludes understanding of the consent materials and research questions or significant medical or neurological disease and possible delirium. While in the Emergency Department, research staff conducted a semi-structured interview including demographic information, brief medical history, assessment of psychiatric symptoms, the STS-3, and the Columbia Suicide Severity Rating Scale (C-SSRS), among other psychometrics. Results: Data from 51 patients was analyzed. SA and SI patients differed in proportions of race and marital status, $p < .01$. We did not find a significant difference between suicidal ideators and suicide attempters on average age in years (SI: 41.68, SA: 35.76), proportion of gender, proportion of Hispanic ethnicity, or severity of suicidal ideation (C-SSRS score: SI: 3.944, SA: 3.933). Conclusion: The demographic characteristics of patients presenting to the ER with SI only differ from those presenting to the ER following SA.

NR2-51

INCREASING THE USE OF RISPERDAL CONSTA AS A TREATMENT REGIMEN: A QUALITY IMPROVEMENT PROJECT

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SUMMARY:

Background: Risperdal Long-Acting Injection, Risperdal Consta, is the first long-acting injectable formulation of a second-generation antipsychotic and has an efficacy superior to that of tablet form. Patient compliance is responsible for most of the increased therapeutic efficacy of Risperdal Consta as defined by rehospitalization rates. This study shows the superior efficacy of Risperdal Consta compared to tab form antipsychotics risperidone and quetiapine. Methods: Rehospitalization rates were determined by analyzing the mean values of the number of hospitalizations for each patient over a 15-month period, from July 2008 to October 2009, and the duration of first inpatient hospitalization. The root cause analysis looks into the reasons for limited use of Risperdal Consta in patient treatment. Result: Fifty-one charts were analyzed for rehospitalization rates of patients on tablet form antipsychotics and 47 charts were analyzed for rates of patients on Risperdal Consta. Of the patients on tab form antipsychotics, 64% had a total of zero hospitalizations, 36% had one or more hospitalizations, and the average duration of first inpatient hospitalizations was 19.5 days. In contrast, of the 47 patients on Risperdal Consta , 87% had a total of zero hospitalizations, 13% had 1 or more hospitalizations, and the average duration of first inpatient hospitalization was 4 days. The root cause analysis of the limited use of Risperdal Consta showed that there is a lack of medication education in both the physician and patient. One concern of clinicians is how to introduce the possibility of changing from oral antipsychotic to a

long-acting injection. Clinicians might also be unwilling to start acute treatment for a patient experiencing a first episode because of potential side effects which is also a common reason for patient reluctance. There is also a stigma involved as the injection forms have been relegated to the most severely ill patients. Conclusion: Risperdal Consta results in lower mean rehospitalization rates and shorter duration of first inpatient hospitalization than the tab forms of risperidone and quetiapine. In other words, the use of Risperdal Consta should be increased to improve patient response. The correction plan for increasing Risperdal Consta use is as follows: the physician should establish a therapeutic relationship with the patient and should consider using an approach called GAIN which includes goal setting and action planning.

NR2-52

ASSESSING CURRENT PHYSICAL RESTRAINT PROTOCOLS AND THEIR USE ON PSYCHIATRIC PATIENTS

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SUMMARY:

The use of restraints in the psychiatric setting aims to therapeutically respond to the needs of agitated mental health patients, ensuring patient safety as well as the safety of others around them. Once a common fixture in the field of Psychiatry, physical restraints have been under increased scrutiny since the latter half of the twentieth century. The Omnibus Budget Reconciliation Act of 1987 was one of the first pieces of legislation which served to restrict the use of restraints, focusing on the care of the nursing home population. More recently the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) has recommended the standards to be used in the psychiatric setting: "restraint or seclusion is limited to emergencies in which there is an imminent risk of an individual physically harming himself or herself, staff, or others, and non-physical interventions would not be effective." We analyzed the charts of patients on physical restraints in the past year at Bergen Regional Medical Center and examined the protocol followed. We performed a root cause analysis on data collected and proposed ways to improve upon existing protocol most consistent with current research and national trends. Of the 209 patients analyzed, 17% were physically restrained, 38% were physically and medically restrained and 112 were physically restrained then transferred to another unit. Of the 38% physically and medically restrained, about 1% had five to six medications added to their treatment. Agitation was the most common reason for drugs given. Precipitating events leading to the patients change in behavior were not documented. *Conclusion*: Our chart review of patients restrained physically and chemically found that most incidences were not properly documented and medical staff did not follow hospital protocols. To improve the quality of service, it is recommended to assess if national and regional standards are met, increase staff training on non-physical techniques, monthly meetings should be held to review any physical restraints used, the documentation, alternatives and other areas for improvement.

NR2-53

A QUALITY IMPROVEMENT PROJECT TO ASSESS THE IMPORTANCE OF SCREENING VARIABLES IN PATIENTS BEING TREATED WITH LITHIUM

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SUMMARY:

Objectives: This is a quality improvement project to assess the importance of screening variables in patients who are being treated with lithium. Our goal is to implement a protocol to improve screening methods for patients who are being treated with Lithium based on current American Psychiatric Association guidelines. Apart from implementing a protocol, we will measure the adverse effects of lithium carbonate and follow-up for duration of 6 months after initial screening is completed. Design: Retrospective chart review. Participants: Participants consisted of 101 patients recently started on Lithium therapy. Methods: An extensive review of literature was done, based on the current American Psychiatric Association guidelines variables that are most important for screening when a patient is being treated with Lithium. Our sample consisted of 101 inpatients admitted to the Psychiatric service at Bergen Regional Medical Center and who have been placed on lithium therapy. We reviewed the electronic medical records focusing on the laboratory tests that were ordered prior to the initiation of lithium therapy.

The screening variables on which the study focused on were CBC, BMP, Thyroid Function Tests, Serum Calcium levels, EKG and Pregnancy Tests in women. Results: The data gathered from the 101 inpatient admissions shows that 72% of patients had their lithium levels checked. Fifty percent had their EKG monitored. Calcium levels were checked in 89% of patients. Thyroid function tests were checked in 74% of patients on lithium. Potassium levels were checked in 91% of patients. Kidney function, as measured by the BUN/Cr ratio, was monitored in 90% of patients and Complete Blood Count was also monitored in 90% of patients. Eighty-one percent of female subjects had a pregnancy test performed. Conclusions: The goal is to implement the protocol for screening that will reduce the incidence of toxicity and side effects related to the use of lithium. Our data suggests that a large majority of patients started on lithium therapy do have their bloodwork monitored for possible complications and side effects of lithium. However, the results demonstrate that the tendency to monitor the various areas of possible complications is far from 100 percent. The goal is to implement a protocol in accordance with the APA Guidelines for the screening prior to commencement of lithium therapy to avoid potential side effects.

NR2-54

ASSESSMENT OF THE IMPORTANCE OF SCREENING VARIABLES IN PATIENTS BEING TREATED WITH VALPROATE

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SUMMARY:

Purpose: To assess the importance of screening of patients who are being treated with valproate. Methodology: Our sample consists of 101 patients in the outpatient psychiatric clinic and 2 of the long-term inpatient psychiatric units at BRMC who are on valproate. We retrospectively reviewed electronic medical records focusing on laboratory tests that should be ordered periodically while on valproate. The screening variables of our focus are complete blood count (CBC), basic metabolic panel (BMP), liver function tests (LFT), ammonia level, amylase, lipase, weight changes, and pregnancy test in females. Results: 101 patients were analyzed and summarized to see if all the necessary screening lab tests are done periodically as they should. During 12 months on valproate, all patients had their BMP checked, and none had their amylase, lipase, or ammonia levels checked. In the first 3 months, between 24-36% had their CBC, LFT, weight checked, and pregnancy tests done. However, only 17% had their valproate levels checked. In the subsequent three months (3-6 months) of therapy, there was a drop of 8-15% in checking the BMI and pregnancy tests. Ten percent of patients' valproate levels were checked. In the 6 to 9 month period, similar percentages of patients had tests done in each category. In the 9 to 12 months interval, there was a significant drop of 15-21% for CBC, LFT, BMI, and the pregnancy test. However, valproate level checks were similar to baseline. The results show that there is a significant lack of follow-up with patients regarding bloodwork while being on this medication with significant known side effects. As time passed, less bloodwork was being done. Discussion: Our goal was to check if all the necessary lab tests were done periodically for patients on maintenance valproate therapy, in order to reduce and highlight the incidence of toxicity and side effects. Our data suggests that a large majority of patients on valproate therapy have their blood work monitored for possible abnormalities that might develop. However, the tendency to monitor the various areas of possible complications is far from comprehensive. The goal is to increase the awareness of the necessity for periodical lab work for patients on valproate therapy and encourage compliance to help avoid potential serious side effects. The results due to increased awareness could be studied further by conducting a follow up study perhaps 6 months to a year down the line.

NR2-55

IMPLEMENTATION OF TWO POLICIES REDUCES PATIENT WAIT TIME IN THE EMERGENCY DEPARTMENT

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SUMMARY:

Background: Lengthy emergency wait times can be detrimental to the well-being of patients, especially those with mental illness. The presence of one or more risk factors, such as major mental health disorder, alcohol dependence and previous suicide or acute psychosocial stressors, can also increase the time needed for careful

assessment and treatment. The demands placed on emergency departments today make it essential that every possible avenue be explored to improve flow and outcome of care. Some studies suggest that the average length of stay in emergency departments across the nation has risen to more than 6 hours and the stay for behavioral health patients is measured in days. There were two methods developed to decrease the Emergency Department wait times: the Extended Care System (ECS) and the Patient Capping System (PCS). The ECS provided an additional resident to cover patients in the ED during shift transition periods, preventing overflow of patients onto the incoming resident. The PCS set a quota on the number of patients that a resident evaluates, encouraging them to work with more efficiency. Methods: Data was collected retrospectively on the amount of time spent in the ED from registration to discharge for 300 patients from Bergen Regional Medical Center. Latency periods were measured between 3 checkpoints: patient registration and medical clearance, medical clearance and psychiatric evaluation, and psychiatric evaluation and discharge. Average latency periods were compared before implementation of ECS and PCS and after. The data was analyzed to determine whether use of these systems decreased wait time in the Emergency Department. Results: Prior to use of the ECS and PCS, latency periods for the 3 checkpoints were as follows: 106 min, 95.8 min, and 275 min, respectively. The overall total wait time was 477 min. After the implementation of ECS and PCS, latency periods for the 3 checkpoints were as follows: 100.4 min, 76 min, and 161 min, respectively. The Overall total wait time was 338 min.

Conclusion: We concluded that implementing ECS and the PCS in the ED significantly decreased latency periods for two of the three checkpoints: between medical clearance and psychiatric evaluation and psychiatric evaluation and discharge. Overall, the ED wait time was reduced by an average of 139 min. Similar systems implemented at other hospitals may also decrease ED wait time, lessening patient frustration and encouraging efficiency for residents.

NR2-56

ASSESSMENT OF APPROPRIATE PRESCRIBING PRACTICES OF SECOND-GENERATION ANTIPSYCHOTICS FOR PSYCHOTIC PATIENTS WITH COMORBID DIABETES MELLITUS

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SUMMARY:

Objectives: Diabetes Mellitus (DM) is becoming widespread in the US with cases to double and costs to triple by 2034. It is recognized that second-generation antipsychotics (SGAs) induce weight gain and cause abnormalities in glucose and lipid metabolism (Metabolic Syndrome). Two of the SGAs, ziprasidone and aripripazole, are acknowledged to be least likely to cause Metabolic Syndrome. Therefore, it is important to assess whether psychotic patients with DM are being treated with the appropriate psychotropic medication. Method: The population consisted of inpatients admitted to Bergen Regional Medical Center (Paramus, NJ) from September 2008 to September 2009 with a DSM-IV diagnosis related to schizophrenia or other psychiatric illness (i.e., schizophrenia, schizoaffective disorder, etc.). One hundred twenty-five patients were selected from the population by simple random sampling and retrospective chart review was done to analyze length of stay (LOS) and highest random blood glucose as well as BMI and medications on admission and discharge. Results: The sample was stratified into two groups. Ninety-six patients with normal glucose tolerance (as defined by the American Diabetes Association as a random blood glucose < 140 mg/dl) were known as the euglycemic group. Twenty-five patients with diabetes mellitus and 4 patients with impaired glucose tolerance (IGT) (random blood glucose = 140 mg/dl) were collectively known as the hyperglycemic group. The hyperglycemic group consisted of 17 males and 12 females with an average age of 51.8 years. Several findings were noted about the hyperglycemic sample. The average LOS was 37.2 days, 4.5% longer than the euglycemic group. Also, the average BMI on discharge was 31.0, significantly higher in comparison to 28.6 in the euglycemic group. On discharge, out of the entire hyperglycemic group, 6.9% were on Clozapine, 27.6% were on Risperidone, 13.8% were on Quetiapine, 3.4% were on Olanzapine, 13.8% were on Ziprasidone, 10.3% were on Aripripazole, and 10.3% were on Paliperidone. Moreover, only 58.6% were discharged on diabetic medications. Conclusion: The results of the study demonstrate that psychiatrists continue to prescribe SGAs with metabolic side effects despite available alternatives. Patients with co-morbid DM are at higher risk for Metabolic Syndrome. Overall, this suggests that physicians should adopt a more structured system for prescribing SGAs for patients with comorbid DM, as well as implement appropriate screening and metabolic monitoring for such patients.

NR2-57

CHOICE OF BRAND NAME VERSUS GENERIC MEDICATIONS PRESCRIBED BY PSYCHIATRIST IN THE OUTPATIENT CLINICAL SETTING

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SUMMARY:

Background: Spending on prescription drugs and new medical technologies has been cited as a primary contributor to the increase in overall health care spending. Since generics are generally priced 30%-60% lower than trade-name counterparts, substantial cost savings could be realized through greater use of generics. The decreased cost to consumer may also improve patient utilization and medication adherence. In this study we examine the prescribing practices of physicians in an outpatient psychiatric clinic setting at Bergen Regional Medical Center. Prior to 1984, generic medications were relatively uncommon. The Drug Price Competition and Patent Term Restoration Act of 1984, known as the Waxman-Hatch Act, were intended to reduce expenditures on prescription drugs by encouraging generic substitution. In response to growing concern of high costs of prescription drugs in 1989; all states had repealed anti-substitution laws in effort to encourage the use of generic medications. The substitution to a generic medication is generally considered a safe practice since generic drugs are copies of brand-name drugs. They have exactly the same dosage, intended use, side-effects, route of administration, risks, safety, and strength as the original drug. Generic substitution by pharmacists does not occur in the majority of the cases; either because of physician prohibition or pharmacist or patient preferences, the actual drug name written on the prescription by the physician still has the greatest impact on which type of drug the patient will receive. Methods: A retrospective review was conducted of prescribed medications in the outpatient clinic at Bergen Regional Medical Center. Over a one month period in June 2009, 84 charts were found in which either antidepressant (48) or anti-psychotics (36) medication was prescribed. Each group was divided into two categories: Brand name and Generic medication. Results: For the 48 prescriptions of antidepressant, 40 were brand name and 8 were generic. For the 36 prescriptions of anti-psychotic medication, 35 were brand name and 1 was generic. The Overall total percentage for the brand name prescriptions are 89% (75/84) and 11% (9/84) for generic medications. Conclusion: The analysis of the data collected shows a significant difference in the prescription rate of brand name medications in both the anti-psychotics and anti-depressant groups. Almost 90% of the times, brand name medications are being prescribed.

NR2-58

THERAPY BITES: PROMOTING COMPETENCY IN PSYCHOTHERAPY THROUGH AN EXPLORATION OF POPULAR FICTION

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SUMMARY:

Through the years psychiatrists have used literature and film to enhance training in psychotherapy and psychiatric assessments. A major concern often reported by psychiatry residents is their timidity in formulating a psychological assessment and treatment plan. Educational emphasis on biological psychiatry and manual-based therapies often leaves residents seeking additional supervision and guidance in their clinical training. With the recent change in requirements of the American Board of Psychiatry and Neurology regarding competency in psychotherapies, it is crucial that psychiatry residents are able to demonstrate the appropriate knowledge of psychological formulations, displaying confidence in their assessments and treatment recommendations. Incorporating popular fiction or media into training can be a useful tool in engaging residents in their development. *USA Today*'s top 100 titles of 2008 were *Twilight, New Moon, Breaking Dawn*, and *Eclipse*, the four novels in the *Twilight* saga by Stephenie Meyer. The *Twilight* saga, vampire fictional literature, is one of the most popular of the past several years. This poster presents a 12-week elective consisting of an interactive literary review involving residents at multiple levels of training and attending physicians. The effectiveness of improving resident knowledge and confidence levels in formulating psychological frameworks, recognizing defense mechanisms and presenting biopsychosocial formulations will be presented. It is imperative that residency training programs continue striving to identify and incorporate innovative ways of enhancing training. This project serves as a model for teaching psychodynamic formulations and developing psychotherapy competency.

NR2-59

UNDERUTILIZATION OF NONPHARMACOLOGIC INTERVENTIONS FOR INSOMNIA BY HEALTHCARE PROVIDERS

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SUMMARY:
Objectives: Research indicates that nonpharmacologic interventions, including Sleep Hygiene Education (SHE), should be implemented as first-line treatment for insomnia, regardless of the cause or associated medical and psychiatric comorbidities [1]. SHE has been shown to be effective as monotherapy [2], and in combination with pharmacotherapy. The purpose of this study was to identify practice gaps in the treatment of insomnia. Method: Five hundred healthcare providers attending a psychopharmacology course responded to three open-ended clinical questions based on a case vignette. The case described a hypothetical patient presenting with major depressive disorder, who returns for three visits over the next three months. Participants were asked to provide a diagnosis, initial treatment intervention(s), and treatment(s) for insomnia. This study focused on participants' reported treatment of the insomnia.
Results: A majority of providers (75.26%) listed pharmacologic monotherapy as their first-line intervention. Fewer providers (19.45%) listed nonpharmacologic monotherapy (SHE, 10.78%; rule-out environmental or medical factors, 7.19%; cognitive behavioral therapy, 0.42%; and psychotherapy, 1.06%). A small minority would implement a combination of pharmacologic and nonpharmacologic treatments (5.29%). Conclusions: While evidence-based literature suggests that SHE be implemented as a first-line treatment for insomnia, a majority of providers in this sample did not indicate that they would utilize this treatment. Providers may underutilize the SHE intervention in this case because the patient's insomnia returned while taking antidepressants, therefore they may assume the medication is the only cause of the insomnia. These data indicate that a practice gap exists regarding the use of nonpharmacologic treatments and that healthcare providers would benefit from educational activities that address the various treatments for insomnia.

NR2-60

POST PEDS PORTAL PROJECT: GENERATING WORKFORCE IN CHILD AND ADOLESCENT PSYCHIATRY

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SUMMARY:
Introduction: Mental health care services for children and their families in the United States are complicated by a longstanding and critical shortage of child and adolescent psychiatrists (CAPs). Although there is an estimated need for 30,000 CAPs in the US, fewer than 7000 are currently in practice. However, 60,000 pediatricians are practicing in the United States, representing a potential pool of physicians who are already committed to the well-being of children and youth and could be trained as CAPs. Typically, pediatricians seeking to become CAPs have needed to complete a general psychiatry residency as well as a CAP fellowship, totaling at least 4 additional years of training. This training pathway is substantially longer than the 3-year fellowships typically required for other pediatric subspecialties. This long duration of training likely discourages pediatricians from pursuing careers in CAP and does not acknowledge their existing skills in caring for the complex physical and emotional needs of young patients. To address this issue, the American Academy of Child and Adolescent Psychiatry proposed a pilot project, the Post Peds Portal Project, which seeks to train pediatricians in general psychiatry and CAP over a 3-year period. The project was approved by the Accreditation Council for Graduate Medical Education (ACGME) in 2007. Hypothesis: Establishment of an alternate pathway will facilitate effective cross-training of pediatricians into CAP and help alleviate the CAP workforce shortage. Methods: Psychiatry Residency Review Committee announcements were reviewed and open discussions were held with Post Peds Portal Project training directors and residents. Results: Five pilot programs were approved for accreditation by the ACGME (first in Nebraska, Ohio, and Pennsylvania, and later in Maine and Rhode Island). Seven residents are currently in training. Training curricula and resident experiences are highlighted in the poster presentation. Conclusions: The Post Peds Portal Project has generated sufficient interest from educational institutions to establish pilot training programs and has been successful in attracting pediatricians into CAP training. Discussion: Although the pilot project has been successful so far, performance of residents on in-training and board certification exams and integration into practice

settings remains to be assessed.

NR2-61

MENTAL HEALTH PROVIDERS' RESPONSES TO A CLINICAL CASE VIGNETTE: TRANSCULTURAL DIAGNOSTIC AND TREATMENT DIFFERENCES

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SUMMARY:
Objective: Research indicates that clinician responses to hypothetical case vignettes can accurately reflect real-life diagnostic and treatment practices (1). Such measures, in turn, can be useful in evaluating the effectiveness of continuing medical education (CME) programs. This study aims to discuss diagnostic and treatment differences between groups of American and Chinese mental health providers, as indicated by their responses to a psychosis case vignette. Method: Seventy Chinese and sixty-two American mental health providers attending CME events in their respective countries reviewed a vignette of a patient presenting with first-episode psychosis. Questions focusing on diagnosis and treatment were presented as the case unfolded. Providers' top three ranked responses were translated and comparatively analyzed. Results: Results confirm significant differences in diagnosis and treatment approaches for this hypothetical patient. Chinese providers were significantly more likely to select schizophrenia as the diagnosis ($z=2.304$, $p<0.001$), whereas American providers more often selected schizoaffective ($z=2.192$, $p<0.001$) and mood disorders ($z=2.488$, $p<0.001$). Chinese providers were significantly more likely to assess for cannabis use ($z=2.372$, $p<0.001$) as their next action step. American providers were more likely to start this patient on antidepressants ($z=1.65$, $p<0.005$). Conclusions: Significant differences were shown between Chinese and American providers in the management of first episode psychosis. Findings suggest real cultural differences in terms of how cases are approached clinically and conceived of diagnostically. Differences may be due to the nature of the training programs in the two countries, and levels of previous provider training. More research is needed to determine the implication of these differences. This study was supported by Independent Medical Education grants from several pharmaceutical companies.

NR2-62

STUTTERING ONSET ASSOCIATED WITH STREPTOCOCCAL INFECTION: A CASE SUGGESTING STUTTERING AS PANDAS

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SUMMARY:
We report the case of a six year-old male with the sudden onset of stuttering approximately one month after a documented streptococcal infection. The child had no known family history of stuttering. Six months prior to an evaluation for stuttering, the boy presented to his pediatrician for complaints of a sore throat, fever and general malaise. A rapid antigen strep test was performed at the time and was found to be positive (Genzyme Strep A Test OSOM). Choosing to avoid medications, the parents declined antibiotics. One month later, the child developed the acute onset of stuttering characterized by sound and syllable repetitions and silent blocking of speech. Three months later, he developed characteristic struggle behaviors of stuttering - facial grimaces and head twitches when a stuttering event occurred while speaking. Five and one-half months after his initial diagnosis of a streptococcal infection, the child continued to have a positive rapid strep test, an antistreptolysin O (ASO) titer of 400 IU/ml (age-specific normal < 200 IU/ml) and an antideoxyribonuclease-B (anti-Dnase-B) titer of 387 U/ml (normal= 0 to 70 U/ml.). He then began amoxicillin/clavulanic acid dosed at 400 mg twice a day for ten days with near resolution of stuttering symptoms within 2 weeks. Streptococcal throat culture after the antibiotic course was negative. The child remained without stuttering symptoms at the time of this submission (six months later). This case illustrates that stuttering in some individuals may be viewed as PANDAS (Pediatric Autoimmune Neuropsychiatric Disorder Associated with Streptococcal Infections) [1] The hypothesis involves that the antibodies created to fight the infection cross-react with the developing basal ganglia—a region of the brain implicated in stuttering etiology [2,3]. PANDAS are characterized by a waxing/waning course, proposed involvement with the basal ganglia, pediatric onset, and neuropsychiatric symptoms often involving tic-like motions, all of which are associated with stuttering. This

case is the first described in the literature of a documented streptococcal infection preceding stuttering weeks prior to onset. This child's recovery may have been spontaneous and unrelated to antibiotic therapy, which, in PANDAS, has been associated with mixed results [4]. Although the concept of PANDAS in other disorders remains open to debate, further research is indicated into this possible etiology of stuttering.

NR2-63

ATTITUDES TOWARDS MEDICATION AMONG TEENAGERS IN A RESIDENTIAL TREATMENT PROGRAM

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SUMMARY:
Patients' attitudes towards medications have been shown to have a clinically significant impact on a number of variables including medication compliance, adherence, and efficacy. The aim of this study was to deconstruct attitudes towards psychotropic drugs amongst an inpatient adolescent population in order to understand these aforementioned phenomena in depth. Research in noncompliance has shown it to be a generally unpredictable trend when tested against common variables such as age, race, socioeconomic status, diagnosis, etc. This study utilized a questionnaire, which included the 30-question Drug Attitude Inventory, as well as a medication adherence scale, and Rosenberg's Self-Esteem and the General Self-Efficacy scales in an attempt to understand the interplay between drug attitudes and adherence with less commonly tested factors such as self-esteem and self-efficacy. The questionnaire was administered to a subset of the inpatient adolescent population at Ironwood Residential Treatment Center taking psychotropic medications for a range of minor psychiatric and behavioral diagnoses. The study demonstrated a variable but often high presence of attitudes in conflict with successful adherence to maintenance medication, and suggested that diagnostic and socioeconomic factors as variable which may be associated with differences in attitude pattern. In conclusion, prescribers may do well to recognize the prevalence and strength of such attitudes affecting adherence to treatment.

NR2-64

CLOZAPINE-INDUCED DOUBLE INCONTINENCE: CASE REPORT

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SUMMARY:
Clozapine-induced double incontinence (both urinary & fecal incontinence) is an extremely rare and under reported adverse effect of clozapine. Only two prior case reports have been published (1,2). To our knowledge ours is the first case report in the U.S.A. We present a 62 year- old white female patient with a diagnosis of chronic undifferentiated schizophrenia, with daily episodes of double incontinence for 7 days, during the phase of titration of clozapine. Complete medical evaluation revealed no abnormalities, which included infectious and inflammatory causes for diarrhea. Patient was on 200 mg of clozapine at that time. Pubmed search revealed that double incontinence can be a rare adverse effect to clozapine. Clozapine dose was tapered down to 150 mg which resulted in complete resolution in double incontinence in 2 days time. We feel this adverse effect is more common than it is reported as most of the patients find it embarrassing to report this. When our patient began to have double incontinence, it was initially thought to be overflow incontinence secondary to urinary retention & constipation as these are common side effects. The exact mechanism of Clozapine causing incontinence is perplexing given its strong anti-cholenergic effect. The susceptibility of certain doses to have a more potent antagonism of adrenergic receptors could possibly explain double incontinence. In our case report we discuss the mechanism of this adverse affect and possible treatments. We also discuss other antipsychotics that could cause the double incontinence.

NR2-65

THE EVIDENCE BASE FOR THE LONG-TERM USE OF ANTIDEPRESSANTS AS PROPHYLAXIS AGAINST FUTURE DEPRESSIVE EPISODES

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SUMMARY:
Context: Antidepressants have proven effective in the treatment of acute depression. However, controversy exists over whether or not antidepressants protect against

future episodes of depression once a patient has achieved sustained remission. A number of controlled studies have been conducted to test the hypothesis that antidepressants actually prevent depression. Objective: We sought to review the literature to assess the evidence for prophylactic use of antidepressants. Data Sources: Articles for review were identified from the Medline and PubMed databases, which were searched from inception to July 1, 2009. We used specific keywords including antidepressants, maintenance treatment, relapse prevention and the generic names of all putative antidepressant medications. We limited our search to human studies published in the English language. When review articles and practice guidelines were identified we manually searched reference lists to include studies not identified by our databases. Study Selection: Articles were screened for randomized, double-blind, placebo-controlled trials in which the combined duration of the continuation and maintenance phases was at least 18 months or longer. 18 studies met selection criteria. Data Extraction: Results from these studies were typically reported in the form of Kaplan-Meier plots (survival curves), which we analyzed systematically. We analyzed original data corresponding to survival rates at various time intervals throughout the studies when such data were available. Results: Patients continued on antidepressants experienced a lower rate of depression relapse than patients switched to placebo by study end in the vast majority of maintenance studies. However, closer analysis of the survival curves and original data revealed that much of the difference in survival resulted from a disproportionate rate of relapse (63-100%) that occurred in the placebo arms within the first 6 months of the studies. There did not appear to be a difference in the proportion of depression relapse (placebo vs. antidepressant) after the first six months in the vast majority of maintenance trials we reviewed. Conclusion: These findings may challenge the hypothesis that antidepressants provide prophylaxis against depressive episodes.

NR2-66

L-LYSINE TREATMENT NORMALIZED SUB-CORTICAL, ACOUSTICALLY ELICITED, MASKING-RESPONSE IN PATIENTS WITH SCHIZOPHRENIA

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SUMMARY:
Introduction: Available antipsychotic treatments lack the ability to alleviate both sensory information processing and cognitive deficits in patients with schizophrenia. The prevailing hypothesis is that these deficits may lead to pre-attentive information processing and consequent cognitive deficits. Both experimental animal studies and clinical human research demonstrate that the brain's nitric oxide signaling (NO) system is involved in the pathophysiology of schizophrenia. Sensory information processing and cognitive deficits are effectively blocked by inhibition of NO-synthesis in rodents, by i.e. L-lysine treatment. Material and Methods: Ten patients with schizophrenia were treated with an add-on of L-lysine, 6 grams/day and placebo for 4 weeks in a crossover, single-blinded design. Sensory information processing, i.e. masking of acoustic stimuli, was measured using an auditory brainstem response (ABRS) audiometry method at baseline, after four and eight weeks of treatment. The ABR registration was analysed by measurement of latencies and amplitudes of peaks and troughs throughout the curves, from the triggering pulse until the ninth millisecond. Results: The four-week L-lysine treatment regimen was well tolerated and caused a significant increase in blood concentration of the amino acid in eight out of ten patients compared to baseline and placebo levels ($p<0.05$). The effect of L-lysine treatment on forward masking was analysed by Wilcoxon signed ranks test, which showed a statistically significant increase, i.e., a normalisation in masking by the L-lysine treatment (N=8, sum of positive ranks=36, sum of negative ranks=0, $p<0.01$). Discussion: In healthy individuals the masking effect is signified by a large change in ABR response in the masking condition compared to the non-masking condition, while patients with schizophrenia display a small change in the masking response. Thus, an increase in the masking response signifies a "normalization" of the masking response. In conclusion, a four week add-on L-lysine treatment, as compared to baseline condition and placebo treatment, significantly normalized sensory information processing in patients with schizophrenia.

NR2-67

AN ASSOCIATION STUDY BETWEEN VARIOUS MONOAMINE TRANSPORTER GENE POLYMORPHISMS AND TREATMENT RESPONSE TO MIRTAZAPINE IN MAJOR DEPRESSION

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SUMMARY:
Background: Initial drug treatment fails in 30-40% of patients with major depression. A genetic polymorphism between individuals may influence the response to antidepressants among patients suffering from depression. This study investigated a possible association of various monoamine transporter genetic polymorphisms with treatment response to mirtazapine in major depressive patients among the elderly.
Method: It was a 6-week naturalistic treatment study with blinded outcome evaluation of 00 Korean inpatient with major depression diagnosed by DSM-IV. Treatment response to mirtazapine was defined as =50% decrease in HAM-D score at 6 weeks. In this study three genetic polymorphisms were selected: serotonin transporter 5-HTTLPR, serotonin transporter 5-HTT intron 2 VNTR, and norepinephrine transporter NET (G1287A). The genotype of patients were determined by the polymerase chain reaction. Result: Response to Mirtazapine was significantly associated with 5-HTTPLR polymorphism (odds ratio [OR], 4.26; 95% confidence interval [CI], 1.35 – 13.41; P = 0.013 by multiple logistic regression). The favorable allele for Mirtazapine was s allele of 5-HTTLPR polymorphism (P = 0.004). A response rate 71.7% (33/46) was associated with the ss genotype, which was significantly greater than the response rate in the sl and the ll genotypes (41.9% (13/31) and 37.5% (8/3), respectively). However, 5-HTT intron 2 VNTR l/s (odds ratio [OR], 1.41; 95% confidence interval [CI], 0.39 – 5.05; P = 0.599 by multiple logistic regression), and NET(G1287A) G/A (odds ratio [OR], 2.28; 95% confidence interval [CI], 0.74 – 7.05; P = 0.152 by multiple logistic regression) showed no statistical significant influences on response rate. Conclusion: Monoamine transporter gene polymorphisms were associated with response to Mirtazapine. The combinations of polymorphisms may be informative for predicting the response and the non-response to Mirtazapine. These findings could benefit the refined antidepressant selection in treatment of depression patients.

NR2-68

ACUTE PSYCHOSIS ATTRIBUTED TO INTERACTION OF ANTITUSSIVE WITH ANTICONVULSANT AND STIMULANT MEDICATIONS

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SUMMARY:
Acute-onset psychosis is treated aggressively with atypical antipsychotics. A minimum of 4 weeks should be expected before major remission of hallucinations and associated symptoms. The following case report describes a 24 year-old female patient with a history of depressive disorder, Asperger's disorder, autistic disorder, and obsessive-compulsive disorder, and attempts to explain how methylphenidate and unlabeled usage of topiramate potentially interacted with pseudoephedrine, dextromethorphan, codeine, and carbetapentane in over the counter cough medicine. Methylphenidate and topiramate have individually been linked to acute psychosis, paranoid delusions and auditory hallucinations. This case may be a good teaching example where we can observe how a patient may benefit from a thorough history and consideration of drug interactions, instead of assuming psychosis may be attributed to extremely rapid-onset schizophrenia and the accompanying drug regime.

NR2-69

CLOZAPINE TREATMENT CAUSES OXIDATION OF PROTEINS INVOLVED IN ENERGY METABOLISM IN LYMPHOBLASTOID CELLS: POSSIBLE MECHANISM FOR METABOLIC ALTERATIONS

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SUMMARY:
Background: There is increasing concern about the serious metabolic side effects and neurotoxicity caused by atypical antipsychotics. We have previously shown, using a novel proteomic approach, that clozapine treatment in SKNSH cells induces oxidation of proteins involved in energy metabolism, leading us to hypothesize that protein oxidation could be a mechanism by which atypical antipsychotics increase risk for metabolic alterations. In this study, the same proteomic approach was used to identify specific proteins oxidized after clozapine treatment in lymphoblastoid cell lines of schizophrenia patients and normal controls. Methods: Cells were treated with 0 & 20 μM clozapine for 24 hrs and protein extracts were labeled with 6-iodoacetamide fluorescein (6-IAF). The

incorporation of 6-IAF to cysteine residues is an indicator of protein oxidation. Labeled proteins were exposed to 2D-electrophoresis, and differential protein labeling was assessed. Results: Increased oxidation after clozapine treatment was observed in ten protein spots ($p<0.05$). Seven different proteins in 10 spots were identified by HPLC-ESI-MS/MS as enolase, triesophosphate isomerase, glyceraldehyde-3-phosphate dehydrogenase (GAPD), Rho GDP dissociation inhibitor, Cofilin, UMP-CMP kinase and translation elongation factor. Discussion: Several of these proteins play important roles in energy metabolism and mitochondrial function. These results further support the hypothesis that oxidative stress may be a mechanism by which antipsychotics increase risk for metabolic syndrome and diabetes.

NR2-70

A POSSIBLE ROLE FOR ANTIDEPRESSANTS IN THE PREVENTION OF LITHIUM-INDUCED DIABETES INSIPIDUS?

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SUMMARY:
Background: Although the syndrome of inappropriate ADH secretion (SIADH) is currently thought to be the mechanism for antidepressant-associated hyponatremia, previous work by our group identified normal serum ADH levels, despite fulfilling other criteria for SIADH, in 3 of 21 cases (14.3%) of antidepressant-associated hyponatremia found on Medline. "Renal ADH hypersensitivity" is a potential explanation for cases of non-SIADH hyponatremia and variability in severity of hyponatremia found with different antidepressants. Nephrogenic Diabetes Insipidus, a condition of reduced renal sensitivity to anti-diuretic hormone (ADH), is estimated to occur in 12% of patients on chronic lithium therapy (> 5 years) in several medium-to-large cohort studies. Objective: To observe whether antidepressant use affects diabetes insipidus incidence in patients taking lithium and thereby potentially verify the existence of antidepressant-associated renal ADH hypersensitivity. Methods: We performed a retrospective cohort study comparing the incidence of diabetes insipidus (DI) in geriatric psychiatry outpatients of the Jewish General Hospital, Montreal, taking lithium alone vs. lithium + SSRIs vs. lithium + other antidepressants. Differences in incidences were then assessed for statistical significance using the Fisher Exact Test (two tailed). Results: 250 charts were reviewed, of which 21 cases of lithium use were identified with the following rates of diabetes insipidus: 2/6 cases with lithium alone, 1/15 cases involving antidepressants (1/11 cases with SSRIs, and 1/6 cases with other antidepressants). Patients were similar in their durations of lithium use, age, medical backgrounds, and other characteristics. The difference between lithium + antidepressants and lithium only groups was closest to achieving statistical significance ($p=0.18$). Conclusion: Although our results suggest differences in diabetes insipidus incidence between antidepressant co-treated and lithium only groups, these were not of statistical significance. Further studies, with larger sample sizes, will be needed to explore the relationship between antidepressant co-administration and lithium-induced diabetes insipidus.

NR2-71

ISONIAZID-INDUCED PSYCHOSIS

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SUMMARY:
Case Report: "Ms. B," a 63 year-old white woman with a history of major depressive disorder, developed an acute onset of psychotic symptoms after she was started on prophylactic isoniazid (INH) for a positive tuberculin (purified protein derivative) test. She was also on pyridoxine (25mg po qd) for prophylaxis against neuropathy associated with INH. Her psychotic symptoms included visual hallucinations of "midgets" coming out of her refrigerator and air conditioner and in her food, and tactile hallucinations of insects burrowing under her skin. She was eventually hospitalized because of worsening of these symptoms. Initially, INH-induced psychosis was not suspected, and she was treated with quetiapine in the hospital for her psychosis. The dose of quetiapine was titrated to 800 mg daily over the course of a few weeks. The intensity of psychotic symptoms decreased after treatment with quetiapine for 7 days, and Ms. B was discharged home. She continued to receive quetiapine at the same dosage in the outpatient clinic for several weeks. However, she continued to complain of bugs infesting her apartment and crawling under her skin. At this point, we considered the possibility that her psychotic symptoms could have been secondary to INH. Her INH was discontinued, and her symptoms resolved completely after 3 weeks. Discussion: With the increasing prevalence of tuberculosis in the United States, and guidelines emphasizing the importance of prophylactic treatment of

latent tuberculosis, more people are expected to receive INH as it continues to be a first-line drug for treatment and prophylaxis. Literature reviews reveal a growing number of cases of isoniazid induced psychosis. Most of the reported symptoms include paranoid delusions, visual and auditory hallucinations, suicidality, irritable mood, and disorientation. INH-associated psychosis has been reported in patients on multiple as well as monodrug therapies and in treatment regimens with and without pyridoxin. The treatments for isoniazid- induced psychosis include discontinuation of INH3 and addition of an antipsychotic, or a combination of both. The suggested mechanism for INH-associated psychosis involves INH's altering the levels of catecholamines and serotonin by inhibiting monoamine oxidase or by inducing pyridoxine deficiency, or both. Although, pyridoxine alone has not been shown to prevent INH-induced psychosis, it may be partially protective. This report adds to a growing body of literature.

NR2-72

DIABETES AND DEPRESSION: IS THERE A LINK?

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SUMMARY:

Objective: Depression is one of the oldest syndromes in psychiatry, having been clearly described by the physicians of antiquity. Diagnosing depression in medical patients is a persistent problem. Diabetes mellitus is a syndrome with disordered metabolism and inappropriate hyperglycaemia due to either the deficiency of insulin secretion or to a combination of insulin resistance and inadequate insulin secretion to compensate . Depressive disorders have been found to occur at increased prevalence rates among patients with Type 1 and Type 2 Diabetes Mellitus. Depression has the additional importance in diabetes because of its association with poor compliance with diabetic treatment, poor glycemic control and an increased risk of micro and macro vascular complications. Depression may be a cause or consequence of hyperglycemia, the causal mechanisms underlying these pathways may or may not be the same, and both the directions and the mechanism may vary over time, between episodes, and both between and within individuals. More than likely, major depressive disorders in individuals with diabetes represent a complex phenomenon resulting from interaction between genetic, biological and psycho-social factors. An accurate estimate of depression prevalence is needed to keep and gauge the potential impact of depression management in patients with co-morbid diabetes. Better recognition and better treatment of depression are important in themselves but they could also improve medical outcome by substantial a portion in patients of diabetes. Methods: Total of 527 cases were screened for major depressive disorder (MDD) by using DSM-IV- based criteria, which is a sensitive and valid method for detecting depression in Diabetes II. Montgomeny Asberg Depression rating scale (MADRS) 56 were used Clinical Global Impression (Severity) (CGI) scale to access severity after major depressive disorder was established by DSM-IV criteria. MADRS has ten items rated for severity on a scale from 0 to 6 with each item having specific distinction for severity. The scale has higher reliability, validity, and consistency, confirmed by numerous studies. CGI is a scale designed to give global information of severity of disease, rated from 1 to 7. Conclusions: Major depressive disorder is inordinately high among the sample of adult diabetic patients occurring at the rates of 2 – 6 times greater than those observed in general population.

NR2-73

CONVERSION DISORDER: A COMMON MISDIAGNOSIS OF PRIMARY DYSKINESIA?

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SUMMARY:

Introduction: Conversion disorders can often mimic organic movement disorders. The diagnosis of conversion disorder is made by ruling out an organic movement disorder, based on clinical correlation of the patient's examination. The following is a unique case report of a female patient admitted into a psychiatric unit for what was thought to be classic conversion disorder secondary to comorbid psychiatric illness, but was determined to be an organic movement disorder. Case Report: A.K. is a 42 year-old female of Pakistani descent admitted to a psychiatric unit for the initial diagnosis of depression and suicidality. During her admission, it was learned that she had prominent tongue protrusions for 9 months. The patient denied any history of drug abuse or psychiatric medication treatment besides lorazepam. Past psychiatric history included numerous suicide attempts and psychiatric admissions. She denied follow-up with a psychiatrist or therapist following her prior psychiatric hospitalizations, stating that her familial social supports were her only

needed counselors. She had no noted familial history of neurological syndromes, nor history of neuroleptic or metoclopramide use. Labs (including infectious titers) and Head CT ruled out medical etiology. Through her admission, it was determined that the patient had oral buccal dyskinesia with dystonic features. The diagnosis was established by forward-protruding tongue movements that limited communication, but did not produce dysphagia. For stabilization, the patient was treated with an SSRI and follow-up with psychiatry and movement disorders centers. Discussion: Psychogenic movement disorders often have comorbid psychiatric illnesses including depression and anxiety. Other movement disorders have been shown to be misdiagnosed as primarily psychiatric illnesses, since occurrence of dyskinesia is often characterized as a psychogenic conversion disorder. The importance of low-dose benzodiazepine use in this patient was notable as the widely-used anxiolytic may have increased her susceptibility to her dyskinesia, as prior studies have suggested a possible causal relationship between benzodiazepine use and dyskinesia. It is suggested that clinicians consider utilization of a multidisciplinary approach and extensive history and physical exam taking in movement disorders with psychogenic disorders as a differential, including consideration of use of less well-known pathophysiologic agents such as low-dose benzodiazepines.

NR2-74

MEDICAL STUDENT EVALUATION OF PSYCHIATRY RESIDENT TEACHING: DOES FEEDBACK MATTER?

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SUMMARY:
Despite psychiatry residents' responsibilities as teachers, many receive limited or no feedback about their teaching skills. Without feedback, residents have little direction to improve their teaching. There are currently no published randomized controlled trials evaluating psychiatry resident teaching in the United States. One randomized controlled trial was performed in the United Kingdom of psychiatry residents teaching medical students interviewing skills after a teaching intervention. Other medical disciplines have used 1-2 day workshops to attempt to improve resident teaching skills. Our study involves surveying medical students after completing the psychiatry clerkship to evaluate their resident's teaching skills. We will compare data for 2008-09 and 2009-10 residents, with the 2009-10 residents receiving feedback half way through the year. Comparison of the medical student evaluation scores of residents who received feedback and those who did not will help establish if providing feedback improves satisfaction with resident teaching. Our hypothesis is that providing feedback to psychiatry residents about their teaching, will lead to improved teaching and medical student education.

NR2-75

A SYSTEMATIC REVIEW OF COLLABORATIVE CARE MODELS IN THE TREATMENT OF MENTAL HEALTH CONDITIONS

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SUMMARY:
Objective: Collaborative chronic care models (CCMs) have demonstrated efficacy in improving quality and outcome in a variety of chronic medical illnesses. However, their efficacy in treating mental conditions has not been comprehensively assessed. This study applies systematic review methods for randomized controlled clinical trials of CCMs, which were published or in press in the peer-reviewed literature that investigated individuals with mental health conditions to assess the effectiveness of CCMs on clinical and economic outcomes as well as quality measures. Methods: CCMs were defined as interventions having at least 3 of 6 core CCM components established by Wagner and colleagues: patient self-management support, clinical information systems, delivery system redesign, decision support, health care organization support, or linkage to community resources, and did not have a mobile community outreach component. Randomized controlled trials of CCMs vs. other care conditions published between January 1, 1960 and November 2, 2009 were identified via Medline, PsychInfo, Embase, the Cochrane database, supplemented by contacts via clinicaltrials.gov. In addition to meeting the Wagner criteria, studies were included if they reported a primary or secondary analysis that included: mental health clinical symptoms, social role function, quality of life, economic outcomes, physical health clinical symptoms, or guideline concordance rates. Results: The literature search yielded 1598 potentially relevant articles. One thousand three hundred eighty were excluded based on review of titles and abstracts, while 218

were retrieved for full text review. One hundred forty-eight articles were excluded based on full text review and 70 articles met inclusion criteria. We found that 80% of studies and analyses were on depression, followed by anxiety disorders and bipolar disorder, with one study on Alzheimer's disease, one on trauma and one on medically unexplained symptoms. Conclusion: Individual studies of collaborative care models have been shown to be effective in management of chronic medical illnesses. Systematic review will illustrate whether such models are candidates for broad implementation across mental health conditions.

NR2-76

RESPONSE TO ECT IN PATIENTS WITH MOOD DISORDER RESISTANT TO THE PHARMACOLOGICAL TREATMENT: CAN IT BE PREDICTED?

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SUMMARY:

Background: Remission rates with ECT are in the range of 70% to 90% and exceed that of any other antidepressant treatment. However, post-ECT relapse is an important problem. Studies that have addressed the prognostic significance of the patient's characteristics for ECT outcome were mostly reviews of case series and reached contradictory conclusions. The aim of this study was to examine the response to ECT in patients with mood disorder resistant to the pharmacological treatment. Methodology: The study involved 21 patients with Treatment Resistant Major Depression (17 unipolar and 4 bipolar) who received ECT in the Department of Psychiatry of the Mayo Clinic Rochester, MN. Hamilton Rating Scale for Depression (HAM-D) was used to assess severity of depression prior to the first ECT treatment (baseline) and after the last treatment. Subjects were subcategorized into groups based on their HAM-D score at the last treatment: Remission was defined as a HAM-D score of 7 or less (group1- 'G1'); partial response was defined as a post-ECT HAM-D score less than at baseline (group 2- 'G2'), and no response or worsening was defined as a post-ECT HAM-D higher than at baseline (group 3- 'G3'). In addition, a retrospective analysis of the electronic medical records was conducted in search of demographic and clinical information. Results: Of the 21 subjects enrolled in the study, 5 dropped out after the first ECT treatment, one died for reasons unrelated to ECT, and for 3 subjects no HAM-D were obtained at the end of the treatment. Out of remaining 12 patients, 5 (G1) reached remission, 6 (G2) had partial response, and 1 had became more depressed than before ECT. Groups did not differ in average age (52.8±22.5 years for G1 and 51.2±9.14 years for G2), length of illness (7.8±12.1 in group 1 and 18.8±6.1 in group 2) and lifetime presence of comorbidity for axis II disorders (50% of group 1 and 40% in group 2). The total number of treatments was 4.5 in G1, 8.2 in G2. Summary: Our findings confirm that ECT is a viable option for the treatment of both unipolar and bipolar depressive patients. Of the 12 study subjects that completed treatment, 11 responded favorably to ECT with 5 reaching remission. Interestingly, those who reached remission tended to have fewer treatments compared to those with partial response. Search for clinical and/or physiologic predictors of response to ECT is necessary to achieve better outcomes and decrease probability of side effects.

NR2-77

TAI CHI CHUAN AS AN ALTERNATIVE TREATMENT FOR TEENAGERS WITH MENTAL ILLNESS: RESULTS FROM A 12-WEEK CONTROLLED PILOT STUDY

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SUMMARY:

Objective: To examine the efficacy of Tai Chi Chuan (TCC) in enhancing self-control behavior and reducing mood disturbances in mentally ill youth in a controlled trial design. Background: Randomized controlled trials have shown the benefits of TCC in improving quality of life and depressive symptoms in adults. Limited non-controlled trials suggest beneficial effects of TCC in children with Attention-Deficit/Hyperactivity Disorder (ADHD) or anxiety [1, 2]. However, most studies were descriptive and lacking objective data of the emotional benefits of TCC for youth. Methods: Twenty-six youth aged 12-18 with at least one DSM IV-TR Axis I diagnosis were recruited and assigned to either a control or TCC group, during the six-week Summer Respite Program at Maimonides Medical Center. A repeated measures experimental design was used to compare TCC vs control activities on symptoms of mood disturbances and conduct at baseline (T0), week 6, and week 12, using the Conners-Wells self-report scale (CWSS) and Beck Youth inventories. The TCC group met twice a week for 60 minutes while the control group carried

out routine activities at the same time. Results: Nineteen youth completed 12-weeks of participation. The 12 TCC sessions improved hyperactivity scores (Means±SD: TCC 45.22±11.02; Control: 57.88±10.67; P = 0.03) and ADHD index scores (Means + SD: TCC 51.89±10.54; Control: 67.38±8.55; P = 0.005) in the TCC group compared to controls at week 6 as measured by CWSS. Post hoc analysis of results suggested additional benefits of TCC in improving cognitive problems in subjects with ADHD. No sustained effect was observed after the 6-week post-practice period (week 12). No subject reported practicing TCC at home without guidance. Conclusions: TCC may show promise in behavior regulation and cognitive improvement in mentally ill youth. Lack of TCC sustaining effect may indicate that a continuous service system is required to provide guidance for TCC practice in the community. Larger patient population, longer study period, and more objective measures are needed to further assess beneficial effects and to assess TCC effects in alleviating mood disturbances. Additionally, efforts should be also focused on unveiling the underlying mechanisms of TCC's therapeutic actions.

NR2-78

CHARACTERISTICS OF A HIGH-RISK OBSTETRICS POPULATION REFERRED FOR PSYCHIATRIC EVALUATION

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SUMMARY:

Objective: Research shows that a substantial number of women seen in obstetric clinics have mental illness, which if left untreated can have a negative impact on them and their families. The collaborative care model has improved outcomes by bringing psychiatric care to the primary care setting. The purpose of this study is to describe a population of high-risk obstetrics patients referred for psychiatric evaluation in an OB clinic. Method: This study is a case review of 149 high-risk obstetric patients referred for psychiatric evaluation in an outpatient OB clinic between 2006 and 2009. Variables to be analyzed include demographics, pregnancy stage and history, psychiatric diagnosis and treatment history, and associated social factors. Results: Patient's ages ranged from 14 to 46 with a mean of 25.8. Most were in their second trimester (N=59, 39.6%), followed by the third (N=55, 36.9%), post-partum (N=17, 11.4%) and first trimester (N=14, 9.4%). Diagnostically, depression (Major Depressive Disorder, Dysthymia, and Depression NOS) was the most common diagnosis on Axis I (N=98, 65.7%). Other diagnoses frequently seen were Anxiety disorders (N=44, 29.5%), Bipolar Disorder (N=24, 16%), Adjustment Disorder (N=17, 11.4%), and Psychotic disorders (N=9, 6%). Most patients had a history of being on psychiatric medications (N=77, 51.7%), but a smaller number continued medications during pregnancy (N=25, 16.8%). Psychosocial factors included history of abuse 56.4% (N=84), history of violence 30.9% (N=46) and history of suicidal ideation or attempt 55% (N=82). There was a significant association between history of abuse and suicidal ideation or attempt (?2=16.5, df=2, N=130, p<.001), and there was also a significant association between history of violence and history of suicidal ideation or attempt (?2=32.6, df=2, N=113, p<.001). Conclusions: The vulnerable population in this study experiences a significant amount of depression, suicidality, abuse, and violence. The results indicate that psychiatric services are needed in the care of high-risk obstetric patients, and that the collaborative care model is a good method for providing mental health assessments in an OB clinic setting.

NR2-79

VALIDATION STUDY OF EDINBURGH POSTNATAL DEPRESSION SCALE (EPDS) AND PATIENT HEALTH QUESTIONNAIRE (PHQ9) IN MADAGASCAR

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SUMMARY:

Background: Perinatal mood disorders are prevalent in 10-15% of the female population in the Western nations. If not adequately recognized and treated, these mood disorders have been demonstrated to have detrimental effects on the maternal, child, and family life on an acute and long-term basis. Many cases of perinatal mood disorder are unnoticed or unrecognized due to underreporting of symptoms, cultural norms/beliefs, stigma, fear of losing child custody, and lack of education. Early identification via valid and reliable screening can be implemented to decrease the perinatal risks and adverse outcomes. The Edinburgh Postnatal Depression Scale (EPDS) is a sensitive screening instrument used to detect depressive symptoms in postpartum women. It has been

translated and validated in seventeen languages, mostly in industrialized nations. The PHQ-9 derived from the Patient Health Questionnaire is based on DSM-IV items. It is not designed specifically for perinatal women, but it is widely used to screen for depression. Little research has been done on developing nations such as Madagascar where there is no valid screening tool for detecting perinatal mood disorders. The purpose of this pilot study is to validate the EPDS and PHQ9 screening surveys for the Malagasy population. Objectives: 1.) To test the feasibility of using these scales translated into Malagasy on a sample of pregnant or postpartum women in Madagascar. 2.) To compare the scores of women on each of the questionnaires to determine how interchangeable they are.
Methods: The two questionnaires were translated into Malagasy and then translated back into English to verify the preservation of the meaning. The Malagasy versions of the EPDS and PHQ-9 were administered to 25 subjects in two hospital and clinic settings in Vohemar and Ansirabe, Madagascar. Each participant completed both surveys. General demographics were obtained from their assigned midwives. The total scores of the questionnaires were compared by the Pearson correlation coefficient. A Kappa Statistic and a Test for Symmetry were used to test the degree to which the responses to seven pairs of similar questions from the surveys agreed. Results: The Pearson correlation coefficient between the EPDS and PHQ-9 total scores was 0.448, explaining only 20% of the variance between the scores. The Wilcoxon Signed Rank Test showed a significant difference in the responses between surveys.

NR3-01

EFFICACY AND SAFETY OF QUETIAPINE FOR DEPRESSIVE SYMPTOMS IN PATIENTS WITH SCHIZOPHRENIA

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SUMMARY:
Methods: Thirty-nine patients fulfilling DSM-IV-TR diagnostic criteria for schizophrenia and had depressive symptoms were studied in a prospective 6-week open-label design using quetiapine monotherapy. Quetiapine was initiated at 100–800 mg/day (baseline) and titrated upwards in response to the clinical status of the patient by the treating psychiatrist. The brief psychiatric rating scale (BPRS), 17-item Hamilton depression rating scale (HAMD-17), Simpson-Angus rating scale, and the Barnes Akathisia rating scale (BARS) were used to assess patients at baseline, week 1, 2, 4, and 6. Results: Thirty patients (76.9%) completed this study. The dose of quetiapine at endpoint was 583 (±235 SD) mg/day. Treatment with Quetiapine was associated with significantly reduced depressive symptoms (HAMD-17 total score and BPRS depression/anxiety subscale) from the first week of treatment. Changes of mean score from baseline to endpoint were 7.8 ± 6.2 for HAMD-17 total score and 3.4 ± 3.6 for BPRS depression/anxiety subscale (LOCF, $n = 39$, $p < 0.001$). Quetiapine was well tolerated, with minimal extrapyramidal symptoms and non-significant increase in body weight (mean increase of 0.8 kg). Conclusion: While the interpretation of findings from the open-label design of this study warrants appropriate caution, the results suggest that quetiapine may be an effective and tolerable treatment for depression in patients with schizophrenia.

NR3-02

EPISTASIS BETWEEN A SET OF VARIATIONS LOCATED IN THE TAAR6 AND HSP-70 GENES TOWARD SCHIZOPHRENIA AND RESPONSE TO ANTIPSYCHOTIC TREATMENT

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SUMMARY:
Objective: Suggestive associations have been reported between trace amines and heat shock proteins, and a disrupted pathophysiology that enhances the risk of psychosis and that modifies responses to antipsychotic treatments. Our group previously reported genetic studies on TAAR6 and HSP-70 separately in patients with schizophrenia. In the current study, we investigated possible epistasis between the same set of variations in a sample of 281 patients diagnosed with schizophrenia and 288 healthy controls. Methods: Sample characteristics, inclusion and exclusion criteria, test batteries and timing in this study have been described elsewhere, as have details related to the selection and genotyping of the investigated variations (TAAR6: rs4305745, rs8192625, rs7452939, rs6903874 and rs6937506; HSP-70: rs562047, rs1061581 and rs2227956) ([Pae et al., 2008a] and [Pae et al., 2008b]). 281 patients with schizophrenia and 288 healthy controls were enrolled in the study. Psychiatrists who conducted the study and performed the tests were blinded to genotype. The positive and negative syndrome

scale (Kay et al., 1988) and the clinical global improvement scale (Guy, 1976) were assessed at the time of admission and discharge. Results: Analysis of the distribution of combined allelic frequencies between cases and controls resulted in the following significant results. A/A genotype at rs452939 located in the TAAR6 coding frame was associated with an increased risk of schizophrenia when associated with C/C and G/C genotypes at rs539689 co-occuring with heterozygosity at rs562047 and homozygosity at rs2227956, or homozygosity C/C at rs562047 and heterozygosity at rs2227956. The analysis of PANSS positive scores detected the following significant associations: (1) a good response profile was detected for homozygosity at rs6903874, rs539689, rs1043618 and rs562047 (C/C, C/C, G/G and C/C, respectively) and (2) combined homozygosity at rs6903874 and rs539689 with heterozygosity at rs1043618 and rs562047. Finally, analysis of the PANSS total scores (Fig. 4) revealed that rs6903874 was associated with a greater treatment effect; however the analysis did not return any testing balanced accuracy level, thus this evidence should be rejected. The inclusion of covariates into the model did not significantly impact the results. The analysis of CGI scores gave no significant results.

NR3-03

CHARACTERISTICS OF CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER WITH AND WITHOUT COMORBID READING DISORDER

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SUMMARY:

Purpose: Attention-deficit/hyperactivity disorder (ADHD) and reading disorder (RD) are often comorbid, and the combination of both conditions may present a challenge to healthcare providers. The objective of this study was to compare demographics, frequency of comorbidities and medication use for children with ADHD with and without RD. Methodology: Using a large managed care administrative claims database (Thomson MarketScan®), we identified children <18 with a coded diagnosis of ADHD in 2006. Patients with autism, mental retardation and/or developmental delay were excluded. Patients with comorbid RD (n=265) were identified, and their demographics, prevalence of comorbid diagnoses, and medication use were compared to those of patients with ADHD alone (n=97,703). Results: Few (0.3%) children with ADHD were identified as having comorbid RD. The ADHD plus RD group was slightly younger (mean age 10.2 vs. 10.8 years) than the ADHD only group, and exhibited a similar (approximately 2:1) male-to-female ratio. Children with ADHD and RD had a higher prevalence of bipolar/mania (9.4% vs. 6.4%, p=0.04), conduct disturbance (15.5% vs. 11.2%, p=0.03), depression (14.3% vs. 9.9%, p=0.02) and other (non-RD) developmental/learning disorders (12.8% vs. 3.3%, p<0.001) than patients with ADHD alone. While no statistically significant difference was observed in the prevalence of other individual co-occurring psychiatric (sleep disorders, anxiety, psychotic disorders, eating disorders, personality disorders) or neurological conditions (seizures, Tourette's syndrome), a higher proportion of children with ADHD and RD (38.1%) had a diagnosis of at least one of these comorbidities than children with ADHD only (26.4%) (p<0.001). Compared to children with ADHD alone, patients with comorbid ADHD and RD were less likely to be prescribed stimulant medications (71.7% vs. 77.1%, p=0.04). Conclusions: RD is infrequently coded in administrative claims, biasing low estimates of the frequency with which RD and ADHD co-occur. Children with ADHD and coded RD diagnoses tend to be younger, on average, and have a higher comorbid burden than children with ADHD only, and are less likely to receive stimulant medications. The clinical importance of these differences is unclear, and further research is needed to understand the unique characteristics and needs of children with comorbid ADHD and RD.

NR3-04

THE ROLE OF ACETALDEHYDE IN HUMAN PSYCHOMOTOR FUNCTION: A DOUBLE-BLIND PLACEBO-CONTROLLED CROSSOVER STUDY

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SUMMARY:

Background: Acetaldehyde, the first product of ethanol metabolization, is a biologically active compound, but the behavioural properties of acetaldehyde in humans are largely undefined. We investigated the acute effects of both alcohol and acetaldehyde on psychomotor functions

related to automobile driving skills. Methods: Twenty-four men were selected through genotyping; half had the ALDH2*1/*1 (active form) genotype and half had the ALDH2*1/*2 (inactive form) genotype. In a double-blind placebo-controlled crossover design, each subject was administered one of the following doses of alcohol: 0.25 g/kg, 0.5 g/kg, 0.75 g/kg, or a placebo in four trials that took place at one-week intervals. Blood ethanol concentration (BEC) and blood acetaldehyde concentration (BAAC) were measured nine times and psychomotor function tests (critical flicker fusion threshold, choice reaction time, compensatory tracking task, and digit symbol substitution test) were assessed seven times in total over 4 hours after study drug ingestion. Results: Following the consumption of alcohol, BEC was comparable in the two subject groups, while BAAC was significantly higher in subjects with ALDH2 *1/*2 than in those with ALDH2 *1/*1. The psychomotor performance of subjects with ALDH2*1/*2 was significantly poorer than that of subjects with ALDH2*1/*1. Significant correlations between psychomotor performance and both BEC and BAAC were observed. However, in the linear regression analysis, BAAC significantly predicted poorer psychomotor performance, whereas BEC was not associated with any measure of psychomotor function. Conclusions: Acetaldehyde may be more important than alcohol in determining the effects on human psychomotor function and skills.

NR3-05

THE ASSOCIATION BETWEEN OBESITY, SUICIDE, BRAIN-DERIVED NEUROTROPHIC FACTOR AND TYROSINCE KINASE B RECEPTOR PROTEIN LEVELS IN MAJOR DEPRESSION

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SUMMARY:
Background: Brain-derived neurotrophic factor (BDNF) and its receptor tyrosince kinase B receptor (TrkB) in mood disorders and antidepressant effects have been intensively investigated. BDNF and TrkB were also associated with eating disorder, obesity, and suicide in other studies. Method: Serum BDNF and TrkB protein levels of 60 inpatients and outpatients diagnosed with major depressive disorder were collected. Men and women with a body mass index (BMI) of ?26.4kg/m2 were classified as obese. Analysis of covariance (ANCOVA) models was performed to examine the differences in BDNF and TrkB between obese/non-obese and suicidal/non-suicidal major depressive patients. P-values <0.05 were regarded as statistically significant. Results: BDNF protein levels appeared lower among obese major depressive patients, but no statistical significance was noted using ANCOVA (F=2.230, P=0.141). BDNF protein levels also appeared lower among major depressive patients without suicide attempt, but no significance was found using ANCOVA (F=0.569, P=0.454). TrkB protein levels, in contrast, appeared higher among obese major depressive patients. Statistical significance was noted using ANCOVA (F=4.137, P=0.047). TrkB protein levels appeared higher among major depressive patients without suicide attempt, but no significance was found using ANCOVA (F=0.747, P=0.391). Conclusion: Our results only found statistical significance in elevated TrkB in obese major depressive patients. No significant relationship was found between BDNF protein level and obesity in major depression. We also did not find a significant relationship between the BDNF protein levels, TrkB protein levels, and suicide history in major depressive patients.

NR3-06

BIOCHEMICAL AND POLYSOMNOGRAPHIC STUDY OF PATIENTS WITH MAJOR DEPRESSION DISORDER AND SOMATOFORM PAIN DISORDERS

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SUMMARY:
Introduction: Chronic pain is a frequent reason for seeking medical care and causes disability, accounting for half of outpatient visits. Fifty percent of depressed patients report multiple unexplained symptoms including chronic pain. Sleep is disturbed in both groups of patients. Methods: We studied three groups: Depression (MDD) (N=20; age M=35.65), Somatoform pain disorders (SPD) (N=20; age M=54.05), and Normal controls (NC) (N=19; age M=39.95), all without co morbid psychiatric disorders. All underwent 8 hour NPSGs, and 7:30 A.M serum plasma levels of cortisol and interleukin-6. Patients were administered the SCID-IV, Hamilton Depression Rating Scale (HDRS), and Screening of Somatoform Symptoms (SOS). Pittsburgh Sleep Quality Index (PSQI) and Insomnia Severity Index (ISI) assessed sleep problems.

Results: REM% was higher in MDD (25.3±6.9) than NC (20.1±4.4) (p<0.05). REM Lat was longer in SPD (149.8±101.1) than NC (113.9±50.9) and MDD (92.9±51.2) (p<0.05). Sleep efficiency was lower in SPD (77.1±14.8) than NC (86.8±6.6) and MDD (82.8±12) (p<0.02). REM periods were higher in MDD (5.4±1.6) than the SPD (4±1.5) and NC (4.6±6) (p<0.03). TWTASO was higher in SPD (84.5±53.5) than MDD (47.5±35.9) and NC (43.7±32.8) (p<0.006) . Cortisol was higher in SPD (17.9±5.8) than MDD (13±5.4) (p<0.02). IL6 was higher in SPD (5±5.1) than NC (2.4±0.5) (P<0.05). PSQI was higher in SPD (27±6) than MDD (22±6.2) and NC (8.4±4.4) (p<0.001). ESS was higher in both SPD (11.1±5.4) and MDD (11.2±5) than NC (5.8±3) (P<0.001). ISI was higher in SPD (17.8±6.1) and MDD (18.1±4.8) than NC (4±3.3) (p<0.001). Conclusion: Cortisol was higher in SPD than MDD patients, possibly reflecting stimulation of the arousal system and explaining their poor sleep efficiency. IL-6 was elevated in SPD patients which may be a useful disease marker. SPD patients had more frequent shorter REM periods which may also explain the unrestorative quality of this sleep.

NR3-07

PLASMA SEROTONIN LEVEL OF KOREAN VIETNAM WAR VETERANS WITH POST-TRAUMATIC STRESS DISORDER AND SYMPTOM SEVERITY

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SUMMARY:

Objective: The overlap in clinical phenomenology and morbidity between post-traumatic stress disorder (PTSD) and such conditions as major depression, anxiety disorders and aggression, in which a serotonin dysfunction is implicated, suggests a role for serotonin in the pathophysiology of PTSD. This study was conducted to examine the relationship between plasma serotonin levels and PTSD symptoms in chronic PTSD patients with long term pharmacological treatment. Methods: Fourteen Vietnam War veterans with chronic PTSD who had concurrent psychopharmacological treatment and 28 non-PTSD patients without trauma exposure were recruited consecutively. History of trauma was assessed by clinical exploration and the Posttraumatic Diagnostic Scale (PDS). Combat exposure scale (CES), Mississippi scale for combat-related posttraumatic stress disorder (M-PTSD), clinician-administered PTSD scale (CAPS), Hamilton rating scale for depression (HAMD), and Hamilton anxiety scale (HAMA) were used to evaluate PTSD symptom severity. For more precise comparison of plasma serotonin, we averaged the result of two plasma serotonin levels, which took with more than 4 weeks gap, and used it. We measured plasma serotonin levels by high performance liquid chromatography (HPLC). Results: The plasma serotonin levels were significantly higher in PTSD group than control group (1st p=0.036, 2nd p=0.006). The score of M-PTSD (p<0.001), CAPS (p<0.001), HAMD (p<0.001), and HAMA (p<0.001) were significantly higher in PTSD group than control group. There were no significant relationships between plasma serotonin and PTSD symptoms. Conclusion: Though the levels of plasma serotonin were higher in chronic PTSD patients with long-term pharmacological treatment (mean 50.2 months) than non-PTSD patients, the core symptoms of PTSD appeared partially in PTSD patients. Throughout analyzing plasma serotonin levels, our research on the change of severity with long-term pharmacological treatment projected a different conclusion than those of past studies. PTSD is a complicated disorder which may likely be related to a variety of neurotransmitter systems. Therefore, further research which investigate relationships with norepinephrine, dopamine, and other neurotransmitters as well as serotonin is needed to improve the treatment of PTSD.

NR3-08

A CORRELATION AMONG PLASMA ASS42, DEPRESSIVE SYMPTOMS, AND COGNITIVE FUNCTION IN THE KOREAN ELDERLY

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SUMMARY:

Objectives: Several longitudinal studies indicated that elevated plasma amyloid beta 42 (Aß 42) levels may be a significant risk factor for the development of AD in the general population. This study aims to investigate whether plasma Aß 42 levels are associated with depressive symptoms and/or cognitive function in community-dwelling elderly. Methods: Subjects were 132 participants of a population-based study of community-dwelling elderly above 65 years old for an early detection screening project in the Inje and Cheolwon areas in Gangwon province. Symptoms of depression were evaluated by SGDS-K (Short Geriatric

Depression Scale of Korean version), and the MMSE-KC (Mini-Mental State Examination-Korean version) scale was used to assess cognitive function. Plasma Aß 42 levels were measured with human amyloid beta ELISA Kit. Results: The elderly with depression (SGDS-K score > 8) had lower plasma Aß 42 than those without depression ($p<0.05$). Plasma Aß 42 levels were positively correlated with SGDS-K score ($p<0.05$). However, MMSE-KC score was inversely associated with plasma Aß 42 level ($p<0.01$). In regression analysis, plasma Aß 42 levels were associated with MMSE-KC (ß= -0.27, F=9.65, $p<0.01$) and SGDS-K (ß= 0.19, F=5.00, $p<0.05$). Conclusion: Depressive symptoms and cognitive decline were associated with high levels of plasma Aß 42 in community-dwelling elderly. Past studies reported that Aß 42 deposits selectively in the AD brain and it is well-established that the CSF Aß 42 level is decreased in subjects with MCI or AD. Other studies suggested amyloid-associated depression, which is associated with poor memory and other cognitive dysfunction in cognitive perspective. However, the difference between the past studies and our research is that the main participants of the past one are based on patients with depression, who got treatment from the hospital, while our research is based on community-dwelling elderly. Therefore, prospective cohort studies may be needed in a large community elderly sample in the future to confirm these associations.

NR3-09

EVIDENCE FOR INTERACTION BETWEEN BDNF PATHWAY GENES AND PERSONALITY IN CHINESE HAN POPULATION

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SUMMARY:

Objective: To explore the role of the single gene including BDNF, PRKCG in BDNF pathways, and analyze the interaction effects between them on personality in Chinese Han healthy population. Methods: Three hundred seventeen unrelated Chinese Han healthy people (male 134, female 183; average age 27.26±8.40 years) were selected. All subjects were assessed by Eysenck Personality Quesrionnaire (EPQ) including three personality dimensions: Neuroticism(N), Introversion-Extraversion(E) and Psychoticism(P). We calculated the standard scores (T) of three dimensions, and divided N and E dimensions into three levels by the T38.5~61.5: Non-neuroticism, moderate and Neuroticism; Introversion, moderate and Extraversion; divided P dimensions into two levels by the T61.5: Psychoticism and Non-psychoticism. BDNF and PRKCG genes polymorphisms were detected by polymerase chain reaction (PCR), including BDNF rs6265?BDNF rs7124442 and PRKCG rs3745406. SPSS13.0 software was used for monofactorial analyses. The UNPHASED program was used to perform the gene-gene interaction analysis among SNPs. Results: 1.) The Hardy-Weinberg equilibrium test showed that the genotypic distributions of BDNF rs6265, rs7124442 and PRKCG rs3745406 in this sample were in HWE, which indicated that the sample can represent the population. 2.) No significant difference was found in distributions of mean age, sex and educational background between different personality groups. 3.) No statistically significant difference of each personality dimension mean was detected between different BDNF rs6265, rs7124442 and PRKCG rs3745406 genotypes and alleles, and there was no statistically significant difference of BDNF rs6265, rs7124442 and PRKCG rs3745406 genotypes and alleles frequency distribution between different personality dimension groups. 4.) UNPHASED program results showed the significant interaction effects between BDNF rs7124442 and PRKCG rs3745406 in Introversion-Extraversion dimension(?2=12.39,P=0.015), and in Psychoticism dimension(?2=9.859, P=0.043). After 1000 times repeating by the permutation testing, the former P value remained significant(P=0.017), but the latter turned negative. In the Neuroticism personality, there are no interaction effects found to be significant. Conclusions: No significant associations were found between BDNF, PRKCG single gene and EPQ personality. Significant interaction effects were detected between them on the Introversion-Extraversion personality in Chinese North Han healthy population.

NR3-10

DIFFUSION TENSOR IMAGING IN STUDYING WHITE MATTER COMPLEXITY: A GAP JUNCTION HYPOTHESIS

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SUMMARY:
Background: Absolute brain size has been found to be a strong determinant of cognitive abilities across primate species. Moreover, within the brain, the prefrontal white matter volume was reported to be disproportionately larger in humans than in other primates, suggesting that prefrontal white matter volume and complexity played a key role in brain evolution. Alternatively, the role of the prefrontal cortex as an executive oversight of posterior regions sheds light on the extent to which the anterior regions of the brain may interconnect relatively to the posterior regions. Hypothesis: Diffusion tensor imaging is a modality that measures fractional anisotropy. Disruption of the integrity of white matter tracts disturbs the planar water diffusion, decreasing the fractional anisotropy. Furthermore, a higher level of fiber tracts intersection results in a decrease of fractional anisotropy. Thus, should the prefrontal white matter possess higher complexity, possibly through tracts intersection and gap junctions, we would predict that healthy rostral white matter tracts linking frontal regions to the rest of the brain would in fact have lower fractional anisotropy in comparison to caudal white matter tracts or corpus callosum. Methods: In order to test the hypothesis that white matter complexity is greater in frontal versus posterior regions of interest, diffusion tensor imaging was used to determine regional fractional anisotropy in 9 healthy bonnet macaques. Four regions of interest were included: anterior limbs of the internal capsule, posterior limbs of the internal capsule, occipital lobe white matter, and the corpus callosum. Results: The fractional anisotropy of the anterior limbs of the internal capsule was lowest compared to all other regions of interest (N-K p<.0001), whereas the fractional anisotropy of the corpus callosum was highest (N-K; p <.0001). The posterior limbs of the internal capsule and the occipital white matter were not distinguishable but exhibited intermediate fractional anisotropy in comparison to the former (N-K; p < 0.0001) and the latter (N-K; p <0.0001). Conclusions: The current study supported the hypothesis that healthy anterior white matter tracts have lower fractional anisotropy in comparison to caudal white matter tracts or the corpus callosum. Moreover, it suggested that the observed fractional anisotropy variation may in part be due to differences in gap junction abundance and state, which remains to be demonstrated.

NR3-11

CORRELATIONS BETWEEN MOOD AND BRAIN GABA LEVELS AFTER YOGA AND WALKING

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SUMMARY:
Background: Yoga and exercise have beneficial effects on mood and anxiety. GABA is reduced in mood disorders and anxiety. The practice of yoga asanas is associated with increased brain GABA levels [1]. Objectives: Are changes in mood and/or GABA levels specific to yoga or related to physical activity in general? Methods: Healthy subjects with no significant medical/psychiatric disorders were randomized to an Iyengar yoga or walking intervention for 60-min. 3x/week for 12 weeks. Mood scales were taken at weeks zero, four, eight, 12 and before each MRS scan. Scan
1 was at baseline. Scan 2 was after 12 weeks and followed by a 60-min. yoga or walking intervention, immediately followed by Scan 3. Results: The yoga subjects (n=19) reported greater improvement in mood (e.g.,
Positive Engagement ?=0.01) and greater decreases in anxiety (?=0.05) than the walking group (n=15). The yoga group showed a trend towards an increase in thalamic GABA levels (p=0.09). There were correlations between the mood scales and GABA levels (e.g., whole group, Scan 2, Tranquility p=0.005). The yoga group had positive associations between the changes in mood scales and changes in GABA levels (e.g., Scan 2-1, Revitalization p<0.001). Conclusions: Although matched metabolically, the yoga intervention had a greater positive effect on mood than the walking intervention, suggesting the effect is not just due to physical activity. There was correlation between mood and thalamic GABA levels in all subjects. Correlation of changes in mood and changes in GABA levels in the yoga group is similar to the pattern seen in the treatment of depressed subjects with SSRIs [2]. These findings suggest that yoga postures should be considered as adjunctive treatments in people with low GABA levels.
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NR3-12

PLAYERS OF FIRST PERSON SHOOTER GAMES SHOW INCREASED ACTIVITY IN FRONTAL BRAIN IN DEFAULT-MODE NETWORK AS SHOWN BY FMRI

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SUMMARY:
Introduction: There is an increased interest in the influence of first person shooter games (FPSG) on the behavior of the players. Recent research shows an increase in aggression due to the intensive use of FPSG but little is known about the influence of these games on the brain activity. Methods: Adult German male users of FPSG (n=14, daily use of Counter Strike M = 5 hours, SD = 2.2 since at least two yrs., age M = 25 yrs. ± 5.8 yrs.) and 14 control subjects (no use of FPSG, age M = 23 yrs. ± 4.2 yrs.) underwent fMRI scanning while they were told to relax and keep their eyes closed. A total of 178 T2*-weighted volumes of the whole brain were recorded. Subjects had to complete the FAF and the Interpersonal-Reactivity-Index (IRI). We identified individual brain sites of the DMN by calculating independent component analysis. Group differences in RS were calculated by random effects analysis. The questionnaire scores were correlated with the individual volumes of the DMN clusters. Results: The groups differed in the aggression scores of the FAF, whereas the FPSG players reached significant ($p<0.05$) higher values in this questionnaire indicating higher levels of felt aggression. The analysis of individual fMRI data revealed robust results for identification of the DMN clusters. The group analysis revealed differences in the frontal part of the DMN, whereas the control group showed significant lower RS. The individual extent of the clusters correlated positive with the impulsiveness ($r=0.394$) and the self aggression ($r=0.533$) scale of the FAF. The control group DMN clusters correlated significantly positive with the self aggression scale of the FAF ($r=0.696$). Conclusion: High activity in the DMN indicates reduced cognitive activity during resting periods. Our results show differences in brain activity during cognitive and motor resting periods between the FPSG users and the control group. This frontal increase in DMN may indicate executive dysfunctions of FPSG users having influence on the high scores in the aggression questionnaire.
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NR3-13

NATURE OR NURTURE? PERSONALITY DIMENSIONS AND FMRI NEURAL REPRESENTATION OF ATTACHMENT

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SUMMARY:
Objective: To determine the influence of genetic and environmental personality dimensions on the neural correlates of the visual processing of attachment figures. Introduction: Personality disorder (PD) has been proposed to have genetic and environmental influences, with the cluster A, B and C groupings having environmental influences and overall PD risk as well as two other specific factors (schizoid-avoidant and borderline-antisocial) having genetic risk factors (Kendler et al, 2008). We have employed functional magnetic resonance imaging (fMRI) to study the influence of personality dimensions on the neural underpinnings of attachment. Method: 20-30 year old female subjects with no psychopathology completed a battery of assessments including SNAP-II to measure PD. Subjects viewed photos of their mother, a close female friend and age matched strangers (old and young). Personality was co-varied with the mother versus others condition and the corresponding regression slope was used to test the hypothesis of a zero regression slope for the personality dimension against the alternative of a positive regression slope. Images were acquired using a Siemens 3T scanner and analyzed using SPM8. Results: Though the genetic dimensions were associated with some significant patterns of activation, it was not consistent for all three dimensions. Environmental dimensions were significantly associated (corrected $p < .05$) with activation as follows: Cluster A: Significant deactivations in the inferior parietal lobule, Brodmann 40, 32 and the anterior cingulate with no significant activations. Cluster B: Activations

in the frontal lobe (precentral gyrus, superior frontal gyrus, medial frontal gyrus) thalamus, anterior cingulate, Brodmann 13, and insula with no deactivations. Cluster C: Activations in the frontal lobe, inferior parietal lobe, Brodmann 4, supramarginal gyrus, middle temporal gyrus and the insula. Deactivations were seen in the parietal lobe (Brodmann 1) and postcentral gyrus and the frontal lobe (precentral gyrus). Conclusion: When looking at personality dimensions in the context of attachment, groupings based on environmental risk factors (the PD clusters) more consistently explain variance in brain activation during an attachment-related viewing task. Interestingly, when viewing photos of the mother versus others, cluster A was associated with only deactivations whereas cluster B was associated with only activations. Cluster C was the only one showing both.

NR3-14

PET-MEASURED OCCUPANCY OF THE D2 RECEPTOR: A COMPARISON OF QUETIAPINE FUMARATE IMMEDIATE- AND EXTENDED-RELEASE FORMULATIONS IN HEALTHY SUBJECTS

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SUMMARY:
Introduction: Developed as an antipsychotic, quetiapine displays moderate, transient occupancy of dopamine D2 receptors. Characterization of norquetiapine indicates that this major human metabolite potently inhibits the norepinephrine transporter and binds to D2 receptors with affinity similar to quetiapine. Clinical pharmacology studies suggest pharmacodynamic differences between the immediate-release (IR) and the recently developed extended-release (XR) quetiapine formulation. The objectives of this study were to further investigate the pharmacokinetics of these formulations, and to relate D2-receptor occupancy to quetiapine and norquetiapine exposures. Methods: Eleven healthy male volunteers, aged 21 to 29 years, underwent PET using the radioligand [11C] raclopride. After baseline measurements, quetiapine XR was administered once-daily for 8 days, with titration to 300 mg on Days 5 to 8. Quetiapine IR was administered at 300 mg daily on Days 9 to 12. PET measurements were repeated after the last doses of XR and IR at predicted times of Cmax. Striatal D2-receptor occupancy was calculated using a reference tissue model. Concomitant pharmacokinetic measurements were performed. Results: For quetiapine XR, mean D2-receptor occupancy in the putamen at Cmax was 32% (SD ±11%; n=11). For quetiapine IR, mean D2-receptor occupancy at Cmax was 47% (SD ±9%; n=10). Quetiapine XR produced lower peak D2 occupancy than quetiapine IR in all subjects. Conclusions: Pharmacokinetic differences between quetiapine XR and IR formulations translate to different profiles of brain receptor occupancy. Quetiapine XR was associated with lower peak D2-receptor occupancy than quetiapine IR at corresponding doses. This observation may provide important mechanistic underpinnings for emerging clinical data comparing the 2 quetiapine formulations.
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NR3-15

THE FEASIBILITY OF IMAGING HUMAN HIPPOCAMPAL SUBFIELDS IN YOUNG ADULTS AT 7 TESLA

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SUMMARY:
Purpose: To establish an imaging approach to visualize the 100 micron thick hippocampal neuron generating, dentate granule cell layer (DGCL), consistently in a clinically feasible magnetic resonance imaging (MRI) scan duration (1); and to assess its sensitivity by quantifying the likelihood that it will be detected in healthy young adults with the hopes of eventually using this technique to evaluate DGCL pathologic changes in neurologic and psychiatric disorders. Materials and Methods: The study was HIPPA compliant and all subjects provided Institutional Review Board written informed consent. Ten healthy volunteers (5 male, 5 female 26±6 years old) were imaged at 7 Tesla using a 24-element head coil-array with 3D T1-weighted MRI for anatomic reference, followed by T2*-weighted gradient-echo (TE/TR= 25/944 ms) imaging at 232 micron in-plane resolution (0.05 mm3 pixels) in coronal and sagittal slabs (17 slices 1 mm thick) over the hippocampus in 14 minutes. The entire study took 45 minutes. Results: The DGCL was consistently visible in all 10 enrolled subjects. All larger subfields were visible in excellent detail and contrast in every subject. Conclusion: The spatial resolution and tissue contrast at ultrahigh field MRI can be used to consistently reveal hippocampal

morphology down to 100 micron subfields in clinically acceptable scan durations. This imaging technique might be used to detect cellular disarray and degenerative changes in this sensitive circuit earlier than at 1.5 T or even 3.0 T. This advancement in brain imaging capability may be the key to early detection and evaluation of disease progression of neurologic and psychiatric disorders that involve the hippocampus, such as schizophrenia (2). This will allow for earlier interventions that will prevent further neuronal degenerative activity that would lead to worsening of symptoms.

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NR3-16

THE SEROTONIN RECEPTOR 2A GENE POLYMORPHISM AND CHILD ABUSE HISTORY ASSOCIATED WITH A HISTORY OF SUICIDE ATTEMPTS AMONG DEPRESSED INPATIENTS

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SUMMARY:

Objective: Caspi et al. showed that individuals maltreated in childhood have higher rates of depression in later life if they are homozygous short of the serotonin transporter gene polymorphism (5HTTLPR). Also, the homozygous long of 5HTTLPR was associated with better SSRI response, and the A/A of the serotonin receptor gene polymorphism (5HT-R 2A SNP rs7997012) was associated with better citalopram response with STAR*D sample than the G/G. However, the effects of the SNP in the moderation of child abuse history on the characteristics of mental illnesses are not well understood. We examined if there are similar gene-environment interactions with the serotonin receptor gene polymorphism. Methods: Retrospective chart review of 447 depressed mood disorders inpatients from 2005-2008. Those who had serotonin receptor genotyping were included. Subjects with each genotype (A/A+A/G, GG) were subcategorized into 2 groups with/without history of child abuse. The history of suicide attempts of each group was compared. Results: Of the 447 patients genotyped for serotonin receptor genes, the history of child abuse was found among 53.7% of patients. 250 Caucasian patients were genotyped for 5HT-R 2A SNP rs7997012. An interaction was found between the SNP and child abuse history influencing the prevalence of suicide attempts. Although A carriers (A/A+A/G) and the G/G did not show the difference in the risk of suicide attempt when there was no abuse history (31.7% versus 35.5% respectively), A carriers showed significantly higher rates of suicide attempt compared to the G/G when there is a history of child abuse (48.4% versus 22.7% respectively, p=0.0050). Conclusions: Our findings showed an interaction between a SNP (rs7997012) in 5HT-R 2A gene and stressful life events. The fact that a same polymorphism is associated with increased risk of suicide attempt with abuse history and better treatment response to SSRI is counter intuitive. STAR*D sample is depressed outpatients, while our sample is depressed psychiatric inpatients, which warrants further investigation for generalizability.

NR3-17

SERT AND BDNF POLYMORPHISMS IN BORDERLINE PERSONALITY DISORDER AND BIPOLAR DISORDER II

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SUMMARY:

Objective: Borderline personality disorder (BPD) and bipolar disorder II (BPII) are relevant clinical problems. There is a controversy between those who consider that BPD is a form of BPII, and those who think that they are two separate entities. Affective instability may be a feature shared by both disorders, while impulsiveness may be more closely associated with BPD. There are positive findings on genetic polymorphisms associated with impulsiveness in BPD, and several candidate genes for bipolar disorder. However, this controversy has not been examined from the genetic point of view. Therefore, it is relevant to compare the distribution of the frequencies of certain gene variants among these clinical populations. The objective of this work was to estimate and compare the allelic frequencies for two candidate genes for psychiatric disorders, in a sample of patients with BPD, another of patients with BPII, and a control sample. We studied the polymorphisms 5HTTLPR of the SERT gene, and Val66Met of the

BDNF gene. Methods: To establish the diagnosis of BPD or BPII we used SCID I and II. Controls were evaluated with MINI. Genotyping was carried out using of PCR or PCR-RFLP. Allelic frequencies were estimated and compared using chi square. A p-value of 0.05 was considered significant. Results: No differences were found between the three populations in the allelic frequency of 5HTTLPR. Regarding Val66Met polymorphism, we found significant differences between BPII patients and control individuals. We did not find significant differences either between BPD patients and controls or between both groups of patients. Conclusions: Our results suggest that BDNF gene may be involved in the production of BPII. The similarities between BPD and BPII samples pose the question regarding common genetic vulnerability factors. Genetic analysis of these relevant clinical populations may clarify the controversy on the nature of these disorders.
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NR3-18

NR3C1+1830C>G POLYMORPHISMS AND MIRTAZAPINE RESPONSES IN PATIENTS WITH MAJOR DEPRESSION

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SUMMARY:
Background: Cortisol and corticotropin-releasing hormone (CRH) affect the serotonin (5-HT) system. During the stress response, glucocorticoids (GCs) stimulate all these features of 5-HT transmission. Conversely, 5-HT transmission is impaired and noradrenergic transmission in the hippocampus is suppressed during chronic psychosocial stress and hypercortisolism, which is similar to the series of events evident during depression. The GR polymorphisms affect GC sensitivity, which is associated with cortisol feedback effects. The degree of cortisol feedback is closely related to the development of depression and may also be affected by antidepressants. Therefore, we hypothesized that the above four GR polymorphisms are associated with the susceptibility to MDD and predict the response to treatment with mirtazapine. Methods: Trained psychiatrists examined all of the subjects using the Structured Clinical Interview for DSM-IV Axis I disorders (SCID-I) and the Korean version of the Diagnostic Interview for Genetic Studies (K-DIGS). The severity of depression was assessed using the 21-item Hamilton Depression Rating (HAMD21) scale. Only subjects with a minimum score of 18 on the HAMD21 scale were enrolled. During the treatment period in the study, all subjects took mirtazapine at a daily dose of 15–60 mg. Clinical symptoms were evaluated using the HAMD21 scale at baseline and after 1, 2, 4, 8, and 12 weeks of treatment. The genotype frequencies were compared using logistic regression analysis, and between-genotype differences in the decrease in the HAMD21 score were analyzed using a linear regression analysis in 271 Korean patients with MDD. Results: The proportion of patients with MDD possessing the G allele was higher in non-remitters (41.6%) than in remitters (24.4%) after 4 weeks of mirtazapine treatment (P = 0.031, odd ratio = 2.38 (1.08 – 5.22). Similarly, the reductions in the HAMD21 scores were smaller in G allele carriers (46.09 ± 2.65%) than those in patients with the CC genotype (54.84 ± 1.99%) after 4 weeks of mirtazapine treatment (P = 0.016). Conclusion: These results suggest that NR3C1+1830C>G affects the outcome of mirtazapine treatment in patients with MDD, and that this polymorphism may be a good genetic marker for predicting the clinical outcome of mirtazapine treatment.

NR3-19

POLIMORPHISMS OF THE LEP- AND LEPR GENES, METABOLIC PROFILE AFTER PROLONGED CLOZAPINE ADMINISTRATION AND RESPONSE TO THE ANTIDIABETIC METFORMIN

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SUMMARY:
Background: The excessive body weight (BW) gain and related metabolic dysfunction observed during atypical antipsychotic treatment may be associated with genetically-based leptin dysregulation (1). This proposal was explored by comparing the anthropometric and metabolic profile and the response to metformin (MET) in clozapine-(CLZ) treated schizophrenia patients according to their polimorphisms to the leptin (LEP-2548/G/A) and leptin receptor (LEPR-Q223R) genes. Methods: Study 1. Fifty-six subjects (84.6% males) undergoing prolonged CLZ

treatment were evaluated in fasting conditions to assess the body mass index (BMI), serum levels of glucose, lipids, leptin, cortisol, the insulin resistance index (HOMA-IR) and the frequencies of LEP- and LEPR polimorphisms. Study 2. After the initial evaluation, 52 subjects (80.7% males) were randomly assigned to MET XR (1000 mg/day) or placebo for 14 weeks. The basal metabolic profile and the response of the BW and biochemical variables to MET were compared among subjects according to their specific polimorphisms. Analysis: Glucose and lipids were quantified by enzymatic methods, and hormones by ELISA. Genotypes were determined by the polymerase chain reaction. Results: Allele distribution was for LEP: 19 (AA) and 37 (AG+GG); for LEPR: 24 (QQ) and 32 (QR+RR). Both distributions did not deviate from the Hardy-Weinberg equilibrium. Study 1. Groups QQ ($p < 0.05$) and GG ($p = 0.05$) displayed the lowest triglyceride levels. No significant differences were observed either in the frequency of the metabolic syndrome (ATP-III) or in individual anthropometric or biochemical variables. Study 2. In the metformin branch the GG group showed a significant increase in glucose levels ($p <0.05$), whereas the QQ group displayed a significant decrease in the HOMA-IR and low density cholesterol levels ($p < 0.05$). No differences were observed in the placebo group. The BMI and BW change did not differ between the genotypes in any study, even after correcting for CLZ dose. Conclusions: In agreement with recent studies in men (2), BW response to CLZ was not related to LEP- and LEPR polimorphisms. However, the genotypes GG and (QR + RR) showed an impaired response to metformin. This result waits for replication in more powered sample studies and balanced gender distribution.

(1) Peña R, et al.

NR3-20

GENETIC STUDIES OF MICRORNAS IN SCHIZOPHRENIA

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SUMMARY:

MicroRNAs (miRNAs) are short, non-coding RNAs that regulate the stability and translation of mRNA targets. Compelling evidence has shown that miRNAs could be involved in the initiation and progression of neuropsychiatric disorders including schizophrenia. Prior to this study, six miRNAs had been reported to show a significantly abnormal expression level in schizophrenic brains. Also, common single nucleotide polymorphisms within two miRNA transcripts have shown genetic associations with schizophrenia. However, it remains largely unknown whether variants in these miRNA genes and/or in their target sites are associated with schizophrenia. Here, we selected the above eight miRNAs, plus 15 of their experimentally validated target sites, as candidate susceptibility factors for schizophrenia, for mutation screening and further association studies in Chinese case-control samples. We identified a new potentially functional variant ss178077483 located in the precursor of mir-30e, which was strongly associated with schizophrenia (allelic $P = 0.00017$; genotypic $P = 0.00015$), with an odds ratio of 4.952 (95 % confidence interval: 1.887–12.998). We also demonstrated that this new variant ss178077483, combined with mir-30e rs7556088 and mir-24-MAPK14 rs3804452, showed a weak gene-gene interaction for schizophrenia risk ($P = 0.001$). These data imply that miRNAs and/or their target sites may play an important role in schizophrenia susceptibility. Further functional characterization of miRNA variants and their influence on target mRNAs may provide underlying mechanisms for the observed associations and disease etiology.

NR3-21

PATIENT AND STAFF PERCEPTIONS OF THE IMPLEMENTATION OF AN ENHANCED DISCHARGE PROCESS FOR INPATIENT PSYCHIATRIC SETTINGS

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SUMMARY:

Objective: As the duration of psychiatric hospitalizations has decreased, engagement in services post-discharge has become increasingly important (Hudson, 2004). Yet many patients discharged from psychiatric hospitals do not receive timely follow-up care (Stein et al, 2007). Few studies have examined interventions to improve rates of engagement following psychiatric hospitalization, and feasibility of implementing such interventions is uncertain. An enhanced discharge process to improve timely engagement after discharge, designed for feasible implementation on inpatient units, was developed after

review of the literature and collaborative process with key stakeholders. This report provides empirical data on the success of implementing key elements of this enhanced discharge process. Methods: Inpatient staff from five psychiatric hospitals implemented the enhanced discharge process. As part of these quality improvement activities, staff and patients routinely completed an 11-item survey about the degree to which the key components of the processes, including promoting consumer empowerment, educating consumers about behavioral health care system, and enhancing pre-discharge communication among providers, patients and support networks, were completed. Responses on the degree to which specific processes were completed were assessed on a 5 point Likert scale, ranging from 4 (Very much) through 0 (Not at all). Results: The majority of enhanced discharge processes were implemented successfully (mean=3.37; sd=.67), according to patient and staff reports, and the reports of consumers and staff were highly correlated ($p<0.001$). However, the practice of engaging families/supports (mean=2.51; sd=1.61) and facilitating communication between patient and outpatient provider (mean=3.19; sd=1.33) were significantly less likely to be successfully implemented ($p< 0.001$) than other processes. Conclusion: Community-academic collaborations, in which the implementation of empirically supported processes are supported and assessed, can inform efforts to improve care in community settings and identify challenges to successful implementation. Better assessing implementation effectiveness is a critical aspect of efforts to examine the impact of empirically supported interventions in real world settings.

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Stein, B.D., Kogan, J.N., Sorb

NR3-22

SUCCESSFUL IMPLEMENTATION OF A GLUCOSE MONITORING PROGRAM IN A COMMUNITY MENTAL HEALTH SETTING

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SUMMARY:

Background: Patients with major mental illnesses are known to have higher mortality rates, primarily associated with increased cardiovascular risk, compared to the general population [1]. In 2004, the American Diabetes Association (ADA) released metabolic monitoring recommendations for this population [2], which includes obtaining baseline and yearly fasting plasma glucose. Identification of metabolic abnormalities, such as elevated fasting plasma glucose, is an important public health screening opportunity in psychiatric patients treated with antipsychotic medications. In the setting of a community mental health center (CMHC) serving approximately 4,000 adult patients across four separate clinical sites (one urban, two suburban and one rural), a quality improvement program was initiated to improve annual glucose monitoring rates in patients receiving antipsychotic drugs. Methods: The plan to monitor the percentage of patients that had at least one fasting glucose test documented within the preceding 12 months was initiated in 2005, with target screening rates set at 70% for 2006 and at 90% for 2007-08. Monitoring rates were compared to a control clinic population, where the physicians also spent ½ day per week at the urban CMHC site, and received the initial education and reminders to monitor their CMHC patients, but not their control clinic patients. In addition to repeated education, the intervention included monthly e-mails to all physicians except the control clinic physicians. These e-mails included a rank-ordering of the monitoring rates relative to that of their peers, offering a public comparison to incentivize improved monitoring rates in the CMHC setting. Results: The average initial (2005) CMHC monitoring rate was 49% with the highest screening rates occurring in the urban and rural sites. By the end of 2006 the average monitoring rate increased to 61%, with monitoring rates increasing at all CMHC sites; one of the suburban sites and the rural site exceeded the 70% screening goal while the other suburban site and urban site did not. In the second year of the program (2007) the overall monitoring rate increased to 82%; the rural site and the one suburban site again met the 90% screening goal, while the other suburban site and the urban site did not achieve the target. In the third year of the program (2008) the overall monitoring rate increased to 88%, with the same trend between the sites.

NR3-23

TREATMENT ADHERENCE AND PERSISTENCE WITH BRANDED ANTIDEPRESSANTS AMONG PATIENTS WITH MAJOR DEPRESSIVE DISORDER AND PAINFUL CHRONIC DISEASES

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SUMMARY:
Objective: This study compared the medication adherence and persistence profiles of 3 branded antidepressants (duloxetine, venlafaxine XR, and escitalopram) for patients with major depressive disorder (MDD) and painful chronic diseases (PCD) in real-world clinical settings. Method: This is a retrospective cohort study using the MarketScan commercial claims and encounter databases. Patients were included in the analyses if they filled any prescription of the study medication during the index period of July 1, 2006 to June 30, 2007, had no record of the use of the study medication in the prior 3 months, were aged 18 to 64 years, and had diagnoses of MDD and PCD of interest [1]. Patients were followed up at 6 months. Adherence was measured using the Medication Possession Ratio at =80% [2]. Persistence was defined as the number of days on the study medication before a prescription gap over 30 days. Results: Of the sample, 6,500 patients were initiated on duloxetine, 3,405 on venlafaxine XR, and 5,618 on escitalopram. Patients on duloxetine had a higher adherence rate (46.03%) than those on venlafaxine XR (42.94%; p=.0033) or escitalopram (37.27%; p<.0001). Patients on duloxetine stayed on the medication longer (117.82 days) than those on venlafaxine XR (114.24 days; p=.009) or escitalopram (105.73 days; p<.0001). After adjusting for demographics and comorbidities, patients on duloxetine still had significantly higher adherence rates and more persistence days than those on venlafaxine XR or escitalopram. In a sensitivity analysis with a 15-day allowable gap for a refill similar findings to the main analyses were found.
Conclusions: Among commercially insured patients with MDD and PCD, patients on duloxetine seem to have better adherence and persistence profiles than those on venlafaxine XR or escitalopram during the first 6 months. Further research is needed to examine the benefits of medication adherence among this population.
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NR3-24

IS "HOME TREATMENT" FOR THE ACUTELY MENTALLY ILL IN A RURAL SOUTHERN GERMAN AREA AS EFFECTIVE AS THE USUAL INPATIENT TREATMENT?

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SUMMARY:
Objective: "Home Treatment" (HT), a home based multiprofessional psychiatric service for the acutely mentally ill, is hypothesised to be an equally effective alternative to traditional inpatient treatment (TAU) in mainly schizophrenia and affective disorders (1). The first HT service in Southern Germany was established in Guenzburg/Bavaria in 2005. This study aimed to compare HT to TAU in two subsequently studied groups of patients with regard to its clinical effectiveness.
Method: We prospectively studied 60 HT patients and 18 comparable patients receiving TAU by use of PANSS, HAMD-21 and HoNOS ratings at admission and discharge. Statistical analysis was performed by random-effects regression models; significance level was set at p<0.05.
Results: In both groups, the majority of patients suffered from affective disorders and schizophrenia (HT 85%, TAU 71%). The mean age was 40 years in both groups. In the HT group, 70% of the patients were female (TAU 61%). The mean treatment duration in the HT group was significantly longer than in the TAU collective (63 versus 38 days). We found significant decreases with regard to HAMD-21 scores in both groups without significant differences between the groups. In both groups, the reduction of the PANSS scores indicated a therapy response which was significantly more pronounced in the TAU group. By contrast, significant improvements concerning HoNOS scores in both groups can be stated – this time with a significantly stronger effect in the HT group.
The regression analyses revealed that employment and higher GAF scores at admission were associated with a higher probability of being allocated to the TAU group.
Conclusions: In accordance with the literature (2) we found that HT seems to be an overall clinically equally effective and feasible alternative to TAU in our clientele. The significantly less pronounced decrease concerning PANSS scores in the HT group despite a longer treatment duration may be explained by the fact that our HT patients had a worse functional status at admission and

therefore could be considered as more chronified than the TAU patients.
Supported by funding from AstraZeneca.

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NR3-25

FREQUENCY AND DURATION OF PHYSICAL RESTRAINTS IN GENERALIZED VERSUS SPECIALIZED EMERGENCY ROOM SETTINGS

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SUMMARY:
Objectives: General hospital emergency departments manage patients presenting with psychiatric emergencies through consultation (the "Generalized" model) or by allocating space and resources specifically to the development of a psychiatric emergency room (the "Specialized" model). The Rhode Island Hospital Emergency Department (RIH-ED) recently implemented procedural changes effecting an overall transition from a Generalized to Specialized model. The purpose of this study was to evaluate the impact of a Generalized vs. Specialized ED on the frequency and duration of physical restraints that occur in the emergency room setting. We hypothesized that the Specialized ED environment would be associated with both decreased frequency and decreased duration of physical restraints, and would also be associated with more frequent administration of psychotropic medication. Methods: This study is a retrospective chart review of patients who required physical restraint in the Generalized ED and Specialized ED settings in the emergency department of a single academic, tertiary care center. All patients who required physical restraints in May 2008 (Generalized ED model) and May 2009 (Specialized ED model) were compared. The primary outcome measure was the frequency of physical restraint use. Results: Frequency of physical restraints decreased 66% with the transition from a Generalized to Specialized ED, from 0.60% (53 of 8551) to 0.20% (18 of 8866) of patients evaluated in the emergency department (Chi2(1)=17.38, p<0.001). Duration of restraints declined from an average duration of 117.6 ??75.4 minutes in the Generalized ED to 79.9 ??54.7 minutes in the Specialized ED, with a trend toward significance (t=1.91, df=59, p=0.06). There was no significant difference in the number of medications administered to patients in the Generalized vs. Specialized ED; however, the Specialized ED was associated with increased use of oral medications (50.0% vs. 20.8%, Fisher's exact test, p=0.031). Conclusions: The Specialized ED setting is associated with fewer episodes of physical restraint as compared to the Generalized ED setting. This finding cannot be accounted for by increased chemical restraint. We conclude that the Specialized ED model of care offers benefits to patient care (decreased patient restraint) that cannot be attributed to changes in prescribing practices.

NR3-26

A DRUG INTERACTION STUDY OF DEXTROMETHORPHAN/QUINIDINE: AN INVESTIGATIONAL AGENT FOR PSEUDOBULBAR AFFECT AND PAROXETINE

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SUMMARY:
Introduction: Pseudobulbar affect (PBA) is a common neurological condition in patients with underlying neurologic disease or insult, such as MS, ALS, or stroke. The involuntary outbursts of laughter and crying that define PBA are incongruent with mood and cause much distress and embarrassment. Although PBA is not a psychiatric disorder, it is often associated with mood disorders. SSRI use, including paroxetine (P), is not uncommon in these patients. Dextromethorphan (DM)/quinidine (Q) is a potential treatment for PBA that has demonstrated efficacy for reducing PBA episodes. Concomitant use of P and DMQ may occur. Because DM is metabolized by CYP2D6, Q is a CYP2D6 inhibitor, and P is both a CYP2D6 substrate and inhibitor, it is important to evaluate potential PK interactions. Methods: Healthy volunteers entered this open-label, randomized, parallel-group study. Group 1 (n=14) received P 20mg qd for 12 days to attain steady state; DMQ (DM 30mg+Q 30mg) was then added bid for 8 days. Group 2 (n=13) received DMQ bid for 8 days to attain steady state; P 20mg qd was then added for 12 days. PK blood sampling was performed at steady state for each agent as monotherapy

(DMQ or P) and as concomitant therapy (DMQ+P) at Day 20. The primary endpoints were the 90% CIs for the ratio of the AUCs (overall exposure) during concomitant therapy vs monotherapy. Additional PK parameters and safety measures (vital signs, ECGs, labs, and adverse events [AEs]) were also assessed. Results: The 90% CIs of the AUCs were outside the predefined range [0.8, 1.25] for all analyses indicating an interaction. At steady state, addition of DMQ to P resulted in increased levels of P, and addition of P to DMQ resulted in increased levels of DM and Q. The mean increase was 30% for P (AUC0-24), 50% for DM (AUC0-12), and 40% for Q (AUC0-12). A subgroup analysis that excluded outliers found similar increases except for P, where a 70% increase in AUC0-24 was demonstrated. Incidence of AEs was increased when P was added to DMQ (30.8% for DMQ alone vs 83.3% with P+DMQ); however, addition of DMQ to P was associated with lower AE incidence (78.6% with P alone vs 64.3% with DMQ+P). Overall, 3 subjects discontinued due to AEs and no serious AEs were reported. Conclusions: Drug interactions between DMQ and paroxetine resulted in an increased incidence of AEs in some subjects. Patients receiving both drugs should be monitored for AEs, with doses adjusted if necessary.
Support: Avanir Pharmaceuticals.

NR3-27

A STUDY OF POTENTIAL PHARMACOKINETIC (PK) AND PHARMACODYNAMIC (PD) INTERACTIONS BETWEEN DEXTROMETHORPHAN/QUINIDINE AND MEMANTINE

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SUMMARY:
Introduction: Pseudobulbar affect (PBA) is a common condition in patients with underlying neurologic disorders including Alzheimer's disease (AD). PBA has been successfully treated with dextromethorphan (DM; an uncompetitive NMDA receptor antagonist/sigma receptor agonist) in combination with quinidine (Q). Memantine is another NMDA receptor antagonist used in AD. It has been considered that PD effects may be enhanced if memantine is used concomitantly with another NMDA receptor antagonist but this has not been systematically studied. Q has a theoretical potential to inhibit memantine excretion. This study was therefore designed to assess PD and PK interactions. Methods: Healthy volunteers were enrolled in this open-label, randomized, parallel-group study. Group 1 (n=23) was titrated to memantine 20mg/day over 3 weeks and continued for an additional 11 days to attain steady-state; DMQ (DM 30mg + Q 30mg) was then added bid for 8 days. Group 2 (n=29) received DMQ bid for 8 days to attain steady-state; memantine was then added according to the same schedule as for Group 1. PK blood sampling was performed at steady-state for each agent as monotherapy and as concomitant therapy. The primary PK endpoints were the 90% CI for the ratio of the AUCs (overall exposure) during concomitant therapy versus monotherapy. Assessments of attention, psychomotor function, postural stability, anxiety, depression, sleep, nausea, and dizziness were used to evaluate PD interactions. Results: Following the addition of DMQ to memantine or memantine to DMQ, the 90% CIs of the AUCs were within the predefined ranges for memantine, DM and the metabolite dextrorphan indicating no drug interaction affected these parameters. The Q AUC ratio was slightly above the predefined CI, but the mean AUC increased only 25%. AE incidence was not increased during concomitant use. Visual analog scales showed no difference between groups in nausea but a slight increase in dizziness at certain times postdose when DMQ was added to memantine. Beck Depression and Anxiety Inventories and Leeds Sleep Evaluation Questionnaire indicated no difference between groups. Tests of motor function, attention and postural stability generally showed either no difference between groups or improvements on some subscales. Conclusions: There are minimal PK and PD interactions between memantine and DMQ suggesting that they can be safely coadministered without dose adjustments.
Support: Avanir Pharmaceuticals.

NR3-28

EMPLOYEE PERPECTIVE ON PATIENT SAFETY INSIDE A BEHAVORIAL HEALTH CLINIC: A CASE STUDY

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SUMMARY:
Objective: Each year in the United States more than a million people seek substance abuse treatment. However, little if

anything is known about patient safety in this population. The purpose of this project was to assess staff perceptions of risk for clients in publicly funded outpatient substance abuse treatment. Method: Participants were treatment counselors and administrative staff at an ambulatory adult substance abuse treatment clinic. Structured interviews focusing on patient and staff safety were conducted with all staff members. Additionally, paper surveys were completed by staff so they could anonymously describe any safety errors they had witnessed. Results: Approximately half the staff members reported that they had never seen an error. Among those who had seen something, the majority reported only witnessing one. Participants believed that sharing information about errors is important. However, discussion of and reporting of errors were less common. Further, systems-wide approaches would seem to be under-utilized as 63% of respondents indicated that they "strongly agreed" or "agreed" with the statement "After an error occurs, an effective strategy is to work harder to be more careful." Qualitative themes from the interviews included balancing a heavy workload with service excellence, differing perspectives between administrative and clinical personnel, high turnover, difficulties surrounding paper charts, need for specialized training for administrative personnel for the specific patient population being served, and the physical design of the environment. Overall, participants' responses to questions pertaining to their experiences suggested that while they assigned a high priority to patient safety in terms of their beliefs, best practices are not always employed. Conclusions: Patient safety within the context of substance abuse treatment is critical to patient outcomes. This case study demonstrates that systems-level problems can impact staff perceptions of and behaviors pertaining to patient safety. While clinic staff consistently endorsed items indicating they considered patient safety a high priority, there were discrepancies between espoused beliefs and behavior when it came to reporting errors or discussing them with colleagues. These discrepancies may be partially due to perceptions that the substance abuse treatment culture in general provides little support for dealing constructively with errors.

NR3-29

PREDICTIVE VALIDITY OF THE REASONS FOR LIVING INVENTORY IN COLOMBIAN PSYCHIATRY PATIENTS WITH SUICIDE RISK

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SUMMARY:
Background: Although suicide is of great public health significance, its clinical management is complicated. The usefulness in clinical practice of self-report questionnaires is questionable. Objective: The aim is to establish the psychometric properties of the Reasons for Living Inventory in psychiatry patients with suicide risk and its predictability for suicide or suicide attempt. Methods: This was a validation study with a prospective design. Patients who assisted to psychiatry consult and their attending psychiatrist found them to have suicide risk were assessed with the Reasons for Living Inventory, Suicide Behavior Questionnaire-Revised, and a semi-structured interview for suicide risk. At 30 days, follow-up was completed with all patients to establish the predictive validity with suicide attempt or suicide. Results: Two hundred seventy-one patients were surveyed. The mean age was 30.0 years old (SD=12.9). Thirty-seven point three percent of the sample were men. The Cronbach's alpha was 0.95. Five factors were found that explain the 84% of the variance. The Cronbach's alpha was between 0.69 and 0.96 for the factors. The Reasons for Living Inventory showed a correlation of -0.55 with Suicide Behavior Questionnaire-Revised the ($p<0.001$) and -0.32 ($p<0.001$) with the semi-structured interview for suicide risk. With cutpoint equal or higher than 219 with a positive predictive value of 2.5% and a negative predictive value of 93.7%. Test-retest reproducibility was 0.74. Conclusion: The Reasons for Living Inventory was useful for the assessment of psychiatry patients with suicide risk. This scale could be applied as a screening instrument in psychiatry patients with suicide risk to predict suicide attempt in the first month of treatment, because of its good negative predictive value. Otherwise those patients who have a score lower than 219 should be assessed and followed up by a suicide specialized team.

NR3-30

THE ROLE OF PERCEIVED SOCIAL SUPPORT AS A RISK FACTOR FOR ADOLESCENT SUICIDE ATTEMPTS: A SYSTEMATIC REVIEW

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SUMMARY:

Objective: To synthesize research on the predictive use of patient perception of low availability of beneficial social support among adolescent suicide attempts (SA). Method: Relevant articles were identified from PsychInfo and PubMed using the terms "social support," "social support network," "buffering hypothesis," and "perceived social support" combined with "suicide attempt," and "suicide." This was supplemented with articles identified in the reference lists of relevant articles. Criteria for inclusion: measurement of patient's perception of social support, inclusion of a specifically SA population, study conducted with adolescent participants (including high school and undergraduate samples). Results: 11 articles were identified as meeting criteria for inclusion. 7 articles found strong correlations between low perceived social support and SA status as well as high predictive ability of with low perceived social support. Effects were generally stronger for support from family members with mixed findings on the role of support from friends. Three articles did not find a significant association between perceived level of social support and SA status. 1 article reported that low perceived social support from family and from friends differentiated multiple from single attempts. Conclusion: There is some evidence of a strong relationship between patient perception of social support and risk of attempting suicide; however several studies did not find this association. The discrepancy may be the result of covariates included in predictive models or the result of different measures of social support. Future research should investigate the mediating pathways between social support, distress, and attempting suicide as well as identifying factors that predict who benefits from what types of family- and friend-provided support.

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NR3-31

LIAISON OPPORTUNITIES FOR PSYCHIATRY: CHALLENGES IN THE NEONATAL INTENSIVE CARE UNIT

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SUMMARY:

Objective: Families of criticallly ill newborns and hospital staff are both under considerable stress during the infant's stay in the Neonatal Intensive Care Unit (NICU). In addition to concerns about morbidity and mortality, during the long hospitalization, concerns about parental coping and parenting as well as staff stress may arise. We sought to characterize NICU staff perceptions regarding various factors which may lead to more challenging interactions. Method: A cross-sectional survey was devised by multi-disciplinary team members, and was reviewed and piloted with a small group of NICU staff. The survey was distributed to staff at both NICUs in teaching hospitals in a large Midwest city. Survey questions inquired about perceptions of challenging interactions based on: infant medical factors, psychological/psychiatric factors, and social factors. Results: Respondents included physicians, nurse practitioners, and nursing staff (N=163). Results indicated a high likelihood of challenging interactions with parents who had paranoid or delusional thoughts, or who hover, repeat questions, interfere with equipment or perceive the staff as inaccessible. From a medical perspective, staff perceptions of challenging interactions were noted when infants are of high medical complexity, have malformations, recent decompensation, or long duration of stay in the NICU. Finally, from a social perspective, parents who have addictions, or cases in which child protective services are involved were more challenging. There was a striking concordance of views among staff with different training and roles in the NICU. Conclusions: Improved medical care, a shorter length of stay and improved developmental outcome for infants may occur related to decreased stress and better interactions, in this often demanding environment. This further understanding of what staff perceive as stressful, provides support for an educational or interventional role by psychiatrists.

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NR3-32

IMPROVING EFFICIENCY AND ACCESS TO MENTAL HEALTH CARE: INTEGRATING MENTAL HEALTH AND PRIMARY CARE SERVICES AT MCGUIRE VETERANS AFFAIRS

MEDICAL CENTER

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SUMMARY:
Integrating mental health care in the primary care setting has been associated with increased access to mental health services, enhanced clinical and functional patient outcomes and higher patient satisfaction. McGuire Veterans' Mental Health Service has taken a leadership role in co-locating mental health care into the primary care setting. This integration is in keeping with a growing body of research that has demonstrated the effectiveness of integrating mental health with primary care in improving health outcomes. Measuring the effectiveness of these models, i.e. timeliness of treatment, will provide incentives for other VA Mental Health Services to co-locate care. Method: We co-located select providers to provide access to comprehensive mental health care in a primary care clinic. We measured before and after implementation of the clinic included numbers of completed consults and rate of consultation completion time for 6 months. Results: The number of consults increased exponentially from inception of the program during the measurement period. Waiting time for new appointments was shortened from a mean of greater than 14 days to 4 days. Conclusion: Co-location of mental health services in primary care has proven to be an effective means of increasing access and productivity. Traditional constructs that separate specialty care services from the primary care setting lead to increased waits and decreased productivity. Innovative systems redesign within the McGuire has led to dramatic improvements in access to mental health care and efficient use of resources.

NR3-33

CLINICAL INDICES OF INSTITUTIONAL STRESS IN RELOCATING TO A NEW HOSPITAL

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SUMMARY:
Relocating an entire state hospital population to a new facility may pose considerable stress for patients and staff. Preparation for a July 2008 transition of 414 patients (57% hospitalized >2 years) to a newly built state hospital proceeded over 18 months. Clinical staff completed several scales for each patient: BPRS; a 4-point transition scale assessing anticipated and then post-move perceived patient difficulty ("none" to "a lot"); and the single-item/5-point Greystone Intrusiveness Measure (GIM). Data are available for 195 patients both before and after the move. Total BPRS decreased from 41.4+13.0 <mean+/-sd> to 34.7+14.6 (paired t=6.5,df 194,p<0.001), and mean GIM from 2.13+1.28 to 1.78+1.12 (t=3.8,df 193,p<0.001). GIM pre-move correlated with concurrent (r=0.43,p<0.001) and post-move (r=.24,p<0.001) BPRS. Anticipated patient difficulty (35% some/11% a lot) was associated with pre-move BPRS (r=.33;p<0.001) and GIM (r=.28,p<0.001), but to only a lesser degree with post-move BPRS (r=.18;p<0.02) and GIM (r=.16;p<0.03). Reported post-move difficulties (23% some/6% a lot) were less than expected (t=3.3,df 194,p<0.001) and not associated with anticipated difficulties (r=0.06,p ns). Only 37% of those predicted were reported to have post-move difficulty. Post-move difficulty was modestly associated with pre-move BPRS (r=0.21,p<0.01) and GIM (r=0.17,p<0.02), more so with the concurrent post-move BPRS (r=0.46,p<0.001) and GIM (r=0.58,p<0.001). Hospital-wide antipsychotic polypharmacy spiked (to 20% greater use) preceding the move, gradually returning toward baseline in the post-move months. The findings suggest that anticipation of the institutionally transforming event was associated with greater clinical stress than the move itself. The extensive hospital planning may account for both high anticipatory stress and reduced adverse consequences post-move. Clinicians appear to have only a modest ability to predict who will have difficulty with clinical transitions.

NR3-34

IS THERE A DIFFERENCE IN TRANSPORTATION OF PSYCHIATRIC PATIENTS TO THE EMERGENCY DEPARTMENT?

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SUMMARY:
Introduction: Patients with psychiatric complaints may be transported to the emergency department by various means: police, emergency medical services, family or walk-in. It is uncertain whether certain patients are transported to the ED, such as agitated or violent patients transported to the ED by police. The objective of this

study was to determine if there is a difference in the type of psychiatric patient transported via EMS as compared to police, family or walk in. Methods: A retrospective consecutive ED chart and EMS run review performed in an urban community teaching hospital with 60,000 annual emergency department visits was performed. Demographic information, history and physical examination, patient and staff injuries and interventions were reviewed. The participants were patients who entered the emergency department with a psychiatric diagnosis. Patients who were seen with other complaints were excluded. The data analysis included descriptives, frequencies, and ANOVA. Results: 300 patients were evaluated: 102 walk-ins, 66 from EMS, 82 from police and 36 brought by family. Patients transported by EMS were mostly male (51.6%), mean age 41.7 yrs, single (77.3%), African-American (71.2%), regular doctor regular (36.4%), psychiatrist (13.6%), admit diagnosis of drug use (42.4%), patients restrained (68.2%), positive alcohol level (42.4%), discharged home (47.0%), cost $6304 and spent 506 minutes in the ED. Analysis of patients transported by EMS versus police, family or walk ins demonstrated significant difference in having a regular doctor, having a regular psychiatrist, drug use, restrained, high alcohol level, marital status, disposition, age and admitting diagnosis using a significance level of <.01. There was no correlation between transport means and urine drug test positive, type of restraint used, patient's violent intent, gender, ethnicity, insurance, cost or throughput time. Due to the small number of EMS and police interventions and injuries that were documented, we were unable to analyze these data elements. Conclusions: This study found that the EMS system is frequently used to transport intoxicated patients, who do not have a regular psychiatrist, have an admitting diagnosis of drug use and are later discharged from the emergency department. These findings have significant ramifications for EMS planning and training.

NR3-35

PHYSICIAN COMPLIANCE WITH REQUIRED TESTING ON PSYCHIATRIC PATIENTS IN THE EMERGENCY DEPARTMENT

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SUMMARY:

Introduction: A protocol for the testing of psychiatric patients in the emergency department was agreed to by a state task force on medical clearance. This protocol required minimal testing to be performed by the emergency department. The use of this protocol was mandated and implemented in one emergency department. The purpose of this study was to determine the compliance with required testing as part of a medical clearance evaluation. Methods – An educational process was performed to educate the emergency physicians with regard to the mandated medical clearance process. An order set and medical clearance document was updated to reflect the mandated testing. This study was a retrospective, before-and-after study of the number and types of testing conducted over a 12-month period for patients presenting with psychiatric complaints. Results: A total of 150 patients were in the "before" group and 150 in the "after" group. There was no significant difference found between psychiatric patients prior and after in terms of the variable of drug use prior to and after use of routine screens, throughput times, disposition from ED, or cost of ED visit. Although the aggregate amount of testing increased, there was no significant difference seen in the number of tests performed before and after protocol initiation. Conclusion: This study did not demonstrate any significant effect of the initiation of a protocol for mandated testing for all patients presenting with psychiatric complaints.

NR3-36

ACUTE CARE MODEL: A NOVEL WAY OF SERVICE PROVISION IN ADULT PSYCHIATRIC SERVICES

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SUMMARY:

Introduction: Mental health services have gone through numerous changes throughout the world in the last century. In Britain, services have undergone remodelling initiated by the National Service Framework (1999). Recently, with the adoption of New Ways of Working, Acute Care Teams have been created integrating in-patient care with crisis resolution and home treatment team. In this model, there is a dedicated medical team for in-patients to facilitate quicker reviews of in-patients and minimise delays in discharges. Being a relatively new model, the effectiveness is yet to be proven.

Aim: Our aim was to evaluate the impact of the Acute Care Model on the Adult In-patient Services at Clatterbridge Hospital, Northwest England. Method: Data was

collected retrospectively from the hospital information system. The outcome measures were: 1) average length of hospital stay; 2) bed occupancy, defined as the percentage of total number of beds occupied; 3) average length of stay of involuntary admissions; 4) total number of admissions, and 5) the 28 day re-admission rate. Data on the above outcome measures were obtained 15 months before and after June 2007, when the Acute Care Model was introduced. Results: There was a reduction in the average bed days spent in hospital, from 51.8 days to 14.7 days (72% reduction). The bed occupancy decreased by 38%. The average duration of stay for detained patients reduced significantly from 81.44 days to 46.25 days (43.21% reduction). These results were in the background of no increase in the total number of admissions and re-admissions. Conclusions: Health care delivery is complex and varies from country to country. Our data suggests that in the UK, the Acute Care Team has a positive influence on services.

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NR3-37

PREDICTORS OF PSYCHIATRIC DISORDERS DURING PEG-INTERFERON AND RIBAVIRIN THERAPY IN PATIENTS WITH CHRONIC HEPATITIS HCV-CORRELATED

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SUMMARY:

Objective: Peg-Interferon (PegIFN) and Ribavirin (Rbv) therapy in patients with HCV chronic hepatitis have been associated with the onset of psychiatric symptoms and syndromes in approximately 20% of the cases (1, 2). The aim of the present study was to evaluate if patients' baseline score of psychometric scales before Peg IFN or Ribavirin therapy might be predictive of psychiatric visit or treatment in the follow-up. Methods: 70 patients with chronic hepatitis and receiving PegIFN or Rbv were followed up for 48 months recording data about psychiatric visits or eventual administration of psychopharmacological treatment. Sheehan Disability Scale (SDS), Mood Disorder Questionnaire (MDQ), Symptom Checklist-90 (SCL-90) and Internal State Scale (ISS) were administered at baseline. Binary logistic regression was performed to evaluate if total and sub-total scores of the administered scales were predictive of psychiatric visit or treatment. Results: Higher scores at SDS at baseline were predictive of psychiatric visit (OR=1.17, p=0.047), but not of receiving psychopharmacological treatment (OR=1.01, p=0.94), suggesting that cross-sectional measures of patients' functioning might be even more significant for psychiatric outcome than other longitudinal psychopathological features. Conclusions: These preliminary data would indicate that higher scores at SDS may be predictive of psychiatric visit in patients with chronic hepatitis receiving PegIFN or Rbv treatment. Further research with larger samples is warranted to confirm the present data.

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NR3-38

CHILDHOOD SEXUAL ABUSE BY PARENTS AND OTHERS CAREGIVERS: INTRA-FAMILIAL CHARACTERISTICS AND BIOMARKERS OF IMMUNE RESPONSE

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SUMMARY:

Objectives: The aim of this study was to determine if children and adolescents sexually abused by parents

and other caregivers have intra-familial violence and biomarkers of immune response. Methods: In a cross-sectional design, a total of 45 children and adolescents who have been sexually abused and 90 children and adolescents not sexually abused were included. Sociodemographic characteristics were obtained by a questionnaire. Peripheral blood samples were obtained to measure plasma concentration of interleukin-6 (IL-6), cortisol, and CD4+ T lymphocyte and CD8+ T cells lymphocyte counts. Results : Children and adolescents who have been sexually abused showed markedly higher rates of parental divorce/ separation, less religion, lower educational background, more prior family history of substance use, more psychiatric disorder, and more parents with childhood maltreatment when compared with the family characteristics of children and adolescents not sexually abused ($p<0.001$). The most frequent age at onset of sexual abuse ranged from 6 to 12 years old. The frequency of recurrence of sexual abuse among children with age ranging from 2 to 5 years old at onset of sexual abuse was 66%, among the children aging from of 6 to 12 years old the frequency was 80.8%, and among the adolescents aging =13 years was 91.3%. The father was the most frequent aggressor followed by the step-fathers, siblings, uncles and cousins. Cortisol levels and CD4+ T observed in the group of sexually abused were lower than the other group, but not significant differences. Higher to CD4+ / CD8+ rates were associated with sexually abused children and adolescents. Conclusion: The health care professionals and social workers must identify, in clinical practice, family structure and resources that could be associated with childhood sexual abuse and make interventions to break the intra-familial violence cycle, and it is vital that children and adolescents who have been sexually abused by parents and other caregivers are detected early on, so as to minimize immunological consequences.

NR3-39

HYPERSENSITIVITY PNEUMONITIS SECONDARY TO CLOZAPINE THERAPY: A CASE REPORT

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SUMMARY:
Background: There have been several previously published cases of medical problems secondary to complications of Clozapine therapy. There have also been several previously published cases of drug-induced hypersensitivity pneumonitis. Few reports exist, however, of Clozapine-induced hypersensitivity pneumonitis. One case was reported in 1998. In this report, a case of hypersensitivity pneumonitis, presumably Clozapine-induced, is described and discussed. The patient resides in a long-term state psychiatric hospital. She had been on Clozapine therapy that had been efficacious for treating symptoms of her schizoaffective disorder. She was discontinued from Clozapine after the development of hypersensitivity pneumonitis. Objective: The purpose of this study is two-fold. The first is to elucidate the effects of Clozapine on the pulmonary system. The effects of Clozapine on this body system have not received the attention that other body systems (e.g. – cardiac, gastrointestinal) have received. The second is a literature review of the side effects of Clozapine. Methodology: The patient's case notes and reports were reviewed and the patient's psychiatrist was interviewed. For the literature review, a PubMed search for English-language articles published from 1974 to 2009 was conducted. Search terms used were "side effects of Clozapine," "Clozapine adverse effects," "Clozapine and hypersensitivity pneumonitis" and "Clozapine and allergic pneuomnitis."
Conclusion: Pneumonitis is a serious side effect of Clozapine and can undermine the treatment of a patient's psychiatric disorder. In this case, despite the development of chronic respiratory symptoms, the patient initially had no insight and did not report her symptoms for several months after development of her symptoms. Careful evaluation of the patient's medication regimen and discontinuation of Clozapine eventually resolved the patient's pneumonitis. Clozapine is associated with a number of medical problems that affect virtually every body system. Careful attention should be placed on the pulmonary effects of Clozapine as well with vigilance towards the connection between the development of pulmonary changes and Clozapine therapy.

NR3-40

TRANSLATIONAL PHARMACOLOGY OF QUETIAPINE AND NORQUETIAPINE: PRECLINICAL FINDINGS SUPPORT MULTIFUNCTIONAL PSYCHOTROPIC PROPERTIES

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SUMMARY:
Introduction: Clinical studies demonstrate that quetiapine is efficacious in schizophrenia, bipolar mania, bipolar depression, major depressive disorder, and generalized anxiety disorder. The pharmacological basis for this broad range of clinical effects is not completely understood. The current experiments evaluated pharmacological assays investigating the receptor-binding characteristics of quetiapine and norquetiapine (the major human metabolite) and compared these with other atypical antipsychotics and standard antidepressants. Methods: In vitro receptor-binding assays utilized cloned human targets including norepinephrine transporter (NET), dopamine D2 receptor, and serotonin 5-HT1A, 5-HT2A, and 5-HT2C receptors stably expressed in CHO or HEK cell lines. In vitro functional studies included uptake-inhibition assays for NET and GTPgammaS assays for D2/D3 antagonist and 5-HT1A agonist activity. Results: Norquetiapine demonstrated high affinity at 5-HT2A receptors (5 nM) and moderate/high affinity at NET (29 nM) and 5-HT2C receptors (76 nM), while quetiapine had moderate affinity at 5-HT2A receptors (29 nM), weak affinity at 5-HT2C receptors (2800 nM), and lacked appreciable affinity at NET. Both quetiapine and norquetiapine showed moderate affinity at D2 receptors (56 nM and 59 nM, respectively) with moderate/low-potency antagonist activity. Both quetiapine and norquetiapine exhibited low affinity at 5-HT1A receptors (1800 nM and 570 nM, respectively) with low-potency agonist activity. Conclusions: These experiments confirm that quetiapine-norquetiapine have multiple pharmacological effects at targets associated with psychotropic drug action. This combination of effects by quetiapine-norquetiapine at dopaminergic, serotonergic, and noradrenergic targets may explain the antipsychotic, antidepressant, and anxiolytic properties of quetiapine.
Supported by funding from AstraZeneca Pharmaceuticals LP

NR3-41

PREDICTORS OF POST-DISCHARGE ADHERENCE TO ATYPICAL ANTIPSYCHOTIC MEDICATIONS IN ADOLESCENT PSYCHIATRIC PATIENTS

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SUMMARY:
Background: Atypical antipsychotic medications are now used for the treatment of mood disturbances in both adult and adolescent patients. However, there are few data on adherence to these medications in adolescents or its relationship to baseline symptom severity, medication dosage, and eventual treatment response in adolescents. This poster will present the results of a 120-day follow-up study examining the symptomatic, dosing, and treatment response predictors of adherence to antipsychotic medications in adolescent patients. Methods: Adolescent psychiatric inpatients with major depressive disorder, bipolar disorder, and conduct disorder were treated with doctor's choice of either quetiapine (n=60) or aripiprazole (n=96). These patients were rated at hospital admission and 30 and 120 days after discharge with the Young Mania Rating Scale (YMRS) and the Hamilton Depression Rating Scale-17 (HAMD-17). They were also assessed for adherence to treatment at the 30 and 120 days post-discharge. Results. Both antipsychotic medications were found to reduce HAMD-17 and YMRS scores from admission to the final post-discharge assessment, using a mixed model repeated-measures analysis (all $p<.005$). Adherence rates were similar at 30 and 120 day assessments: Quetiapine 53%; aripiprazole 69%; quetiapine 48%; aripiprazole 64%. More severe symptoms at psychiatric admission on the HAM-D and higher discharge doses of medication predicted greater adherence to quetiapine at both 30 and 120 days post discharge. These two variables did not predict adherence to aripiprazole and the baseline YMRS did not predict adherence to either treatment. The average dose of quetiapine administered at discharge was only 83 mg in patients who stopped taking the medication, while patients who remained adherent were treated with an average dose of 240 mg. Implications: Both of these medications were found to have efficacy in this open design. Low doses of quetiapine, probably not aimed at primary psychiatric symptoms such as depression, were associated with development of early non-adherence. However, patients with more severe depression manifested extended adherence to quetiapine and adherence to both medications was quite stable from 30 to 120 days after discharge. These data suggest that patients with clear symptomatic targets may receive greater long-term benefits from atypical antipsychotic medications, possibly justifying the risks associated with these treatments.

NR3-42

THE IMPACT OF PATIENTS' EXPECTATIONS ON CLINICAL RESPONSE: RE-ANALYSIS OF DATA FROM THE HYPERICUM DEPRESSION TRIAL STUDY GROUP

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SUMMARY:
Background: Patient belief about assigned treatment in double-blind trials may influence outcome. We reanalyzed data from a multicenter randomized placebo-controlled comparison trial of St. John's wort (SJW) versus sertraline for major depressive disorder (MDD) to determine whether patients who believed they were receiving active therapy rather than placebo obtained greater improvement of symptoms, independent of assigned treatment. Methods: 340 adults with MDD and baseline scores of 20 or greater on the 17-item Hamilton Depression Scale (HAM-D-17) were randomized to either SJW 900-1500 mg/d, sertraline 50-100 mg/d, or placebo for 8 weeks. At week 8, patients were asked to guess their assigned treatment. The Intent-to-Treat (ITT) sample included 243 subjects with at least one post-baseline visit for which guess data were available. Univariate ANOVA was used to determine whether treatment assignment moderated the effect of belief on clinical improvement. Logistic regression examined whether treatment assignment moderated the effect of belief on response (50% or greater decrease in HAM-D-17 score) and remission (final HAM-D-17 score <8). Results: Significant differences in clinical improvement were found when comparing belief in SJW ($p<0.001$) or sertraline ($p=0.001$) against placebo, with the strongest improvement in the SJW-believing group. Response rates were significantly stronger for subjects guessing either of the active treatments ($p<0.001$ for SJW and for sertraline) versus placebo, and there was also a significant advantage for subjects guessing SJW versus sertraline (Fisher's $p=0.049$). The association between belief and improvement remained significant when controlling for assigned treatment ($p<0.001$). A significant association with response was seen only for treatment guess ($p=0.003$, 95% CI=0.588), but not for assigned treatment. No significant associations were found for remission rates. Conclusions: Patient expectations regarding treatment may exert a greater influence on clinical outcome than the actual medication received. Further research into factors contributing to the observed efficacy of antidepressants is warranted.

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NR3-43
SIMPLIFYING ANTIPSYCHOTIC POLYPHARMACY REGIMENS FOR PATIENTS WITH CHRONIC MENTAL ILLNESS

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SUMMARY:
Introduction: Polypharmacy has been often used in the treatment of psychotic disorders. Evidence supporting this practice is still limited as the clinical efficacy remains unclear. This treatment strategy is limited as it is supported generally by open label studies and case reports. The purpose of this study is to evaluate the usefulness and need of antipsychotic polypharmacy as a treatment. Method: We evaluated patients in the Maimonides Day Hospital Program who were taking 2 or more antipsychotics. In accordance with hopes of better quality of care we switched patients to only 1 antipsychotic. Our sample included 24 patients who were switched. 18 of these patients were followed for six months after the switch. These patients had been on 2 or more antipsychotics for at least 2 months prior to the switch and they had been clinically stable in that they were not hospitalized prior to the switch for a minimum of 2 months.
Results: Eighteen of the patients were followed on a single antipsychotic for 6 months after the switch with 5 having dropped out prior to 6 months. Four of the 5 were discharged from the clinic between 3 to 5 months after the switch and one discontinued her medication after the switch. One patient could not tolerate the switch and remained on polypharmacy. With respect to the 18 patients followed for 6 months we compared psychiatric symptoms at baseline after the switch. Using paired t-tests and Wilcoxon signed ranks test there were no changes in psychiatric symptoms as assessed with the PANSS at 6 months on monotherapy. However waist circumference was significant on monotherapy vs baseline (M=40.53 SD 6.74 vs 42.08 SD $p=.004$). There was a trend toward lower triglyceride levels on monotherapy ($p=.07$). Additionally among the 18 followed the 4 people hospitalized 6 months prior to the switch and one hospitalization within the 6 months follow-up. Conclusion: For the 18 patients studied,

monotherapy did not worsen psychiatric symptoms and brought some improvement in metabolic parameters

NR3-44

EFFECTIVENESS OF SWITCHING FROM ARIPIPRAZOLE TO ZIPRASIDONE IN PATIENTS WITH SCHIZOPHRENIA

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SUMMARY:
Objectives: Aripiprazole and ziprasidone are the second generation antipsychotics with the lowest risk for metabolic disturbances. This study aimed to evaluate the effectiveness of switching to ziprasidone in patients who had insufficient response or intolerance to aripiprazole for treatment of schizophrenia. Methods: Nineteen patients receiving aripiprazole treatment for schizophrenia participated in this open-label, 12-week study. Outcome measures included the Positive and Negative Syndrome Scale, Social and Occupational Functioning Assessment Scale, Calgary Depression Scale for Schizophrenia, Beck Depression Inventory, and Subjective Wellbeing under Neuroleptics Scale. Safety measures included metabolic parameters and scales to evaluate extrapyramidal side effects. Results: After switching to ziprasidone from aripiprazole, significant improvement of scores on the negative symptom subscale of the Positive and Negative Syndrome Scale, the Social and Occupational Functioning Assessment Scale, the Calgary Depression Scale for Schizophrenia, and the Beck Depression Inventory were observed at the study end-point evaluation. Metabolic parameters including body weight, waist and hip circumference, fasting blood glucose, and ALT showed statistically significant decreases. However, serum prolactin levels were significantly increased, and sedation was the most common adverse event. Conclusions: Switching to ziprasidone in patients with schizophrenia who showed insufficient response or intolerance to aripiprazole improved depression, negative symptoms, and metabolic disturbances. However, sedation and hyperprolactinemia were commonly associated with the switch to ziprasidone.

NR3-45

DRUG USE AMONG SOCIAL NETWORK MEMBERS OF PATIENTS WITH CO-OCCURRING SUBSTANCE USE DEPENDENCE AND BIPOLAR DISORDER

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SUMMARY:
Background: Prior research suggests that drug use among peers has a powerful influence on the initiation of drug use (Valente TW, Gallaher P, Mouttapa M, 2004. Using social networks to understand and prevent substance use: A transdisciplinary perspective. Subst Use Misuse. 39, 1685-1712). In this exploratory analysis, we assessed the effect of drug use among social network members on recovery from drug use disorders in patients with co-occurring bipolar disorder. Methods: Patients (n=57) enrolled in a group therapy study completed a social support interview (Clifford PR, Longabaugh R, 1991. Manual for the Important People and Activities Instrument, Center for Alcohol and Addiction Studies, Brown University, Providence, RI) at intake, during treatment, and at 1-year follow-up, as well as measures of substance use and mood. Results: Patients who reported having 1 drug user in their social networks at intake had few days of drug use during treatment and follow-up, as did patients with no drug users. However, naming >1 drug user predicted more days of drug use over the next 15 months. Patients who consistently included multiple drug users in their social networks had more days of drug use per month than those who never or only occasionally reported >1 drug user. Multivariate analysis showed that patients who consistently named multiple drug users in their social networks had a marked increase in drug use over 15 months, while those not naming multiple drug users had a small decline in drug use over time. Mood episodes were not related to drug user or bipolar disorder among social network members. Conclusions: These findings suggest that multiple drug users in social networks of treatment-seeking drug users may be an indicator of poor drug use outcomes; efforts to reduce the association with these drug users may be useful.

NR3-46

L-METHYLFOLATE PLUS SSRI OR SNRI FROM TREATMENT INITIATION COMPARED TO SSRI OR SNRI MONOTHERAPY IN A MAJOR DEPRESSIVE EPISODE

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SUMMARY:
Objective: To evaluate the efficacy of L-methylfolate in combination with a SSRI or SNRI compared to SSRI or SNRI monotherapy from treatment initiation in adults ages 18-70 treated at an outpatient psychiatric clinic for a major depressive episode (MDE). The primary outcome measure was improvement in the Clinical Global Impression- Severity (CGI-S) scores as demonstrated by a = 2 point reduction from baseline. Methods: The study was a retrospective single site chart review. Eligible patients had a primary diagnosis of Major Depressive Disorder (MDD) with a single or recurrent MDE and a CGI-S score of =4. Exclusion criteria included folic acid >400 mcg per day during treatment, psychotic features, bipolar disorder, current or past treatment with VNS, ECT or TMS, and current antipsychotic therapy. Randomly selected charts were divided into a combination group (SSRI or SNRI combined with L-methylfolate 7.5mg-15mg) (n=96) and a monotherapy group (SSRI or SNRI monotherapy) (n=147). Fisher exact test, chi score, student t-test and Kaplan-Meier statistical methods were used to assess group differences in categorical and continuous variables and to compare time to CGI-S improvement between groups. Results: 243 patients (mean age 43.0 + 11.9 years, 160 female) were included in the trial. L-methylfolate in combination with antidepressant therapy was found to be more effective than antidepressant monotherapy in improving CGI-S scores within 60 days. Eighteen point one percent of the L-methylfolate combination group (n=17) showed a =2 point reduction in CGI-S compared with 7.04% of the control group (n=10) (p<0.01). The time to major improvement for patients in the L-methylfolate combination group was significantly (p=0.03) shorter (median 177 days) than that for patients in the antidepressant monotherapy group (median 231). There was no significant difference in side effects between the L-methylfolate combination group and the antidepressant monotherapy group (p=0.21). Conclusion: The significant improvement in CGI-S score from baseline to endpoint in the L-methylfolate group suggests that L-methylfolate when combined with antidepressant therapy from treatment initiation is effective in reducing symptoms of MDD. The shorter time to improvement in the combination group implies that combination strategies from the start of treatment may be a more time-efficient approach than antidepressant monotherapy.

NR3-47

RESPONSE AND SYMPTOMATIC REMISSION WITH OPEN-LABEL COADMINISTRATION OF GUANFACINE EXTENDED RELEASE AND STIMULANTS FOR ADHD

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SUMMARY:
Introduction: Attention-deficit/hyperactivity disorder (ADHD) is often treated with combination therapy with a stimulant and a nonscheduled medication despite limited research supporting the practice. This open-label, 9-week, dose-escalation study assessed the safety of the selective alpha-2a agonist guanfacine extended release (GXR) when used with methylphenidate (MPH) or amphetamine (AMP). This analysis characterizes the proportion of patients with a clinically meaningful response to GXR when used with MPH or AMP in children and adolescents with suboptimal response to MPH or AMP alone. Methods: Subjects were children and adolescents aged 6-17 years with ADHD whose symptoms were inadequately controlled despite use of MPH or AMP for =>1 month. Subjects continued treatment with MPH or AMP and received GXR 1 mg/d. GXR dose was increased by 1 mg/wk to the highest tolerated dose (<=4 mg/d), which was continued through week 6, then decreased. Effectiveness measures included the ADHD Rating Scale IV (ADHD-RS-IV) and Clinical Global Impression-Improvement (CGI-I) scale. Treatment response was defined as a score of 1 or 2 on the CGI-I scale and a reduction in ADHD-RS-IV total score of =>30% at endpoint (the last postbaseline assessment while on treatment). Symptomatic remission was defined as a reduction from an ADHD-RS-IV total score =>24 at baseline to an ADHD-RS-IV total score <=18 at endpoint.
Results: At endpoint, 73.0% (46 of 63) of subjects in the overall study group met the criteria for treatment response. For subjects treated with GXR combined with MPH or AMP, 77.8% (28 of 36) and 66.7% (18 of 27) of subjects met criteria for treatment response, respectively. In the overall study group, 68.1% (32 of 47) of subjects met criteria for symptomatic remission. In the subgroups of subjects receiving GXR combined with MPH or AMP, 69.0% (20 of 29) and 66.7% (12 of 18) of subjects met criteria for treatment response, respectively. Conclusions: A substantial proportion of subjects treated with GXR in combination with a stimulant achieved treatment

response or symptomatic remission. These results suggest a benefit of coadministration of GXR with stimulants for the treatment of ADHD in children and adolescents with ADHD who had suboptimal response to a stimulant alone. A well-designed and controlled study should be performed to further assess the efficacy, safety, and tolerability of coadministration of GXR with stimulants.

NR3-48

EFFECT OF AGE ON ARMODAFINIL PHARMACOKINETICS IN HEALTHY SUBJECTS

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SUMMARY:

Background: The pharmacokinetics of medications may differ with age due to changes in physiological function, including decreased hepatic function, which can affect systemic exposure. The non-amphetamine, wakefulness-promoting medication, armodafinil, the longer-lasting isomer of modafinil, undergoes substantial hepatic metabolism. Armodafinil has been shown to significantly improve wakefulness in patients with excessive sleepiness associated with treated obstructive sleep apnea, shift work disorder, or narcolepsy. Armodafinil is also being studied in patients with excessive sleepiness associated with jet lag disorder or traumatic brain injury and in patients with bipolar disorder or schizophrenia. The present study evaluated the effect of age on the pharmacokinetics of armodafinil at steady state. Methods: Healthy men, aged 18-45 years (n=25) and 65 years and older (n=25), received once-daily armodafinil for 7 days. Armodafinil was administered at 50 mg on day 1, 100 mg on day 2, and 150 mg for the remaining 5 days. Beginning on day 7, pharmacokinetic samples were taken over 72 hours. Ratios of the geometric means of the two age groups and 95% confidence intervals were calculated for area under the plasma concentration-versus-time curve for 1 dosing interval (AUC0-t) and maximum plasma concentration (Cmax). Tolerability was assessed throughout the study.

Results: Pharmacokinetic data from "young" subjects aged 18-45 years (n=25), "young elderly" aged 65-74 years (n=17) and "old elderly" aged >/=75 years (n=7) were analyzed. In the combined elderly group (65 years and older), statistically significant increases were observed in both the AUC0-t (1.14, 95% CI: 1.03, 1.25) and Cmax (1.15, 95% CI: 1.08, 1.24) ratios relative to the young subjects. Steady-state AUC0-t and Cmax were approximately 10% higher in young elderly and 27% higher in old elderly subjects compared with young subjects. Armodafinil was generally well tolerated. Conclusions: At steady state, systemic exposure to armodafinil is increased in elderly subjects, especially subjects aged >/=75 years, compared with young subjects. Dose adjustment should be considered when administering armodafinil to elderly patients.

FUNDING SOURCE: Sponsored by Cephalon, Inc.

NR3-49

AN OPEN-LABEL, 8- WEEK, FLEXIBLE DOSE TRIAL OF ESCITALOPRAM (LEXAPRO®) IN COMORBID MAJOR DEPRESSION WITH MULTIPLE SCLEROSIS

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SUMMARY:

Aim: The primary objective of this study is to assess the effectiveness and tolerability of escitalopram in improving symptoms of Major Depression in patients with Multiple Sclerosis (MS). The secondary objective is to assess improvement in the quality of life. Background: MS, a demyelinating disease of the central nervous system, is a chronic disabling disease of the central nervous system, affecting 1 in 1000 people in Western countries. Persons who have MS seem to have a higher prevalence of depression and have been associated with decreased adherence to treatment, functional status, and quality of life. Methods: Fifteen subjects between the ages of 18 and 70 years with documented MS, a DSM-IV episode of non-psychotic Major Depression and a HAMD score of =14 score on the 17-item scale were included in this study. Patients with a neurologically confirmed diagnosis of MS underwent consenting, diagnostic verification recording of vital signs (height weight, pulse, blood pressure, body temperature, and respiratory rate), laboratory testing (CBC with differential, liver, kidney and thyroid function tests, serum electrolytes, lipid profile) and EKG. Subjects went on to receive escitalopram (flexible dose schedule) 10-20mg in an open-label fashion for 8-weeks. No other psychotropic medications was permitted during the study. Participants were monitored for efficacy with

Hamilton Depression Rating Scale- 17-item (HAM-D 17 item), Clinical Global Impression of Severity (CGI-I and CGI-S) and Improvement, Beck Anxiety and Depression Inventory (BDA and BDII), Expanded Disability Status Scale (EDSS) and McGill Quality of Life Scale (McQLS). Safety evaluations including vital signs, neurological exam and weight, and spontaneously reported adverse events were performed. Compliance was measured by pill count. Results: Preliminary Analysis showed that 66% of patients went on to achieve response which was defined as a 50% or greater reduction in HAMD- 17 scores from baseline to end of treatment. 50% went on to achieve remission defined as a HAMD-17 score. No significant changes were evident on the Beck Anxiety Inventory or the McGill Quality of Life Indices. Conclusions: There has not been much evidence that antidepressants are useful in treating depression in patients with MS. Results from this small sampled study demonstrates that escitalopram maybe a viable treatment option for this population.

NR3-50

EFFECT OF ARMODAFINIL ON QUETIAPINE PHARMACOKINETICS IN PATIENTS WITH SCHIZOPHRENIA

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SUMMARY:

Background: Armodafinil is being studied as an adjunctive treatment for negative symptoms in patients with schizophrenia. Quetiapine, an atypical antipsychotic, is metabolized via cytochrome P450 (CYP) 3A4, an enzyme known to be induced by armodafinil. This open-label study evaluated the effect of daily administration of armodafinil on the steady-state pharmacokinetics (PK) of quetiapine in patients with schizophrenia. Methods: Adult patients with clinically stable schizophrenia (n=38) who were receiving stable daily doses of quetiapine (>/=300 mg/d for >/=28 days) were eligible for enrollment. Quetiapine was administered at 2100 on each study day. Armodafinil was administered at 0800 daily starting at 100 mg on Day 7 and was titrated in 50 mg increments every 2 days starting on Day 8 until the 250 mg target dose was reached. PK sampling was performed over a 24-hour period following quetiapine administration on Days 5 and 38. Quetiapine PK parameters were estimated using noncompartmental methods and results were dose-normalized, as appropriate, to 300 mg. Schizophrenia symptoms were monitored using the Positive and Negative Syndrome Scale (PANSS) and the Scale for the Assessment of Negative Symptoms (SANS). Tolerability was assessed throughout the study, including a follow-up 7-10 days after discharge on Day 40. Results: Twenty-five patients were evaluable for PK comparison following multiple-dose administration of armodafinil concomitantly with quetiapine compared with quetiapine alone. Statistically significant decreases in the maximum plasma concentration (Cmax) of 45% and in the area under the plasma concentration-versus-time curve over 24 hours (AUC0-24) of 42% were observed. The most common adverse event reported was dizziness (14%) versus headache (24%) following administration of quetiapine alone compared with coadministration of quetiapine and armodafinil, respectively. No change was seen in schizophrenia symptoms as assessed by PANSS and SANS.

Conclusions: Adjunctive armodafinil treatment results in a decrease in steady-state exposure to quetiapine in patients with schizophrenia. Patients should be monitored and quetiapine dose adjusted if necessary.

Funding Source: Sponsored by Cephalon, Inc.

NR3-51

BETAHISTINE SAFELY MITIGATES OLANZAPINE ADVERSE: ROLE OF HISTAMINE RECEPTORS IN WEIGHT GAIN AND SOMNOLENCE

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SUMMARY:

Background: Second generation antipsychotic drugs (SGAs) are highly efficacious for treatment of schizophrenia and bipolar disorders. Yet their benefit is accompanied by rapid and extensive weight gain, mainly attributed to inhibition of hypothalamic H1 receptors (H1R). The risk of exposing psychiatric patients to obesity and diabetes has prompted issuance of warning labels by the FDA and publication of consensus guidelines by the NAASO, the ADA and the APA. Betahistine is a centrally acting H1R agonist and H3R antagonist used for the treatment of vertigo. Aim: To investigate the role of histaminic receptors in Olanzapine-induced weight gain and somnolence in humans through administration of Betahistine. Clinical Outcomes: (1) A Phase Ib double blinded study was conducted to assess the safety, drug-drug interactions and pharmacokinetics of betahistine and olanzapine co-administration. Subjects were randomized to betahistine

(144 mg/day) or matching placebo for a one-week run-in period, followed by co administration of olanzapine (up to 7.5 or 10 mg/day) for three weeks. Betahistine was safe and well-tolerated throughout the study. Adverse events (AE) observed in the Betahistine/Olanzapine arm were similar in frequency, type and severity to AE in the placebo/Olanzapine arm and were mainly related to the Olanzapine. Furthermore, analysis of the intent to treat (ITT; N=46) population revealed a significantly lower weight gain in the Betahistine/Olanzapine group (1.2+1.3 Kg) when compared to the placebo/Olanzapine arm (1.9 + 0.9 Kg; $p<0.05$). Moreover, the frequency of subjects in the placebo/Olanzapine arm that gained > 2.0 Kg was 52%, was substantially higher when compared to the Betahistine/Olanzapine arm (23%; $p= 0.043$). Somnolence, as measured by Epworth Sleepiness Scale increased by 1.7 + 2.3 units in the Betahistine group and by 3.6 + 3.1 units in the placebo group ($p=0.041$). (2) A double-blinded, randomized, placebo-controlled Phase II study, to evaluate safety and weight mitigation by Betahistine (48 mg/day) when administered for 16 weeks in addition to olanzapine in patients suffering from schizophrenia, was terminated mid-way (N=35) due to low recruitment. Nevertheless, Kaplan-Meier analysis of the time it took subjects to reach >7% weight gain, showed smaller weight gain rate in the treatment group (p-value = 0.055). Betahistine did not interfere with the antipsychotic effect of Olanzapine as measured by PANSS.

NR3-52

AN IN-DEPTH CARDIOVASCULAR STUDY OF LONGER-TERM TREATMENT WITH LISDEXAMFETAMINE (LDX) IN ADULTS WITH ATTENTION DEFICIT HYPERACTIVITY DISORDER (ADHD)

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SUMMARY:

Background: Short-term safety and efficacy data supports stimulant medications to be among first line treatment in adult ADHD. However, there is specific concern regarding the cardiovascular safety of these agents. Few investigations have employed methodology outside of office-based vital sign assessments (Schubiner, 2006). The aim of this study is to use novel methodology to assess the cardiovascular impact of an extended-release amphetamine in a sample of healthy adults with ADHD. Methods: Subjects are a well-characterized sample of healthy adults with DSM-IV ADHD. Excluded are subjects with significant medical or psychiatric conditions. This study is IRB-approved; all subjects completed informed consent. Study physicians prescribe LDX to maximum daily dose 70mg, during 6 months of open treatment. Medication is provided. Subjects discontinue due to lack of efficacy, non-compliance or serious adverse experiences. Prior to medication, vital signs, electrocardiogram (ECG), laboratories and non-invasive cardiopulmonary exercise testing (CPET) are completed. All assessments are repeated at endpoint/early termination. We hypothesized that CPET would be informative as to the cardiovascular response to exercise on LDX, without significant changes in ventilatory and gas exchange measures. All analyses were last observation carried forward. An alpha-level of 0.05 was used; all statistical tests were two-tailed. Results: 15 subjects who signed consent, 8 subjects completed the study. No subject discontinued due to cardiovascular adverse effects. Mean age at baseline was 36 years. LDX was effective; mean ADHD rating score significantly decreased at endpoint ($p<0.001$). At rest, heart rate and oxygen uptake were significantly increased at endpoint ($p<0.05$). At peak exertion, cardiovascular variables were not significantly changed. Heart rate after exertion was significantly increased at endpoint; less change (recovery) towards resting rate ($p<0.05$). There were no clinically significant changes in ventilatory or pulmonary variables, nor laboratories or electrocardiogram. Conclusions: This pilot study assessed the longer-term cardiovascular impact of lisdexamfetamine (LDX) in a small sample of healthy adults with ADHD. Consistent with our hypotheses, heart rate recovery was significantly reduced at study endpoint. Also consistent was the lack of significant differences in other CPET parameters, laboratories and electrocardiogram.

NR3-53

POINT OF CARE LITHIUM MONITORING: QUANTITATIVE DETECTION OF LITHIUM USING MICROCHIP CAPILLARY ELECTROPHORESIS

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SUMMARY:

Objective: The objective of this study was to demonstrate the ability to measure lithium levels outside a laboratory

in one droplet of blood by using an office-based or home-based portable device using novel lab on a chip nanotechnology. New micro-technologies enable minimal invasive techniques without clinical laboratory facilities, providing direct feedback of lithium levels to patient and clinician. Method: Lithium values in whole blood (n=283), and fingerstick blood (n=386) samples have been measured in a method comparison study. For each measurement one droplet of blood is injected in a new disposable chip. The different ions in the blood sample are separated under influence of an electric field. Concentrations are determined using conductivity detection. Lithium levels from the same blood samples were also conventionally measured using flame photometry on an IL 943 Flame Photometer. Results: We found good correlation between measurements obtained by the new and conventional techniques. For serum (corr. coeff R=0.99), whole blood (corr. coeff R=0.96) and finger stick blood (corr. coeff tbd, currently being analyzed) results are within 0.1 or 10% mmol/L at 95% confidence. These results are within CLIA standards for clinical use. Conclusion: It is possible to reliably measure lithium levels in only one droplet of serum or whole blood using a small portable microchip capillary electrophoresis system. The current detection range is from 0.2 mmol/L through 4.0 mmol/L. Accuracy and precision are within CLIA standards for clinical use. Discussion: The use of lithium is still restricted due to the small therapeutic window and the necessity of laboratory facilities. Currently the costs of this new technology are still higher than conventional measurement. The results of our study enable the further development of a point of care diagnostic tool for lithium detection at home or in clinical settings, either for routine monitoring or frequent instant testing under special circumstances such as pregnancy, concurrent medical illness, or signs of toxicity. With the point of care technology, safer use of lithium is possible even when laboratory facilities are not easily available.

NR3-54

THE MAINTENANCE RATE OF ARIPIPRAZOLE AMONG SCHIZOPHRENIC PATIENTS WITH DIFFERENT ILLNESS DURATION AND EXPERIENCE OF NEUROLEPTICS DURING 6 MONTHS

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SUMMARY:

Object: The illness duration and experience of neuroleptics can be predictors in the treatment response to antipsychotics in schizophrenic patients. Aripiprazole is known as a dopamine partial agonist or stabilizer which is unique compared to the other conventional or atypical antipsychotics. We investigated the effectiveness of aripiprazole in schizophrenic patients with different illness duration and experience of neuroleptics. Method: We reviewed medical records of 49 patients who were diagnosed as schizophrenic according to DSM-IV-TR criteria and newly prescribed with aripiprazole. We collected the following data from each patient: age, sex, illness duration (year), past treatment history, clinical global impression – severity (CGI-S) scale (baseline and endpoint), maintaining state of aripiprazole at end point. We stratified each patient into one of three groups (acute neuroleptic-naïve (ANN): N=16, acute neuroleptic-experienced (ANE): N=14, and chronic neuroletpic-experienced group (CNE): N=19) according to illness duration and past treatment history. We analyzed the differences in maintenance rate and mean change of CGI-S score among three groups. Result: In all three groups, aripiprazole showed significant clinical improvement (mean CGI-S score change >2, p <.001). There were no significant differences in efficacy of aripirpazole among the three groups (p=.652). And aripiprazole showed high maintenance rate in both the ANE (86%) and CNE (68%) groups. Although statistically not significant, ANN group showed relatively lower maintenance rates (44%) than the other two groups (p=.051). Conclusion: Aripiprazole can be an equally useful antipsychotic agent in treatment of schizophrenic patients with variable illness duration and neuroleptic-experience due to its unique dopaminergic action mechanism. The reason of lower maintenance rates of aripiprazole in ANN group in our study can be explained by the lack of treatment experience and poor insight other than drug effectiveness.

NR3-55

INFLUNCE OF ANTIPSYCHOTICS AUGMENTATION ON TREATMENT ADHERENCE IN TREATMENT OF MAJOR DEPRESSIVE DISORDER WITH ANTIDEPRESSANTS

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SUMMARY:
Objectives: Since the 1950s, various antidepressants have been used for treatment of depression, but satisfactory remission and recurrence rates have still not been achieved. Antipsychotics augmentation therapy is one of the new treatment strategies that has been suggested to increase effectiveness. This study was designed to evaluate the differences of treatment adherence between an antipsychotics augmentation group and and antidepressants monotherapy group through retrospective chart review. Methods: We chose olanzapine as the antipsychotics augmentation agent, which is the first FDA approved agent as olanzapine/fluoxetine combination in treatment of bipolar depression. Venlafaxine XR, which is a serotonin norepinephrine reuptake inhibitor was chosen because it has few side effects and is suggested to be more effective than SSRIs for the treatment of severe depression. We collected the data from medical records of patients who visited the psychiatric outpatient clinic of Bongseng Hospital and were prescribed venlafaxine XR alone, or a combination of venlafaxine XR and olanzapine on their first visit, between August 2006 and August 2008. In each group, 40 medical records were collected consecutively. The degree of adherence was measured by medication possession ratio (MPR) and actual days of coverage. The degree of CGI-I, CGI-S scores and dosages of each medication were also assessed monthly for 6 months. We used chi-square test and t-test to analyze group differences in demographic data and treatment adherence. Results: In cases of one visit, 10 patients were from augmentation group and 15 patients were from monotherapy group. In cases of patients who had been treated at other hospitals, 25 were in the augmentation group and 15 were in the monotherapy group (p=0.038). The mean of first dosages of venlafaxine XR was higher in the monotherapy group than in the augmentation group (48.7 vs 37.5mg) (p=0.003). All olanzapine dosage was 1.25mg except one case. Follow-up times were higher in augmentation group than monotherapy group (8.05 vs 5.32 times) (p=0.004). CGI-S score of augmentation group was significantly greater than of monotherapy group. (4.5 vs 3.9) (p<.001). CGI-I score of augmentation group was significantly lower than monotherapy group at the end of the first month (1.88 vs 2.54) (p=0.002). The augmentation group showed significantly higher MPR than monotherapy group (0.5795 vs 0.4057) (p=0.03). In actual days of coverage, the augmentation group was also higher than the monotherapy group.

NR3-56
PANAX GINSENG AUGMENTATION OF SUBSYNDROMAL DEPRESSIVE SYMPTOMS (SSD) IN SCHIZOPHRENIA: A MULTI-SITE RCT STUDY

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SUMMARY:
Introduction: Recent studies highlight Subsyndromal Depressive Symptoms (SSD) in schizophrenia carry substantial impairment. There is a paucity of controlled studies targeting neurosteroids in SSD.We hypothesize that Panax Ginseng, the prototypal phyto-neurosteroid, modulating Protein Kinase C and NMDA-glutamate systems, is efficacious in SSD in schizophrenia. Objective: To examine efficacy and safety of Panax Ginseng (PG) in improving the SSD in schizophrenia and to delineate the link of baseline neurocognition and SSD. Method:: In our 8-week randomized placebo-controlled dose-finding trial, we recruited schizophrenia patients with HAM-D > 8 maintained on atypical antipsychotics. Subjects were randomized into 3 groups: 1) Placebo; 2) 100 mg po once daily Ginsana-115 (standardized formulation of Panax Ginseng capsules, Boehringer-Ingelheim-Pharmaton, Switzerland); and 3) 200 mg po once daily Ginsana-115. For SSD, we administered a 31-item HAM-D for SSD measure consisting of key domains related directly to SSD: depressed mood, guilt feelings and hopelessness, computerized Neuro-cognitive Screening (NCS), and SANS, BPRS, at weeks 0, 2, 5 and 8. Results: We randomized 39 subjects for 3 groups: mean age 38.0 +/- 9.9 yrs. At baseline, an inverse correlation was found between global NCS score and Anxiety/somatization subscale HAM-AS (Pearson correlation coefficient -0.57) {p < 0.000). Attention working memory task inversely correlated significantly (p < 0.001) with HAM-AS subscale: the higher level of anxiety-depressive symptoms, the worse the cognitive performance. Between-subject t-test showed Ginsana-200 mg significantly (p< 0.05) reduced total HAM-D score (Cohen's effect size 0.90), and significantly reduced Flat Affect of SANS (Cohen's effect size 0.87). One hundred mg Ginsana-115 improved facial memory NCS. Within subject analysis indicated that Ginsana-115 at daily dosage of 200 mg significantly (P < 0.05) improved global SANS and BPRS. Response rate (50% reduction in HAM-D) was 50% for 200 mg Ginsana-115 vs 9 % for placebo. No serious adverse events

were reported: constipation and dry month occurred in <10% of subjects. Conclusion: Ginseng appears to be a safe and promising augmentation therapeutic strategy for SSD in schizophrenia. Supported by Stanley Medical Research Institute MD USA.

NR3-57

LONG-TERM WEIGHT LOSS EFFECT OF ADJUNCTIVE ZONISAMIDE IN PSYCHIATRIC PATIENTS: A RETROSPECTIVE CHART REVIEW

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SUMMARY:

Background: It is well known that a lot of psychotropic medication is associated with weight gain and metabolic syndrome. However, the efficiency and safety of pharmacological treatments for obesity in patients with psychiatric disorders have not yet been established. Some studies on zonisamide have demonstrated its potential efficacy of weight loss. Therefore the authors examined the long-term efficacy and tolerability of zonisamide by a retrospective longitudinal analysis of a large series of patients who take psychotropic medications. Methods: The data were based on the systemic review of the charts of the psychiatric outpatients who had taken zonisamide for treatment of migraines, binge eating, and obesity. Eighty-two patients who reported unwanted weight gain from the introduction of psychotropics were included, who met DSM-IV criteria for schizophrenia (N=25), bipolar disorder (N=10), major depressive disorder (N=30), and anxiety disorder (N=17). The primary efficacy of zonisamide for weight control was evaluated by body mass index (BMI) and the second measures of safety and tolerability were discontinuations for adverse events and the severity of psychiatric symptoms, which were assessed by CGI-S thorough chart review. Results: The mean age was 41.9 ± 13.1 years old. The mean final dose of zonisamide was 143.3 ± 70.6 mg/day ranging from 50 mg to 300mg for a mean treatment duration of 7.1 months. In this study, zonisamide demonstrated a significant reduction in BMI from 27.6 ± 4.5 to 26.9 ± 4.6 (P<0.001) with a mean weight loss of 0.8 ± 1.7 kg. A significant reduction in CGI-S score was observed from 3.84 ± 0.87 to 3.30 ± 0.81 (P<0.001). Twenty-two percent (N=18) of patients reported side effects of zonisamide and 10 patients discontinued zonisamide treatment early due to side effects. Conclusion: Adjuvant treatment with zonisamide showed a significant weight loss in the patients who had suffered from unwanted weight gain due to psychotropic medications. Moreover, its treatment is generally safe and well tolerated without negative effect on the psychiatric symptoms.

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NR3-58

MENTAL STATUS IN NMS

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SUMMARY:

Objective. Diagnosis of the neuroleptic malignant syndrome (NMS) by DSM-4 criteria relies primarily on biological markers. We explored the correlations of changes in mental status to NMS diagnosis in a sample of suspected NMS cases. Method. Data from a national survey of suspected NMS cases from various centers across the US and Canada were analyzed (N=194, age 16 to 90 years, average = 42.5, SD=17.2; 123 men, 71 women). Their diagnoses involved mostly schizophrenia (24.7%), bipolar mood disorder (15.5%), organicity (14.4%), unspecified psychosis (10.3%), or depression (8.8%). We examined the phi correlations of NMS diagnosis to the following 13 parameters of mental status: Decrease in level of consciousness, Drowsiness, Alertness, Incoherence, Delirium, Coma, Agitation, Confusion, Mutism, and being Withdrawn, Disoriented, Obtunded, or Irresponsive. Results: Almost all patients with suspected NMS (171 of 194, i.e., 88.1%) met DSM-IV criteria for NMS. Changes in mental status (as evidenced by at least one of the 13 signs) were present in approximately 65.5 % of the 194 patients with suspected NMS and in 67.7% of those classified as NMS by DSM-IV. Yet none of the correlations of the 13 parameters of mental status to the diagnosis of NMS was significant (all were at p>.05, 2-tailed). The correlations were extremely low (phi<.10)

and/or negative (e.g., with delirium, phi= -.12). The correlation of overall mental status (sum of all 13 signs) to NMS diagnosis was low and nonsignificant (point biserial r=.08, p=244), perhaps because we statistically compared the patients classified as NMS by DSM4 only to patients with very similar syndromes initially suspected to be NMS (these may also often show changes in mental status): no normal control group was used. Conclusions. The low and non-significant correlations imply that changes in mental status are not unique to NMS: they emerge also in similar syndromes, thus making the differential diagnosis arduous.

NR3-59

WOMEN'S AND MEN'S DEPRESSIVE SYMPTOMS AND FUNCTIONAL RECOVERY FOLLOWING CORONARY ARTERY GRAFT (CAG) SURGERY

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SUMMARY:
Objective: To examine depressive symptoms in men and women during early home recovery following CAG surgery.
Method: Consecutive 128 patients (mean age=63.3 ± 9.8 years, 98 men and 30 women) who gave informed consent were examined in a follow-up visit a month after discharge from a Canadian University Hospital. Their functional recovery, fatigue, vigor and attendant symptoms of depression, anxiety, 'state' pessimism and physical distress were assessed prospectively with rating scales. We first statistically estimated the best predictors of Functional Status, Fatigue and Vigor via regression analyses. Then statistical correlations of individual depression scale items with key predictors and outcomes were explored separately for both sexes. We controlled for the effect of age, left ventricular ejection fraction, number of grafts and presurgical symptomatic status via partial correlations. Results: Affective distress (p<.005) (especially state pessimism as defined by Beck's cognitive triad), physical distress (p<.005) and its statistical interaction with state pessimism (p<.02) emerged as significant correlates of physical functional recovery (e.g., activities of daily living). With respect to gender differences, depressive symptoms were more likely (p<.05) to be associated with Physical Distress and Fatigue measures in males and Vigor measures in females. Women significantly (p<.05) more often than men expressed pessimistic cognitions (i.e.have no control over anything, feel maimed or disfigured, a negative view of self and discouraged about the future). Their gloomy views of life's worth significantly (p<.01) correlated with measures of Fatigue, Vigor and physical functional recovery. Conclusions: Suboptimal functional recovery is associated with higher levels of depression and of perceived physical distress: psychological counseling early in recovery could play a preventative role, especially if tailored to gender-specific concerns.

NR3-60

PSYCHOLOGICAL DISTRESS IN WOMEN WITH DUCTAL CARCINOMA IN SITU AND EARLY INVASIVE BREAST CANCER

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SUMMARY:
Objective: There is accumulating evidence that women with non-invasive breast cancer (Ductal Carcinoma In Situ, DCIS) have elevated distress similar to that of women with later stage disease. Surgery, radiation and chemotherapy are associated with the increased anxiety and depression in breast cancer patients. We examined mood and psychiatric symptoms in women with DCIS (Stage 0) and Early Invasive Breast Cancer (EIBC, Stages I-II). Methods: Seventy women with early stage breast cancer (Stages 0-II) were recruited from out-patient clinics. Mean age was 57.4. Seventeen percent were diagnosed with DCIS, 49% with Stage I, and 34% with stage II. Participants underwent a structured interview and were administered the Brief Symptom Inventory (BSI), Profile of Mood States (POMS) and a measure of physical functioning. Women with DCIS were compared with women with EIBC to determine if there were differences in treatments, demographic characteristics, prior psychiatric history, time since diagnosis and other variables. Linear Model Multivariate Tests were run to see if any factors predicted scores on BSI and POMS. Then patient scores on each scale were compared with normative data from non-patient controls and psychiatric outpatients. Results: There were no differences between women with DCIS and EIBC on race, age, marital status, education, previous psychiatric history or substance use, and time since diagnosis. There were differences in treatments between groups. Women with DCIS were more likely to receive lumpectomy while women with EIBC were more likely to receive mastectomy, axillary dissection, and chemotherapy. Breast

cancer stage did not predict distress, but lumpectomy and mastectomy did. Lumpectomy was significantly associated with anxiety, depression, and hostility on the BSI. Mastectomy was significantly associated with anxiety and depression on the BSI. Women in our sample had distress falling between that of normal women and psychiatric outpatients. Conclusions: Our findings support the work of others that women with DCIS have distress comparable to women with EIBC, and that treatments affecting the breast (lumpectomy and mastectomy) are associated with breast cancer patients' distress. There may be differences in the nature of the distress, for example women with lumpectomy scored higher on anger. Further work needs to be done to better understand the distress and create interventions to reduce it.

NR3-61

DOES A SELF-REPORT MEASURE (RSQ) AND THE AAI EVALUATE THE SAME DIMENSION OF SECURE ADULT ATTACHMENT?

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SUMMARY:

Objective: To assess the correlation between self-report and the AAI as measures of attachment in women 20-30 years old. Introduction: Since its entry into psychological assessment, attachment in adults has generated a variety of measures purporting to evaluate the same construct. Literature reviews comparing self-report and the AAI indicate that there are inconsistent findings in correlating these measures (Roisman 2007). Method: We analyzed data from a current study on attachment in adult women, using the coherence of mind measure from the AAI, which is considered the principal score in assessing an individual's state of mind with respect to attachment (Dykas et al. 2006) and the following scores from the Relationship Style Questionnaire (RSQ), a commonly used self-report measure of attachment: secure, preoccupied, dismissing, and fearful (n=10). Data was analyzed using SPSS 16.0 bivariate correlation analysis using a two-tailed test of significance.

Results: The mean RSQ secure score was 3.78 (SD=.61) and the mean dismissing score was 3.72 (SD=.76). The mean AAI coherence of mind score was 6.25 (SD=1.80) and did not correlate with secure attachment in RSQ. Dismissive attachment was significantly positively correlated with coherence of mind (Pearson's r = .665, p < .05). Within the RSQ, secure attachment was negatively correlated with dismissive attachment (Pearson's r = -.319, p<.05). Conclusion: The coherence of mind dimension of the AAI in women 20-30 years old may not be measuring the same secure dimension in the RSQ. Further research is needed to understand what underlying constructs these measures identify and how they might differ across populations.

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NR3-62

ECONOMY AND SUICIDE IN COLOMBIA: RELATIONSHIP BETWEEN MACROECONOMIC VARIABLES AND SUICIDE RATE

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SUMMARY:

Objective: To establish the association between the main macroeconomic variables and suicide rate in Colombia since 1994 to 2008. Method: An ecological study was done to explore the relationship between main macroeconomic variables (Gross Domestic Product, GDP, GDP growth, unemployment rate, no formal employment rate, inflation rate, GINI coefficient, poverty index, nominal annual devaluation, US dollar market exchange rate, public spending on health as proportion of the GDP and active interest rate) and suicide rate in Colombia. A multiple lineal regression was applied to identify and adjust significant associations on variables which showed Pearson correlation (r) higher than 0.300 and p lower than 0.050. Results: Suicide rates ranged from 4.03 to 5.26 per 100,000 inhabitants. Significant associations with suicide rate were poverty index (beta standardized = 0.636) and nominal annual devaluation (beta standardized = 0.284), after adjusting for unemployment rate. Conclusions: Poverty index and nominal annual devaluation are related to suicide rate. Changes in country economics may influence some mental health indicators.

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NR3-63

FROM WINDY STORM TO TOTAL DARKNESS: THE EFFECT OF A COMMUNITY-WIDE BLACKOUT ON ED VISITS AND PSYCHIATRIC ADMISSIONS TO AN URBAN UNIVERSITY HOSPITAL

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SUMMARY:
Background: On September 14th, 2008, the remnants of Hurricane Ike brought 70 miles-per-hour winds to Ohio, leaving nearly 1 million citizens without electricity. Studies assessing the effect of natural disasters and blackouts on visits to emergency department and admissions to psychiatry are limited, and additional research would increase understanding of this issue. Research question: When a blackout occurs, how is the frequency of ED visits and psychiatric admissions affected? Objective: To study the effect of a community-wide blackout on the number of subsequent ED visits and psychiatric admissions. Hypothesis: Presence of blackout will result in a difference in the frequency of ED visits and psychiatric admissions on days affected compared to the daily mean number of ED visits and psychiatric admissions during September 2008. Methods: Study was approved for exemption by University Hospitals Case Medical Center IRB. Anonymous patient census data stored regarding daily number of ED visits and psychiatric admissions at University Hospitals Case Medical Center, Cleveland, Ohio, was collected. The time period of interest was September 2008. The number of ED visits and psychiatric admissions occurring the night of the blackout and the first full day was compared to the mean number of ED visits and psychiatric admissions for September 2008, and a Z-score was used to assess for statistical significance.
Results: On September 14th, 2008 there were 94 ED visits, and 84 ED visits on September 15th. The September 2008 mean number of ED visits was 85.5. The two-tailed Z score for September 14th is 2.884, and for September 15th is 2.327, with corresponding statistically significant p-values <0.005 and <0.02, respectively. On September 14th, 2008 there were 0 psychiatric admissions, and 3 psychiatric admissions on September 15th. The September 2008 mean number of ED visits was 2.13. The two-tailed Z score for September 14th is 8.455, and for September 15th is 3.45, with corresponding statistically significant p-values <0.003 for both days. Conclusion: There is a statistically significant increase in ED visits the night of the blackout, and statistically significant increase in psychiatric admissions the first full day following the blackout. There is a statistically significant decrease in ED visits the first full day after the blackout.

NR3-64

WITHDRAWN

NR3-65

A COMPARISON OF RAPID TITRATION QUETIAPINE AND HALOPERIDOL IN AGITATED ADULTS IN AN EMERGENCY SETTING

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SUMMARY:
Background: Intramuscular (IM) benzodiazepines and/or haloperidol alone or with benzidiazepine are frequently used to treat agitation. Based on emerging literature regarding quetiapine use for the control of anxiety we examined quetiapine use as a possible alternative in selected cases. Methods: This study was a single-blind randomized study comparing quetiapine PO (300 mg) with a combination of haloperidol, benztropine mesylate (2 mg) and lorazepam (2 mg) administered IM (the routine treatment in this setting) to treat agitated patients seeking care in a busy psychiatric emergency setting. Male or female patients, aged 18 to 60 years, agitated and/or aggressive were selected if they had a Positive and Negative Syndrome Score –Excited Component (PANSS-EC) (excitement, hostility, tension, uncooperative, poor impulse control) total score of equal to or greater than 15, a Clinical Global Impression of Change (CGI-C) of 5 or less. Patients deemed competent were randomized

to receive Quetiapine 300 mg PO or haloperidol 5 mg, benztropine mesylate 2 mg, or lorazepam 2 mg given by the IM route. Two scales, PANSS-EC and CGI-C were used to assess patients in the trial. The primary outcome measure was PANSS-EC at 2 hours after administration of the medication. The secondary outcome measure was a binary indicator of improvement defined as a CGI-C score of "much improved" or "very much improved" at 2 hours and/or a 20% reduction in PANSS-EC 2 hours following administration of the medication. Both scales were measured at baseline, and at 1, 2, 4 and 8 hours after medication. Results: Sixty-eight patients were included in the study. There were no significant treatment group differences in baseline PANSS-EC, baseline CGI-C, mean age, and in the proportion of males. There was no significant difference in the primary outcome measures and the secondary outcome measures also did not yield a significant treatment difference. There was, however, a significant within-group decrease from baseline for both treatments. Discussion: The present study suggests that in general the two treatments were equivalent. The haloperidol mixture did have an advantage on one of the secondary outcome measures i.e. a binary indicator of improvement defined as a CGI-C score of "much improved" or ''very much improved "at 2 hours and / or a 20% reduction in PANNS –EC 2 hours following administration of the medication.

NR3-66

USE OF A PREDICTIVE ALGORITHM AND AN AUTOMATED TELEPHONE SCREENER TOOL IN IDENTIFYING MISDIAGNOSED BIPOLAR DISORDER PATIENTS

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SUMMARY:

Background: Patients with bipolar disorder (BD) spend more time (31.9%) in the depressed phase than in other symptomatic phases, often resulting in misdiagnoses of major depressive disorder (MDD). Objective: To assess the direct costs associated with misdiagnosis of BD patients and to examine the applicability of a predictive algorithm and telephonic screener to identify misdiagnosed patients. Methods: Administrative claims data from US commercial health plans were used to identify patients (18–65 years) with claims for MDD (296.2x-3x, 311. xx, 298.0x, 300.4x, 309.0x-309.1x) but no claims for BD (296.0x-1x, 296.4x-8x) from January 1, 2007 through December 31, 2007. Patients were identified as being at high risk of misdiagnosis via a predictive model, followed by screening for BD using a modified version of the Mood Disorder Questionnaire. BD patients at high risk of misdiagnosis received automated telephone calls requesting their voluntary participation in a 5-minute telephone screen. Annualized mental health-related costs between patients screening positive versus negative for BD on the telephone screen were compared. Results: Among 10,799 patients (mean age 41 years, 65% male) at high risk for BD misdiagnosis via the predictive algorithm, 1350 with usable contact information were reached and 423 completed the telephonic screen (participation rate 32%, 423/1350). Of patients completing the survey, 123 screened positive for BD (screen positive rate 28%). One-year mental health-related prescription and medical services costs were significantly higher in patients screening positive for BD ($7286) versus patients screening negative ($3974, P<0.05).

Conclusions: Misdiagnosis is associated with higher medical costs, and claims data-based predictive algorithms, when used in conjunction with automated telephone screeners, may be used in practice to identify BD patients at high risk of misdiagnosis.

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NR3-67

METHODOLOGIC APPROACHES TO THE NATURALISTIC ASSESSMENT OF CLINICAL UTILIZATION AND OUTCOME OF A DEVICE-BASED TREATMENT IN CLINICAL PRACTICE

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SUMMARY:

Objective: Transcranial magnetic stimulation (TMS) was introduced into clinical practice in the US in 2008 for the treatment of patients with pharmacoresistant major depression. The introduction of a device-based therapeutic into clinical practice presents challenges and opportunities that differ from those associated with the more common experience of the introduction of a new psychopharmaceutical agent (e.g, the requirement for standardized clinical training on the safe use of the device). Interestingly, the existence of a electronically-based therapeutic provides unique opportunities for direct observation of the treatment experience. In this report, we summarize the early patterns of use and clinical experience

with this novel technology, and consider the methodologic and practical implications of this approach for naturalistic studies of clinical practice. Methods: Treatment utilization was examined at 45 clinical sites using TMS in routine clinical practice in the US. Actual device activity was electronically recorded in the device itself after each individual treatment session and later downloaded from the device in a HIPAA-compliant manner and then pooled across all clinical sites. Information included basic demographics and diagnoses. In addition, device operational information included the number of treatment sessions per patient, and the specific device parameters used.

Results: Between January and September 2009, information was obtained on 327 patients. A total of 8,367 treatment sessions were recorded. Median age of the population was 52 years (60% female). Eighty-seven percent of patients met ICD-9 diagnostic criteria for a recurrent, non-psychotic major depressive episode. The average number of treatment sessions per patient was 25. Conclusions: The introduction of a device-based therapeutic in clinical psychiatric practice creates unique demands to ensure adequate standardization of technical use. The preliminary information summarized here demonstrates the feasibility of obtaining accurate clinical treatment information of the use of TMS in a naturalistic setting.

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NR3-68

MEDICATION ADHERENCE AND PERSISTENCE AND PSYCHIATRIC HOSPITALIZATION IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

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SUMMARY:

Objective: Adherence to medication therapy for a sufficient duration is important in the treatment of major depressive disorder (MDD) [1,2]. This study examined the association between adherence and persistence with antidepressant therapy and psychiatric hospitalization in the 1-year follow-up period after initiation. Method: In a large US commercial managed-care claims database, 14,438 patients with at least one claim with a diagnosis of MDD (ICD-9-CM: 296.2 and 296.3) were initiated on a branded antidepressant (duloxetine, venlafaxine XR, or escitalopram) during 2006. All of the patients had no active prescription of the 3 study medications for 6 months prior to initiation and had continuous enrollment for 12 months prior to and post-medication initiation. Adherence in the post 6 months was defined as Medication Possession Ratio =0.8, and persistence was defined as the length of therapy without exceeding a 30-day gap. Psychiatric hospitalization in the post 1 year was examined. Results: During the first 6 months after initiation, 50.0% of patients were adherent to medication treatment; average length of treatment was 111.6 days. Compared to non-adherent patients, adherent patients had lower rates of psychiatric hospitalization (5.4% vs. 9.0%, p<.0001). Psychiatric hospitalization rates significantly declined with length of treatment. After adjustment for demographics, comorbidities, and prior hospitalization and emergency room visit, adherence was associated with reduced psychiatric hospitalization (OR=0.65, 95%CI=0.56-0.74). Compared to patients with treatment persistence <31 days, patients with persistence >90 days were 52% less likely to be psychiatrically hospitalized (p<.05). Conclusions: Our findings suggest that adherence and persistence with antidepressant therapy for at least 3 months during the first 6 months after medication initiation are associated with reduced psychiatric hospitalization in the 1-year follow-up period.

Funded by Eli Lilly and Company.

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NR3-69

NICOTINE DEPENDENCE, ADAPTIVE FUNCTIONING, AND PSYCHOPATHOLOGY AMONG PSYCHIATRIC INPATIENTS

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SUMMARY:
Farrell's British survey study found that psychiatric disorders are more frequent in nicotine-dependent population (22%) than in those free of nicotine dependence (12%). Objective: We evaluated whether the extent of nicotine dependence is correlated with the level of the patient's current psychopathology and adaptive functioning. Method: Sixty-four psychiatric inpatients (26 females, 38 males, aged 18 to 65, average = 40.2 years, SD=12.4), mostly diagnosed with schizophrenia (32.8%), depression (26.6%), or bipolar disorder (18.8%) were rated on the Brief Psychiatric Rating Scale (BPRS), Global Assessment of Functioning (GAF), Hamilton Rating Scale for Depression (HRSD), and all completed the Fagerstrom Test for Nicotine Dependence. Only 35.9% were non-smokers: their Fagerstrom score was coded as zero. Mean duration of smoking among the smokers was 19.2 years, SD=10.7. Results: A significant Pearson correlation was found between Fagerstrom and scores on GAF (r=.22, p=.04, 1-tailed) but none of Fagerstrom to BPRS and HRSD. The relationship of duration of smoking to GAF, HRSD, and BPRS was not significant. We subsequently calculated partial correlation coefficients to control for possible bias of age (older patients had more years to smoke but are not necessarily more psychiatrically ill) but also obtained only non-significant coefficients. It is noteworthy that the correlation of GAF to nicotine dependence was significant within the group diagnosed with schizophrenia (r=.45, p=.042) but not in those with depression (r= -.07, p=.39). Conclusions: The extent of nicotine dependence was not associated with more severe psychopathology but correlated with adaptive functioning among patients with schizophrenia: those more dependent showed higher levels of functioning, however, research with a prospective design is needed to determine whether our finding is confounded by a "healthy survivor bias" (see Lecacheux et al, 2009).

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NR3-70

COMPLEMENTARY USE OF TAI CHI IMPROVES RESILIENCE, QUALITY OF LIFE, AND COGNITIVE FUNCTION IN DEPRESSED OLDER ADULTS

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SUMMARY:
Background: Fewer than 50% of elderly depressed patients achieve remission and functional recovery in response to first-line antidepressant pharmacotherapy. Complementary mind-body interventions can improve partial response to antidepressants via stress-reduction, improved physical functioning, increased socialization, and reduced risks of polypharmacy. This is the first randomized trial of Tai-Chi-Chih used to treat geriatric depression comparing the efficacy of the two alternative treatment strategies designed to achieve symptomatic remission and improvement in resilience and function. Methods: One hundred twelve older adults with major depression aged 60 years and older were recruited and treated with 10 mg of escitalopram for the first six weeks. Seventy partial responders to escitalopram continued to receive 10 mg of escitalopram a day and were randomly assigned to 10 weeks of either complementary intervention using: 1.) Tai Chi Chih for 2 hours per week; or 2.) Health Education Program for 2 hours per week. All participants received comprehensive evaluations of depression, anxiety, resilience, health-related quality of life, and cognition. Results: Both Tai Chi (TC) and Health Education (HE) participants demonstrated comparable improvement in the severity of depression (mean Hamilton Depression rating scale scores of 6.0 in both groups; p=0.99). However, subjects in the Tai Chi group demonstrated significantly greater improvement in resilience (mean score of 70.2 vs. 65 in the HE group; $p<0.05$), health-related quality of life (SF-36 scores mean wellbeing scale scores of 80 versus 66; $p<0.05$), and measures of executive cognitive function (Strop mean errors scores of 0.03 compared to 0.4 errors in the HE group, $p<0.05$). Conclusion: Complementary use of mind-body exercise combined with standard antidepressants may provide additional improvement in clinical outcomes of geriatric depression such as resilience, quality of life and cognitive function.

NR3-71

ARIPIPRAZOLE AND HALOPERIDOL IN THE TREATMENT OF DELIRIUM AND ITS SUBTYPES

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SUMMARY:
Objectives: To compare the safety and efficacy of Aripiprazole and Haloperidol in the treatment of delirium and its motoric subtypes. Methods: We collected sociodemographic data and medical variables in addition to systematically rating all patients with delirium with the MDAS, KPS and abbreviated UKU at baseline (T1), 2-3 days (T2) and 4-7 days (T3) and created a delirium database. For this analysis we extracted all data containing Aripiprazole (ARI) and case matched the data to Haloperidol (HAL) treated subjects. Results: We were able to retrieve 21 patients treated with Aripiprazole (ARI) and 21 case matched subjects treated with Haloperidol (HAL). The mean age and baseline MDAS scores were not significantly different between groups. Over the course of treatment MDAS scores improved from and 18.1 to 8.3 (ARI) and 19.9 to 6.8 (HAL), delirium resolution rates were 76.2% (ARI) and 76.2% (HAL). In hypoactive delirium the MDAS scores improved from 15.6 to 5.7 (ARI) and 18.8 to 8.1 (HAL), delirium resolution rates were 100% (ARI) and 77.8% (HAL). In hyperactive delirium the MDAS scores improved from 19.9 to 10.2 (ARI) and 20.8 to 5.8 (HAL), delirium resolution rates were 58.3% (ARI) and 75% (HAL). There were no significant differences in treatment results between ARI and HAL. Treatment with HAL caused more EPS. Conclusion: Aripiprazole may be equally as effective as Haloperidol in the management of delirium and its subtypes. Treatment with Haloperidol resulted in more side effects.

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NR3-72
FACTORS ASSOCIATED WITH LOW DELIRIUM RESOLUTION RATES

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SUMMARY:
Objectives: To identify factors interfering with the resolution of delirium as measured with the Memorial Delirium Assessment Scale (MDAS). Methods: We analyzed our delirium database in respect to delirium resolution. All subjects in the database were recruited from all psychiatric referrals at MSKCC. Measures used were Memorial Delirium Assessment Scale (MDAS) and the Karnofsky Performance Status Scale (KPS), at baseline (T1), 2-3 days (T2) and 4-7 days (T3). We compared the resolution of delirium (RD) with the non-resolution of delirium (NRD) in respect to sociodemographic and medical variables. Results: We retrieved 111 subjects from our delirium database, including 26 patients with non-resolution of delirium (NRD). The mean age of NRD was significantly higher with 71.3 years than RD with 63.8 years. There was no significant difference in respect to the presence of brain metastases between NRD and RD. A history of dementia was significantly more present with 42.3% (NRD) compared to RD with 12.9%. There was no significant difference in respect to single etiologies or the sum of etiologies. MDAS scores improved from 20.1 at baseline to 15.2 at T3 in the NRD cohort compared to 17.7 and 5.7 in the RD cohort. KPS scores were significantly higher in RD than in NRD at T3 (35.1 and 26.2). Significance of Results: In the delirium sample from our delirium database, advanced age and a history of dementia were associated with lower delirium resolution response rates.

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NR3-73
META-ANALYSIS OF PLACEBO RESPONSE IN ANTIPSYCHOTIC TRIALS

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SUMMARY:
Objective: Large placebo response in antipsychotic trials presents a major challenge for psychopharmacologic drug development. The objective of this analysis was to identify predictors of placebo response in antipsychotic trials. Method: We searched the MEDLINE database for RCTs published from 1966 to 2008, supplemented by other electronic databases and hand search. Data were extracted from published (English) RCTs of antipsychotic treatment in schizophrenia and schizoaffective disorder (SAD). In this analysis, placebo response in short-term treatment (2 to 12 weeks) was defined as mean change from baseline in BPRS total score (derived from PANSS in 11 studies). The systematic review used a weighted mean and 95% confidence interval (CI) based on a random effects model. A meta-regression analysis was performed to identify influential moderators of placebo response. Patient-level analysis was conducted to identify additional predictors, based on data from 1 long-term trial and 2 identically-designed, short-term trials in the ziprasidone clinical trial database. Results: A total of 1246 placebo-treated patients from 41 RCTs had valid BPRS total scores with a median placebo group size of 20. Demographics included: weighted mean age 38, duration of illness 16 years, and 77% male (median). The weighted mean baseline, endpoint, and reduction in BPRS were, respectively, 48.58, 46.10, and -2.59 (95% CI -4.08, -1.09). The average effect size was 0.27 (-0.44, -0.11) and heterogeneous across studies (p<0.001). Meta-regression analysis showed that greater placebo response was associated with shorter trials (p<0.001), community hospital (or mixed) treatment settings (p=0.02), more recently published studies (1990-2009) (p<0.01), and higher baseline severity score (p<0.01). Analysis of patient-level PANSS total score, however, showed no improvement over a 1-year period in the higher baseline PANSS subgroup using GMM. Analysis of the placebo arms in the 2 short-term ziprasidone trials showed placebo responses in SAD bipolar patients were significantly lower than schizophrenia patients. Conclusions: Our findings suggest that treatment settings, trial duration, schizoaffective bipolar diagnosis, and baseline level of symptom severity might influence the magnitude of placebo response.
Supported by funding from Pfizer, Inc.

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NR4-01
EVALUATION OF THE EFFICACY OF EXTENDED RELEASE QUETIAPINE FUMARATE (QUETIAPINE XR) FOR THE TREATMENT OF PATIENTS WITH MDD

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SUMMARY:
Objectives: Approximately 60% of treatments investigated for MDD fail to separate from placebo (PBO) on primary endpoint. Once-daily extended release quetiapine fumarate (QTP XR) was evaluated as monotherapy (50, 150, and 300mg/day) or adjunct treatment (150 and 300mg/day) in patients (pts) with MDD. Methods: Data from 8 (7 acute; 1 maintenance) placebo (PBO)-controlled studies of QTP XR were analyzed. Primary endpoint: change from randomization in MADRS score (acute); time from randomization to depressed event (maintenance). Statistical methods: ANCOVA for difference between QTP XR and PBO in LSM change in MADRS total score from randomization to study end (acute); hazard ratio (HR) for time to recurrence of a depressed event (maintenance). Results: 4 monotherapy studies were significant in favor of QTP XR, MADRS LSM vs PBO: Study 1 (QTP XR 50, 150, and 300mg/day, -2.50, p<0.05; -3.44, p<0.001 and -3.11, p<0.01); Study 2 (QTP XR 150 and 300mg/day, -3.63, -4.11; both p<0.001; duloxetine -3.46, p<0.01); Study 3 (QTP XR 150/300mg/day, -3.39, p<0.01); and Study 14 (QTP XR 50-300mg/day, -7.54, p<0.001). Study 4 (monotherapy) was a failed study in which both QTP XR and the active comparator escitalopram failed to separate from PBO (QTP XR 150/300mg/day, -1.61, p=0.174; escitalopram, -1.13, p=0.346). Studies of adjunct QTP XR also significant in favor of QTP XR: Study 6 (QTP XR 150mg/day, -1.90, p=0.067; 300mg/day, -2.99, p<0.01) and Study 7 (QTP XR 150 and 300mg/day, -3.05, -2.73; both p<0.01). QTP XR significantly increased the time from randomization to a depressed event (Study 5); HR (95% CI): 0.34 (0.25, 0.46). Safety and tolerability findings in all studies were consistent with the known profile of QTP. Conclusions: In patients with MDD, QTP XR was consistent in significantly improving depressive symptoms in 6 out of 7 acute studies. QTP XR maintenance therapy significantly reduced risk of a depressed event, demonstrating relapse prevention.
Research funded by AstraZeneca.

NR4-02

EFFICACY AND TOLERABILITY OF VILAZODONE, A DUAL-ACTING SEROTONERGIC ANTIDEPRESSANT, IN THE TREATMENT OF PATIENTS WITH MAJOR DEPRESSIVE DISORDER (MDD)

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SUMMARY:
Objective: To assess the efficacy, safety, and tolerability of vilazodone HCl (VLZ), a dual-acting SSRI and 5-HT1A receptor partial agonist, in the treatment of MDD. Method: This phase 3, randomized, double-blind, placebo (PBO)-controlled study enrolled patients (pts) 18-70 years of age with MDD and a baseline HAM-D-17 score =22. Patients received VLZ or PBO QD titrated to 40 mg over 2 weeks and continued for up to 8 weeks (n=463; 388 completers). The primary objective was to assess VLZ efficacy measured by change in MADRS score. Secondary efficacy measures included MADRS response, HAM-D, HAM-A, CGI-S, and CGI-I. Safety and tolerability assessments included treatment-emergent adverse events (AEs) and labs, ECGs, and the Changes in Sexual Function Questionnaire (CSFQ). Results: VLZ-treated patients had significantly greater improvement from baseline in MADRS total score at endpoint (P=0.009) than PBO (ITT, LS mean changes, –13.3 and –10.8, respectively). Significantly more VLZ-treated than PBO patients (44% vs 30%, P=0.002) were MADRS responders (decrease in MADRS total score =50%). VLZ-treated pts also had significant improvements from baseline in HAM-D-17 (P=0.026), HAM-A (P=0.037), CGI-S (P=0.004), and CGI-I (P=0.004) at endpoint vs PBO. Discontinuations due to AEs were VLZ 9.3% and PBO 4.7%. The most frequent AEs in VLZ vs PBO pts were headache (13% vs 10%), nausea (26% vs 6%), and diarrhea (31% vs 11%) (>93% of these judged to be mild or moderate in intensity). There were no clinically significant changes in weight, vital signs, ECGs, or labs. No clinically significant treatment-related effects on sexual function were seen on the CSFQ in males or females. Libido decrease was the most common AE related to sexual function (11 [4.7%] VLZ pts and 0 PBO pts). Conclusions: Vilazodone treatment was associated with significant improvement in depression and anxiety symptoms and was safe and well tolerated in this study of adult patients with MDD. PGxHealth, LLC funded the study.

NR4-03

A 6-WEEK RANDOMIZED DOUBLE-BLIND PLACEBO-CONTROLLED TRIAL OF ZIPRASIDONE FOR THE ACUTE DEPRESSIVE MIXED STATE

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SUMMARY:
Objectives: We examined the efficacy of ziprasidone versus placebo for the depressive mixed state in patients with bipolar II disorder or unipolar depression. We chose ziprasidone due to its biochemical profile which may suggest both antidepressant as well as antimanic properties. Methods: This four-site, block randomized, double-blind, placebo-controlled study randomized 74 patients, (Drug=36, placebo=38, 54% women, 57% African-American, mean age 38.7 years) to Ziprasidone (40-160 mg/d) or placebo for 6 weeks. Eligible patients had diagnoses of Bipolar Disorder Type II or unipolar major depressive disorder and met DSM-IV criteria for a major depressive episode, while also meeting 2 or 3 (but not more or less) DSM-IV manic criteria. Primary outcome measured the change in baseline Montgomery-Asberg Depression Rating Scale (MADRS). Secondary measures tracked changes in Clinical Global Impression (CGI-I and S), QIDS (Quick Inventory of Depressive Symptomatology Self Report), Hamilton Scale of Anxiety (HAM-A) and Mania Rating Scale (MRS) scores. The mean dose of ziprasidone was 122.4 mg/day. Results: General Linear model employing repeated measures ANOVA showed a significant reduction in MADRS scores from baseline to end of treatment in the Ziprasidone (baseline MADRS= 23.19 +/- 6.18, end of treatment MADRS= 10.73 +/-9.91) compared to the placebo group (baseline MADRS 24.73 +/- 8.03, end of treatment MADRS 19.35 +/- 8.42) ($F = 8.27$, $p<0.01$). Reduction in QIDS from baseline favored drug over placebo ($F=6.92$, $p<0.01$). Responders on CGI-I Overall were greater in drug group (62%) versus placebo (15%) ($p<0.01$). There was no significant difference in CGI-S, MRS and HAM-A change scores from baseline to end of treatment. Safety: There was no significant weight change from baseline to end of treatment in the ziprasidone versus

placebo group. Overall ziprasidone was well tolerated. Side effects reported by 5% or more subjects were insomnia, sedation, irritability, dry mouth and increased appetite in both drug and placebo groups.

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NR4-04

EFFECT OF CHILDHOOD TRAUMA ON THE COURSE OF BIPOLAR DISORDER

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SUMMARY:

Introduction: Few investigations have examined the impact of childhood trauma and domains of childhood abuse on outcome in bipolar disorder. The aim of this study is to research the impact of childhood trauma on the characteristics of clinical course and episodes of bipolar I disorder. Methods: Between the dates of January and April 2009, 116 patients who had been diagnosed with bipolar I mood disorder based on DSM-IV-TR criteria in the euthymic state were included in the study. A structured form designed for the long term and follow-up evaluation of mood disorders (SKIP-TURK), Young Mania Rating Scale, Hamilton Depression Scale and Childhood Trauma Questionnaire were used. Results: In this study, it was found that 61.2% of the bipolar patients had any childhood abuse. The patients who had childhood abuse had a higher ratio of committing suicide. There were significant differences between patients with and without childhood abuse in committing suicide (p=0.003), and the number of total episodes (p=0.026) and depressive episodes (p=0.019). It was found that the patients who had sexual abuse by family members had more manic episodes as the first episode and patients who had emotional abuse had more mixed episodes as the first episode. A significant difference was found between first degree relatives with and without a psychiatric illness in the physically abused (p=0.044). A highly significant relationship was determined between committing suicide and the subtypes of childhood abuse, including physical abuse (p=0.0001), emotional abuse p=0.002, and sexual abuse by a family member (p=0.026) or stranger (p=0.001). When four groups of patients include rapid cycling, rapid cycling plus mixed episodes, mixed episodes without rapid cycling or mixed episodes were evaluated according to the types of childhood trauma, the ratio of emotional abuse and neglect, there was significantly higher in the patients with rapid cycling plus mixed episodes (p=0.018) and the patients with only mixed episodes (p=0.049) than the other groups of patients. Conclusion: The patients with the rapid cycling and mixed episodes of bipolar disorder who had childhood abuse could have poor clinical outcome. It should be considered that these groups of patients are evaluated by different methods for the treatment such as psychoeducation and psychotherapy.

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NR4-05

OSTEOPOROSIS RISK BURDEN IN DEPRESSED MIDLIFE OUTPATIENTS

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SUMMARY:

Introduction: Middle-aged mood-disordered patients are at increased risk for osteoporosis as they share general population risks of genetic and lifestyle factors, and have additional risk factors related to affective illness and its treatment. Yet little confirmatory data is available supporting these associations gleaned from the literature. The purpose of this project was to systematically examine osteoporosis risk factors via personalized screening to determine if osteoporosis prevention programs in mood-disordered mid-life patients are warranted. Methods: As part of a prospective cross-sectional study, mood-disordered men and women ages 40 to 60 years were recruited from 2 university programs: 1) a psychiatric partial hospital program, and 2) an urban neighborhood family medicine center. The MINI was utilized to confirm a primary Axis I disorder of major depression; structured interviews additionally captured demographics, historical,

lifestyle and medication exposure risk. Results: Nineteen (95% women) depressed outpatients completed a historical risk factor assessment visit; mean age was 47.8 (range 40-58). The sample was ethnically diverse (68% Caucasian, 21% African American; 5% Hispanic/Latino and 5% Native American) and predominantly unmarried and low income, with half receiving disability equally for emotional or physical health reasons. The number of risk factors per subject ranged from 10 to 27; the most highly prevalent risks included: 89% history of SSRI treatment, history of major surgery; 68% decreased weight bearing exercise, antipsychotic exposure; 64% low vitamin D levels. Conclusions: Mood-disordered patients have a high number of lifestyle and medical risk factors elevating likelihood for osteoporotic fracture at younger ages, warranting preventive counseling to reduce risk for osteoporosis. Recommendations for DXA screening to confirm low bone mass or osteoporosis include: Recommendations for improving bone health are at increased risk for osteoporosis. Lifestyle interventions for the general mid-life population are appropriate for this population and include calcium and vitamin D supplementation, enhanced physical activity, and coordinated primary care follow-up. These interventions additionally promote overall physical and metabolic health, also of concern in depressed adults who have high rates of comorbid physical illnesses.

NR4-06

EXTENDED RELEASE QUETIAPINE FUMARATE AS ADJUNCT TO ANTIDEPRESSANTS IN MDD: POOLED ANALYSIS IN PATIENTS WITH LOW AND HIGH LEVELS OF BASELINE ANXIETY

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SUMMARY:

Objectives: Patients with MDD with high levels of anxiety typically experience more severe depression and functional impairment than those with low anxiety. Quetiapine fumarate (QTP XR) adjunct to antidepressant (AD) therapy in patients with MDD and inadequate response to AD was evaluated in patients with high or low baseline anxiety levels.

Methods: Pooled data from 2 similar 6-week, double-blind, randomized, placebo (PBO)-controlled trials (Studies 6 and 7) in patients with inadequate response to AD were analyzed. Patients received QTP XR (150 or 300 mg/day)+AD or PBO+AD. Secondary analyses in patients with high or low baseline anxiety levels (HAM-A total score >/=20 and <20) included change at Week 6 in: MADRS total (primary), HAM-A total and CGI-S total scores. Results: For patients with baseline HAM-A total score >/=20 (n=433), adjunct QTP XR 300mg/day (-15.92, p<0.05) but not 150mg/day (-15.20, p=0.122) significantly reduced MADRS total scores vs PBO+AD (-13.49) at Week 6. Adjunct QTP XR 300 mg/day significantly improved HAM-A (-12.19, p<0.05) and CGI-S scores (-1.68, p<0.05) vs PBO+AD (-14.18, -1.37, respectively) at Week 6; reductions with adjunct QTP XR 150mg/day: -11.70 (p=0.082) and -1.60 (p=0.131). For patients with a baseline HAM-A total score <20 (n=486), adjunct QTP XR 150 (-13.99, p<0.001) and 300mg/day (-13.98, p<0.001) significantly improved MADRS total scores vs PBO+AD (-10.83) at Week 6. Adjunct QTP XR 150 and 300 mg/day significantly improved HAM-A (-6.59, p<0.01; -6.48, p<0.05) and CGI-S scores (-1.63, p<0.001; -1.52, p<0.01) vs PBO+AD (-4.93, -1.16, respectively) at Week 6. Reported AEs were similar in both baseline anxiety level groups and consistent with the known tolerability profile of QTP. Conclusions: In patients with MDD and inadequate response to AD therapy, adjunct QTP XR was effective at reducing depressive and anxiety symptoms in patients with high (300 mg/day) and low (QTP XR 150 and 300 mg/day) levels of baseline anxiety.

Research funded by AstraZeneca.

NR4-07

THE IMPACT OF STRESS FACTORS ON HPA FUNCTION IN PATIENTS WITH DEPRESSION AND NEUROSIS: STUDY WITH THE USE OF DST

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SUMMARY:

Objectives: The aim of study was the analysis of the relationship between disturbances in hypothalamic-pituitary-adrenal (HPA) axis functioning and clinical symptoms as well, in patients with depression in comparison to both healthy population and these treated for neurosis. Methods: We examined 36 patients with depression- MDD, 22 treated for anxiety and depressive disorder-neurosis, and 36 persons as a control group. The average age was 34.9 years (SD=12.8). To measure cortisol level, blood samples were collected twice daily: at 8:00 am (K1) and 4:00 pm (K2). Dexamethasone Supression Test

was performed using 1 mg of dexamethasone (K3 and K4). Stress load in childhood was assessed using Early Trauma Inventory (ETI). The level of depression and anxiety was estimated with the use of HADS, STAI and Beck's scales. The influence of the stress factors experienced during the last 12 months on the mental condition was measured with the use of Social Readjustment Scale (SRS). Results: The average morning cortisol concentration before dexamethasone suppression appeared to be the lowest for depression: K1=187.2 ng/ml and evening one for depression and neurosis: K2=86.5 ng/ml. The lowest suppression occurred at depressive patients: K3=41.2 ng/ml and K4=31.8ng/ml. The highest suppression occurred in control group: K3=12.7 ng/ml and K4=18.7 ng/ml. Neurotic patients obtained average results. The higher depressiveness and apprehensiveness, the lower cortisol suppression (higher K3 and K4 concentration). The relation revealed itself most in the group of healthy people. Actual stressors (SRS) and sexual abuse in childhood (ETI IV) worsened the suppression among the depressive patients (higher K3 and K4 results). Conclusion: The results are confirmed by information about the relation of functioning of HPA axis and stressors at depressive patients, in contrast to neurotic patients.

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NR4-08

EXPECTANCY EFFECTS AND TREATMENT OF DEPRESSION: COGNITIVE AND NEURAL MECHANISMS

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SUMMARY:

Background: Depression remains a significant public health problem, as 120 million people worldwide suffer from MDD and only 51% of patients are likely to experience remission of their depression after 4 sequential trials of antidepressant medications. The placebo effect represents a potent treatment for MDD—placebo response in acute randomized controlled trials (RCTs) of antidepressant medications averages 30%, and meta-analyses have estimated the proportion of medication response attributable to placebo to be 50-75%. Patient expectancy is the mechanism of placebo effects in antidepressant RCTs and has been positively associated with medication response. Method: Preliminary results will be presented from a clinical trial and integrated functional Magnetic Resonance Imaging (fMRI) study randomizing adult outpatients with MDD to 8 weeks of treatment in high vs. low expectancy conditions. Included patients are men and women aged 18 to 65 years with unipolar MDD (DSM-IV) and 24-item HRSD score = 16. Expectancy is measured using items 2 and 4 of the CES, which measure the subject's expected likelihood and magnitude of improvement, respectively. Subjects are randomized to (1) Placebo-controlled Track (random assignment to escitalopram or placebo), or (2) Comparator Track (random assignment to escitalopram or citalopram) and are informed of their Track assignment but are blinded to their specific treatment assignment. Subjects are treated for 8 weeks with the study medication and are classified as responders (50% decrease from baseline HRSD) or remitters (HRSD < 7). Well-validated fMRI paradigms are used to investigate the activity of neural circuits underlying subjects' response to emotional stimuli, reward processing, and memory retrieval. Results: Analyses of preliminary data indicate that randomization to placebo-controlled vs. comparator administration of medication significantly affects subjects' expectations of therapeutic improvement and the outcome of antidepressant treatment. Significant amygdala activation was associated with viewing sad and fearful human faces, NAcc/VS activation with the anticipation and receipt of monetary rewards, and PFC activation during recall of emotionally valenced words. Depressed patients at baseline appear to demonstrate differences in neural activations compared to controls, and depressed patients with high as compared to low expectancy appear more similar to normal controls.

NR4-09

IMPROVEMENTS IN COGNITIVE FUNCTIONING DURING INPATIENT HOSPITALIZATION FOR UNIPOLAR AND BIPOLAR DEPRESSION WITH AND WITHOUT PSYCHOTIC FEATURES

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David Abramson, M.D., Maurizio Fava, M.D.

SUMMARY:
Objective: 1. Examine the response of cognitive functioning over the course of inpatient treatment of patients with major depressive disorder or bipolar disorder, depressed type with and without psychotic features. 2. Determine the impact of psychosis on cognitive functioning pre and post treatment.
Introduction: Several studies have demonstrated cognitive impairment in patients with mood disorders during the acute phase. However, less is known about the course of cognitive functioning with treatment, particularly with regards to the presence of psychotic symptoms. Methods: Subjects included 39 patients admitted to an inpatient unit at Massachusetts General Hospital. All participants met DSM-IV criteria for major depressive disorder or bipolar disorder, depressed type, with or without psychotic features based on SCID-I/P interview. Severity of depression and psychosis were determined by the HAM-D-17 and BPRS respectively. Neuropsychological evaluations were determined by a battery of assessments. Results: Pre-post analysis indicated that this cohort of patients experienced significant improvement in depression over the course of treatment (pre mean = 24.00 ± 5.84, post mean = 11.54 ± 6.82; paired t = 7.76, p < .001) as measured by the HAM-D 17. Paired t-tests revealed that patients also experienced significant improvement from pre-to-post on tasks of executive functioning (paired t = 2.31, p = 0.04), memory (paired t = 5.47, p < 0.01), and psychomotor functioning (paired t = 3.05; p = 0.01); however, there were no significant improvements in attention or visuospatial scores. Additional post-hoc analyses compared differences in cognitive functioning at time of admission across individuals with and without psychotic features. Higher scores on the BPRS on admission were associated with significantly lower scores for executive function (r = -0.52, p = 0.01), memory (r = -0.49, p = 0.02), and attention (r = -.50, p = .059), after controlling for HAM-D 17 scores. These relationships were no longer significant post treatment. This pilot study was funded by a private donation. Conclusions: 1. There was a corresponding improvement in executive functioning, memory, and psychomotor speed with improvement in depression. 2. Psychotic features predicted significantly lower scores for executive function, memory, and attention at baseline, but did not predict cognitive functioning post treatment.

NR4-10

COMPARISON OF SAFETY, EFFICACY, AND TOLERABILITY OF MODIFIED AND IMMEDIATE RELEASE ESCITALOPRAM AND PLACEBO IN ADULTS WITH MAJOR DEPRESSIVE DISORDER

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SUMMARY:
Objective: To compare the efficacy, safety, and tolerability of escitalopram modified release (MR) 28 mg/d, escitalopram immediate release (IR) 10 mg/d, and placebo in adults with major depressive disorder (MDD). Method: An 8-week double-blind, multicenter, randomized, placebo-controlled, parallel-group, fixed-dose study comparing escitalopram MR 28 mg/d, escitalopram IR 10 mg/d, and placebo. Eligible patients (18-65 years) had DSM-IV-TR–defined MDD, MADRS total score =26, QIDS-SR score =15, and score =2 on Item 1 of the HAMD24. Primary efficacy: MADRS total score change from baseline to Week 8 (LOCF). Safety/tolerability assessments: adverse event (AE) reports, clinical and laboratory parameters, and safety rating scales. Results: Of 877 randomized patients (mean baseline MADRS total score=32.5), 25.4% discontinued prematurely (placebo, 24.1%; MR, 28.0%; IR, 23.7); the between-group differences were not significant. Mean change in MADRS total score was statistically significantly greater for both escitalopram MR and IR compared with placebo at every visit (LSMD at Week 8: -3.3 and -2.9, respectively; P<.001). No significant differences between the MR and IR groups were detected on any efficacy parameter. Most common treatment-emergent AEs in either escitalopram group (=5% and greater than placebo) were headache, nausea, diarrhea, insomnia, dry mouth, somnolence, fatigue, and nasopharyngitis. Rates of discontinuation due to AEs were 3.2%, 7.1%, and 5.0% for placebo, escitalopram MR, and escitalopram IR, respectively.
Conclusions: Escitalopram MR 28 mg/d and escitalopram IR 10 mg/d compared with placebo demonstrated significant improvement on all key efficacy parameters and both were well tolerated. No significant improvements were noted with escitalopram MR relative to escitalopram IR. Supported by funding from Forest Laboratories, Inc.

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NR4-11

GENOTYPIC AND PHENOTYPIC CYP2D6 POOR METABOLIZER STATUS AMONG OUTPATIENTS WITH DEPRESSION TREATED WITH VENLAFAXINE

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SUMMARY:
Objective: The prevalence of the CYP2D6 poor metabolizer (PM) genotype is 5% to 10% in the general population;the prevalence in patients treated for depression is unknown. Chronic administration of concomitant medications can inhibit CYP2D6 activity, converting the phenotype of an individual with a non-PM genotype to a PM phenotype. Comorbid conditions are common in patients with depression, increasing the likelihood of concomitant medication use. The objective of this study was to determine, in a clinical sample of depressed outpatients treated with venlafaxine extended release (VEN ER), the prevalence the CYP2D6 PM phenotype, based on plasma O-desmethylvenlafaxine (ODV) to VEN ratio (ODV/VEN), compared with the prevalence of the actual CYP2D6 PM genotype. Method: This was a multicenter, open-label, single-visit study in adult patients(age=18 years) treated with VEN ER (37.5 to 225 mg/d) for up to 8 weeks. A 15-mL blood sample for phenotype and CYP2D6 genotype determinations was drawn 4 to 12 hours after the patient's last VEN ER dose. Plasma ODV and VEN concentrations were determined for each patient, and phenotype was assigned. PM status was defined as ODV/VEN <1 based on published data [Nichols, 2009]. CYP2D6 genotype was determined for each patient. Agreement between phenotype and CYP2D6 genotype classifications was assessed using McNemar's test.All concomitant medications were allowed, except for desvenlafaxine(Pristiq®)or generic VEN ER. Results: Both ODV/VEN ratio and genotype results were available for 900 patients. In this clinical sample of patients with depression treated with VEN ER, 243/900 (27%) patients were classified as phenotypic PMs based on ODV/VEN ratio, whereas 35/900 (3.9%) were classified as CYP2D6 genotypic PMs (McNemar's test, P<0.0001). In all, 34/35 (97%) patients genotyped as CYP2D6 PMs had a PM phenotype, however 209/865(24%) genotypic non-PM patients also were classified as phenotypic PMs. Genotypic CYP2D6 intermediate metabolizers (IMs) were more likely than extensive metabolizer EMs to be classified as the PM phenotype; 49/81 (60%) genotypic IMs had a PM phenotype compared with 159/748 (21%) genotypic EMs. Conclusions: A significant percentage of patients with CYP2D6 non-PM genotype were converted to phenotypic PM status, which may affect the tolerability and efficacy of VEN ER for those patients. Phenotype conversion in this population may be due to the use of concomitant medications to treat comorbid conditions. Sponsored by Pfizer, formerly Wyeth Research.

NR4-12

ANALYSES OF THE EFFECT OF ZIPRASIDONE ON AGITATION IN ACUTE BIPOLAR MANIA USING CLINICIAN-RATED PANSS AND SADS-C PROXY MEASURES

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SUMMARY:
Introduction: Agitation is commonly observed in patients being treated for acute bipolar mania. It is difficult to determine to what extent the observed agitation is part of the symptomatology or is a result of the treatment. Analyses examining reports of agitation in clinical trials fail to objectively describe the effect of treatment on agitation measures. Benzodiazepines are frequently used in both clinical practice and clinical trials, further complicating our understanding of the effect of atypical antipsychotics on agitation. In these analyses we sought to examine the effect of ziprasidone on items from the PANSS and the SADS-C, which may most closely approximate objective measures for agitation in acute bipolar mania. We also looked at the possible contribution of concomitant benzodiazepines to this effect. Methods: Pooled data from two 21-day, placebo-controlled trials of ziprasidone (80–160 mg/d) for the treatment of acute bipolar mania were examined to determine the effects of ziprasidone on symptoms of agitation. Items from the PANSS and SADS-C used as a

proxy measure of agitation were: PANSS items (evaluated days 7, 14, and 21) poor impulse control, anxiety, tension, uncooperative, excitement, and hostility; SADS-C items (evaluated days 2, 4, 7, 14, and 21): insomnia (and initial, middle, and terminal insomnia), subjective anger, agitation, irritability, somatic anxiety, and psychic anxiety. Benzodiazepine use, which was limited to the first 9 days of the studies, was compared between ziprasidone and placebo subjects. Results: Ziprasidone subjects experienced significant ($p < 0.05$) reductions versus placebo subjects in several agitation-related items at early time points, including PANSS poor impulse control (days 7 and 14), anxiety (day 7), uncooperative (day 7), and hostility (day 7); as well as SADS-C insomnia (days 2, 4, and 7), initial insomnia (day 4), middle insomnia (days 4, 7), subjective anger (days 4, 7, 14), and agitation (day 2). The use of benzodiazepines was similar between ziprasidone and placebo subjects (46.2% vs 50.0%, respectively). Conclusions: These findings suggest that ziprasidone resulted in significant decreases in several agitation-related items at early time points in the treatment of acute bipolar mania. The fact that rates of benzodiazepine use were similar between ziprasidone and placebo subjects suggests that the observed reduction in agitation was due to ziprasidone alone.

Supported by Pfizer Inc.

NR4-13

TREATMENT OUTCOMES BASED ON DISEASE SEVERITY FOR SUBJECTS WITH BIPOLAR I DISORDER TREATED WITH ZIPRASIDONE PLUS A MOOD STABILIZER

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SUMMARY:

Background: In a 6-month, randomized, placebo-controlled, double-blind trial enrolling subjects with bipolar I disorder and a Mania Rating Scale (MRS) score = 14, ziprasidone was found to be an effective and well-tolerated treatment in combination with a mood stabilizer. [1,2] To elucidate the profile of subjects who received the most benefit from ziprasidone, treatment outcomes across a spectrum of illness severity were determined. Methods: We compared the proportion of subjects who were randomized to double-blind treatment (subjects achieving = 8 consecutive weeks of stability with open-label ziprasidone [80–160 mg/d] and lithium or valproate) and the proportion who relapsed during double-blind treatment for the most severely ill quartile (baseline MRS = 26) and decile (baseline MRS = 30). All p values were calculated using the Fisher exact test.

Results: Rates of stabilization were similar for patients with an MRS score < 30 (209/512, 40.8%) when compared with rates for patients with baseline MRS = 30 (30/71, 42.2%), $p = 0.90$; stabilization rates were 175/420 (41.7%) and 64/163 (39.3%) for subjects with MRS scores < 26 and MRS = 26, respectively ($p = 0.64$). Among subjects with MRS scores < 30, relapse rates were lower for those randomized to ziprasidone (21/114, 18.4%) compared with those randomized to placebo (30/95, 31.6%), $p = 0.04$; the same was true for subjects with MRS scores = 30 (relapse rates: ziprasidone: 4/13, 30.8%; placebo: 6/15, 40.0%), but this difference was not statistically significant ($p = 0.71$). Among subjects with MRS score < 26, relapse rates were lower for those randomized to ziprasidone (14/93, 15.1%) compared with those randomized to placebo (28/82, 34.1%), $p < 0.01$; for subjects with MRS scores = 26, relapse rates were 11/34 (32.4%) and 8/28 (28.6%) for ziprasidone and placebo, respectively ($p = 0.79$). Conclusion: These analyses indicate that ziprasidone, when added to lithium or valproate, was equally effective in stabilizing both mild to moderately ill subjects and severely ill subjects. Mild to moderately ill subjects randomized to continue on ziprasidone were significantly less likely to relapse compared with placebo subjects. With the much smaller sample size of the severely ill group, separation was not demonstrated.

Study supported by Pfizer Inc.

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NR4-14

SIGNIFICANT BIPOLAR RISK FACTORS IN PATIENTS PRESENTING A CURRENT MAJOR DEPRESSIVE EPISODE

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SUMMARY:
Objective: The objective of this study was to evaluate the characteristics of patients presenting with a current major depressive episode (MDE) who were assigned a diagnosis of bipolar disorder (BD) using different diagnostic algorithms, and thus to determine the most explicative bipolar risk factors in these patients. Methods: An international cross-sectional epidemiological study was carried out in eighteen countries in Europe, Asia and North Africa. These data come from an analysis of patients recruited between April 2008 and May 2009. Community- and hospital- based psychiatrists included consecutively in a patient registry all adult patients consulting with a diagnosis of MDE (DSM-IV criteria). At this consultation, participating psychiatrists completed a questionnaire on patients' clinical features which enabled a diagnosis of BD to be assigned using three different algorithms (DSM-IV-TR, modified DSM-IV(m-DSM-IV) and Bipolarity Specifier). Results: A total of 5635 MDE patients were included. Overall, 1645 (39%) received a clinician's diagnosis of BD, 16% fulfilled DSM-IV-TR criteria for BD, 31% fulfilled m-DSM-IV criteria and 47% fulfilled the Bipolarity Specifier criteria. Using these different algorithms, several variables could be identified as risk factors for bipolar disorders. The variables most strongly associated with a diagnosis of BD according to DSM-IV, m-DSM-IV and the Bipolarity Specifier compared to patients with unipolar depression were a family history of mania (Odds Ratio(OR): 2.2; 2.4; 3.8 respectively), at least two mood episodes in the past (OR: 2.6; 2.9; 2.1 respectively), the occurrence of first psychiatric symptoms before the age of 30 years (OR: 1.5; 1.4; 1.7 respectively), a switch to mania/hypomania (OR: 0.6; 4.9; 9.5 respectively) and mixed states during current depressive symptoms (OR: 1.4; 1.4; 2.2 respectively). A history of suicide attempts appeared to be significantly associated with a diagnosis of BD according to m-DSM-IV (OR: 1.2) and the Bipolarity Specifier(OR: 1.2). Conclusions: The description of patients diagnosed with BD according to different algorithms identified a number of shared risk factors for BD. Systematic screening for such risk factors may contribute to improved diagnosis. This study was funded by Sanofi-Aventis.

NR4-15

POOLED ANALYSIS OF THE EFFICACY OF DESVENLAFAXINE 50 MG COMPARED WITH PLACEBO IN THE PATIENTS WITH MODERATE OR SEVERE MAJOR DEPRESSIVE DISORDER

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SUMMARY:
Objective: To characterize the efficacy of the serotonin-norepinephrine reuptake inhibitor (SNRI) desvenlafaxine (administered as desvenlafaxine succinate) in patients with moderate or severe major depressive disorder (MDD). Methods: Data from 3 double-blind, fixed-dose studies in outpatients with Diagnostic and Statistical Manual of Mental Disorders (DSM) defined MDD were pooled. Patients were randomly assigned desvenlafaxine (50 or 100 mg/d) or placebo; this report summarizes findings with 50 mg/d. The primary end point was improvement in 17-item Hamilton Rating Scale (HAM-D17) scores from baseline in patients with moderate (HAM-D17<25) or severe (HAM-D17=25) MDD. Secondary outcomes included the percentage of patients who achieved response (=50% reduction in HAM-D17), remission (HAM-D17=7), and improvement in total scores of the Clinical Global Impression-Improvement (CGI-I), Sheehan Disability Scale (SDS), Covi Anxiety (COVI), and World Health Organization Well-being Index (WHO-5). Changes from baseline in scores were evaluated using analysis of covariance. Fisher's exact test compared response and remission values. Tolerability assessments included treatment-emergent adverse events (TEAEs), discontinuation due to AEs, and taper/post-study-emergent AEs. Results: This analysis included 933 patients (moderate on desvenlafaxine 50 mg=294; severe on desvenlafaxine 50mg=168). Desvenlafaxine improved HAM-D17 scores vs placebo in patients with moderate (difference adjusted means [95% CL] = ?1.82 [?3.10, ?0.55]; P=0.003), and severe MDD (?1.89 [?3.75,?0.03]; P=0.046). Desvenlafaxine significantly improved CGI-I (P=0.003), SDS (P<0.001), COVI(P=0.014), and WHO-5 (P<0.001) scores vs placebo in moderately depressed patients. A greater percentage of desvenlafaxine-treated patients with moderate MDD achieved remission (35% vs 28%; P=0.044) or response (55% vs 47%,respectively; P=0.05) vs placebo. Secondary outcomes in severely depressed patients did not differ significantly. TEAEs reported by =5% of desvenlafaxine-treated patients were nausea, dizziness, insomnia, hyperhidrosis, constipation, fatigue, and decreased appetite. Rates of discontinuation due to AEs were 4.5% for desvenlafaxine 50mg/d and 4% for placebo. Taper/post-study-emergent AEs reported by =5% of desvenlafaxine patients were dizziness, nausea, and drug withdrawal syndrome. Conclusions: Desvenlafaxine 50 mg/d significantly improved depressive symptoms in patients with moderate or severe MDD.
Sponsored by Pfizer, formerly Wyeth Research

NR4-16

RURALITY, SUICIDE AND THE AVAILABILITY OF MENTAL HEALTH PROVIDERS

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SUMMARY:
Suicides in the U.S. are more commonly observed in rural as compared to urban locations. Geographic, sociocultural and psychological factors have been implicated in the causation of this excess mortality. Objective: The purpose of the present study was to examine the association between population density, the availability of mental health providers and suicide rates. Method: The rates of suicide (deaths per 100,000 population) were obtained from the National Center for Health Statistics and Bureau of Census Data, for each of the 51 US states in the year 2004. These were correlated with the population density (persons/square mile) and the number of mental health providers per 100,000 population. Results: Alaska, the state with the lowest population density (1.2 people/square mile) also has the highest suicide rate (23.1 deaths/100,000 population. Conversely, the District of Columbia, which has the highest population density (9316 people/square mile) has the lowest suicide rate (5.3 deaths/100,000 population). Overall a powerful negative correlation was observed between the rate of suicide and population density (r=-0.641, P<0.01). Similar and striking negative correlations emerged between the distribution of psychiatrists (r=.59, p<0.01), psychologists (r=0.34, p<0.05) and social workers (r=0.42, p<0.01) and suicide rates. Discussion: Complex biopsychosocial, geographic and cultural factors may contribute to the higher rate of suicide in rural populations. The present study suggests that access to mental health care may be a relevant factor. The delivery of psychiatric services to rural communities using telehealth may bridge the current gap in available mental health care.

NR4-17

THE PREVALENCE AND CLINICAL CONSEQUENCES OF CONCURRENT HYPERTENSION IN PATIENTS WITH BIPOLAR DISORDER

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SUMMARY:
Patients with bipolar disorder suffer a disproportionate burden of cardiometabolic disorders. The pathogenesis and clinical consequences of these comorbid medical conditions on the expression and course of bipolar disorder have not been satisfactorily elucidated. Objective: The purpose of the present study was to determine the prevalence and examine the clinical correlates of cardiometabolic disorders in patients hospitalized with bipolar disorder. Methods: All patients who were hospitalized on an inpatient psychiatry unit in mid-Michigan for the treatment of bipolar manic and mixed states during calendar years 2002 to 2006 were invited to participate in the study. Following stabilization, the patients completed a brief inventory which included demographic, disease and treatment variables. The DSM-IV-TR psychiatric diagnoses and Young Mania Rating Scale ratings were completed by a psychiatrist. Results: A total of 99 patients were included in the study. Forty-five percent were hypertensive. As expected, the patients with hypertension were older; mean age 44 (SD=11) versus 37 (SD=12) years. They were more obese; mean BMI 33 (SD=9) versus 28 (SD=8). The patients with hypertension had an earlier mean age of onset of bipolar disorder: 24 (SD=9) versus 29 (SD=12) years; F=4.0, df=1, p=0.05. They achieved higher mean mania ratings than the others; 40 (SD=8) versus 35 (SD=8), F=4.55, df= 1, p=0.04. Discussion: As expected the prevalence of hypertension was higher in this cohort than in the general population. An earlier age of onset of bipolar disorder was predictive of the future development of hypertension. The presence of concurrent hypertension was associated with more severe mania ratings, and longer hospital stays. Is it conceivable that the prevention of hypertension may modify the expression and outcome of treatment in patients with bipolar disorder?

NR4-18

EFFICACY OF ADJUNCTIVE ARIPIPRAZOLE IN MAJOR DEPRESSIVE DISORDER: A POOLED RESPONSE QUARTILE ANALYSIS (CN138-139, CN138-163 & CN138-165)

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SUMMARY:

Objective: Evaluate the proportion of patients receiving adjunctive (adj) aripiprazole who achieve various levels of response, and the time course of those improvements. Methods: Data were pooled from three nearly identical studies consisting of an 8-week prospective antidepressant treatment (ADT) phase to document inadequate response (Phase B) and a 6-week, randomized controlled phase (Phase C) using adj placebo or adj aripiprazole (2–20 mg/day) [1,2]. Quartile response categories were defined based on percent reduction in Montgomery Åsberg Depression Rating Scale (MADRS) at weekly timepoints, relative to the end of Phase B: [1] Minimal Response (=<25%), [2] Partial Response (>25% to <50%), [3] Moderate Response (=>50% to <75%), and [4] Robust Response (=>75%). Proportion of adj placebo (n=525) versus adj aripiprazole (n=540) patients achieving each response category was compared for each category using the Cochran-Mantel-Haenszel test, and changes from baseline in mean MADRS score at Weeks 1 to 6 (Phase C) were compared using analysis of covariance. Results: Compared with ADT alone, adj aripiprazole treatment was associated with a significantly greater proportion of patients achieving a partial response (23.9% versus 17.9%, p=0.017), moderate response (23.1% versus 15.0%, p<0.001), and robust response (14.3% versus 7.4%, p<0.001). Likewise, compared to ADT alone, adj aripiprazole treatment was associated with a significantly lower proportion of patients achieving a minimal response (38.7% aripiprazole vs. 59.6% placebo, p<0.001). The time course of improvement for partial, moderate, and robust aripiprazole responders showed significant improvements in their change from baseline MADRS scores as early as Week 2 or 3 versus those responding to adj placebo. Conclusions: The majority of inadequate responders who continued on adj placebo were minimal responders (60%). In contrast, 60% of patients treated with aripiprazole rapidly achieved partial, moderate or robust response status.

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NR4-19

DULOXETINE 60 MG/DAY FOR THE PREVENTION OF DEPRESSIVE RECURRENCES: POST-HOC ANALYSES FROM A RECURRENCE PREVENTION STUDY

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SUMMARY:

Purpose: To assess the efficacy of duloxetine 60 mg/day in the prevention of depressive recurrence in patients with major depressive disorder (MDD). Methods: Patients having had at least 3 episodes of MDD in the past 5 years received open-label (OL) duloxetine 60 to 120 mg/day for up to 34 weeks. Patients who continued to meet response criteria were then randomized to either duloxetine or placebo for up to 52 weeks of double-blind maintenance treatment. Only patients taking duloxetine 60 mg/day during the OL phase and randomized to duloxetine (ie, those remaining on 60 mg/day dose) or placebo were included in this post-hoc analysis. The primary outcome measure was time to recurrence of a major depressive episode. The 17-item Hamilton Rating Scale for Depression (HAMD17) was used to evaluate depressive symptoms. Global and physical functioning was assessed using the Clinical Global Impressions of Severity (CGI-S) scale and Sheehan Disability Scale. Pain was evaluated using Visual Analog Scales. Safety and tolerability were assessed via analysis of treatment-emergent adverse events (TEAEs), vital signs, and weight. Results: A total of 124 patients were randomized to duloxetine 60 mg/day (n = 64) or placebo (n = 60). Time to a depressive recurrence was significantly longer in duloxetine-treated patients compared with placebo-treated patients (P = .001). During the double-blind maintenance phase, 12.5% of duloxetine-treated patients experienced a depressive recurrence compared with 31.7% of placebo-treated patients (P = .004). The HAMD17 total score and most of its subscales as well as the CGI-S significantly worsened in the placebo group compared with the duloxetine 60-mg/day group. There were no significant differences between treatment groups in TEAEs, discontinuations due to adverse events, vital signs, or weight.

Conclusion: Treatment with duloxetine 60 mg/day was associated with a longer time to depressive recurrence and a significantly lower recurrence rate compared with placebo.

Funding: This work was sponsored by Eli Lilly and Company and Boehringer Ingelheim GmbH.

NR4-20

EFFICACY OF DULOXETINE ON FUNCTIONAL IMPAIRMENT IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

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SUMMARY:
Patients with major depressive disorder (MDD) often have a reduced ability to function socially, maintain and enjoy relationships and work. This was a pooled analysis of data from two separate 9-month studies conducted under the same protocol in patients with MDD (DSM-IV-TR) to examine the efficacy of duloxetine 60 mg/day (N=518) versus placebo (N=258) on impairment in functioning. Pooling the data from these studies was specified a priori in the protocol to allow for increased power to detect differences between duloxetine and placebo on secondary and exploratory objectives. Measures included in this analysis were: the Sheehan Disability Scale (SDS); the Social Adaptation Self-evaluation Scale (SASS) to assess social behavior; Massachusetts General Hospital Cognitive and Physical Functioning Questionnaire (CPFQ); and the Profile of Mood States - brief form (BPOMS) subscales Vigor/Activity (VA) and Fatigue/Inertia (FI) used as surrogate measures of function. Mean changes from baseline were analyzed using a mixed-effects model repeated measures approach (MMRM). An analysis of covariance (ANCOVA) using a last observation carried forward (LOCF) approach was conducted as a sensitivity analysis. Endpoint for this analysis was at week 8. At baseline patients had moderately severe levels of SDS global functional impairment scores (18.3±6.9). At endpoint, there was significant improvement from baseline (MMRM) with duloxetine treatment on the SDS global (p=.002), SASS total (p<.001), and BPOMS VA (p=.012) and FI (p=.006) subscales. At endpoint (LOCF imputation), duloxetine-treated versus placebo-treated patients had significantly greater improvement from baseline on the SDS global; SASS total; CPFQ total; and BPOMS subscales VA and FI. In conclusion, these results suggest that treatment with duloxetine may improve functional impairment in patients with MDD. Support/funding: Lilly USA, LLC.

NR4-21

EFFECTS OF EXTENDED RELEASE QUETIAPINE FUMARATE ON LONG-TERM FUNCTIONING AND SLEEP QUALITY IN PATIENTS WITH GENERALIZED ANXIETY DISORDER (GAD)

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SUMMARY:
Objective: GAD is a chronic condition requiring effective long-term treatment to reduce symptoms and improve functional disability. This analysis evaluated the effects of once-daily quetiapine XR (QTP XR) maintenance treatment on functioning and sleep quality in patients (pts) with GAD.
Methods: This was a time-to-event, double-blind, randomized-withdrawal, parallel-group, placebo (PBO)-controlled maintenance study (D1448C00012) of QTP XR monotherapy in GAD. Following open-label run-in (4-8 wks) and a 12-18-wk stabilization phase (QTP XR 50, 150 or 300mg/day), eligible pts (HAM-A <=12; MADRS <=16; CGI-S <=3) were randomized to QTP XR or PBO (last open-label dose) for <=52 wks. Primary outcome: time from randomization to first anxiety event. Secondary outcomes included: change from randomization to each assessment in functioning (SDS) and sleep quality (PSQI).
Results: 433 stabilized pts were randomized to continue QTP XR (n=216) or switch to PBO (n=217) [mean (SD) dose 162.8 (88.3) mg, and 165.1 (95.6) mg, respectively]. Risk of an anxiety event was significantly reduced for QTP XR vs PBO (HR=0.19 [95% CI: 0.12, 0.31]; p<0.001). SDS total scores were significantly better maintained with QTP XR vs PBO (mean change: -0.19 vs 1.01; p<0.05). QTP XR was significantly better than PBO at maintaining the non-work-related SDS domain score 'family life/home responsibilities' (-0.13 vs 0.32, p<0.05), but not 'social life' (0.05 vs 0.34, p=0.114). QTP XR was significantly better than PBO at maintaining the work-related SDS domain score 'days lost' (-0.05 vs 0.11, p<0.05), but not 'work/school' (-0.10 vs 0.29, p=0.051) or 'days underproductive' (0.06 vs 0.13, p=0.619). PSQI global scores were also better maintained with QTP XR vs PBO (0.39 vs 1.60, p<0.001]). Conclusion: In pts with GAD, QTP XR (50-300mg/day) monotherapy was effective in maintaining improvements in several domains of functioning and sleep quality throughout long-term randomized treatment.
Funded by AstraZeneca

NR4-22

A 1-YEAR OPEN-LABEL STUDY ASSESSING THE SAFETY AND TOLERABILITY OF VILAZODONE IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

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SUMMARY:
Objective: Vilazodone HCl is a dual-acting SSRI and 5-HT1A receptor partial agonist that has been studied in two 8-week, phase 3 studies in adults with major depressive disorder (MDD). The objective of this study was to assess the long-term safety profile of vilazodone (VLZ). Method: This 52-week, open-label, multicenter study enrolled MDD patients 18-70 years of age with scores =18 on HAM-D17 at screening and baseline. The VLZ dose was titrated to 40 mg QD by day 14 and then continued for up to 52 weeks (safety population, n=599; completers, n=254). Drug safety was assessed by measurement of treatment-emergent adverse events (AEs), lab tests, physical exams, vital signs, weight, ECGs, discontinuations due to AEs, and the Changes in Sexual Function Questionnaire (CSFQ). Secondary outcome measures included MADRS, CGI-S, and CGI-I. Results: Discontinuations due to AEs in =1% of patients were nausea (1.3%), diarrhea (1.2%), and anxiety (1.0%). Most AEs (85.1%) were of mild or moderate intensity; severe AEs occurred in 14.9% of patients (severe AEs =1% incidence: psychiatric, 4.5%; gastrointestinal, 3.5%; and nervous system, 2.7%). The most frequent AEs were diarrhea (35.7%), nausea (31.6%), and headache, with most (98.7%, 100%, 98.7%, respectively) rated mild or moderate in intensity. Most serious AEs (33 in 23 patients) were judged by investigators as not or unlikely to be related to VLZ. Lab, ECG, and vital sign abnormalities were considered to be not clinically relevant. Decreased libido was the most frequent AE related to sexual function (4.2% of patients). CSFQ scores improved in males and females over the 52 weeks. MADRS mean total scores (OC) were: baseline, 29.9 (n=596); week 8, 11.4 (n=447); week 24, 8.2 (n=313), and week 52, 7.1 (n=254). CGI-I and CGI-S scores also improved. Conclusion: In this study, vilazodone 40 mg QD treatment of adults with MDD for up to 1 year appeared to be well tolerated. PGxHealth, LLC funded the study.

NR4-23

ATTRIBUTES OF RESPONSE IN DEPRESSED PATIENTS SWITCHED TO TREATMENT WITH DULOXETINE

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SUMMARY:
Purpose: To assess the clinical outcomes associated with response in depressed patients with pain switched to duloxetine. Methods: This 8-week, multicenter, single arm, open-label clinical trial included outpatients from Brazil, Canada, China and Korea (N=242) with major depressive disorder switched to duloxetine 60 mg/day after failing selective serotonin reuptake inhibitor (SSRI) or serotonin and norepinephrine reuptake inhibitor (SNRI) treatment. The primary analysis compared mean change from baseline in Brief Pain Inventory – Modified Short Form (BPI-SF) interference score between responders (=50% reduction from baseline on the 17-item Hamilton Depression Rating Scale [HAMD17] Maier subscale) and non-responders after 4 weeks of duloxetine treatment. Responders and non-responders (received duloxetine 120 mg/day for the final 4 weeks) were also compared on depression, anxiety, pain and functional outcomes after 8 weeks. Longitudinal outcomes were analyzed using mixed-effect models with repeated measures. Results: Pain interference improved from baseline in responders (N=108) and non-responders (N=85) after 4 weeks of duloxetine treatment, with greater reductions in responders (BPI-SF mean difference 1.01 [95% CI 0.42 to 1.61]; p<0.001). Reductions in pain interference remained greater in responders versus non-responders after 8 weeks, albeit with a smaller mean difference between groups (0.68 [95% CI 0.03 to 1.33]; p=0.042). Greater improvements in depression, anxiety and function were observed in responders versus non-responders after 8 weeks via HAMD17 total, Hamilton Anxiety Rating Scale total, Clinical Global Impressions of Severity and Sheehan Disability Scale scores (all p<0.001). Conclusion: In patients switched from SSRIs/SNRIs to duloxetine 60 mg/day for 4 weeks, Maier subscale responders showed greater improvement in pain interference than non-responders. Both groups had clinically significant improvements in pain, depression, anxiety and function over 8 weeks. Supported by Eli Lilly and Company.

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NR4-24

THE CORRELATION BETWEEN WHITE MATTER TRACT INTEGRITY OF ANTERIOR CINGULATE AND THYROID FUNCTION IN PATIENTS WITH MAJOR DEPRESSION

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SUMMARY:
Introduction: Recent studies of aim mutations in the SLC16A2 gene suggested that white matter abnormalities would be associated with thyroid function test (TFT) abnormalities which could delay myelination. Functional imaging studies demonstrated that depression was characterized by functional disconnection between frontal and limbic regions. Lower fractional anisotropy (FA), representing lower tissue organization, was observed in dorsolateral prefrontal cortex (DLPFC) and anterior cingulate cortex in old patients with depression. These findings support the hypothesis that altered connectivity between brain regions contributes to the risk of depression. In diffusion tensor studies, the patients with major depression showed a trend for lower values of fractional anisotropy (FA) in the left sagittal stratum, right cingulate cortex and posterior body of corpus callosum, compared to healthy controls. We hypothesized that the FA values of frontal and limbic regions in MDD patients with unstable TFT files (abnTFT-MD) would be lower than MDD patients with stable TFT files (nlTFT-MD). In addition, FA values in abnTFT-MD would be negatively correlated with BDI scores and frequency of admission. Methods: Fifteen abnTFT-MD and twenty nlTFT-MD were recruited. For two years, thyroid indices (T3, T4, and TSH). Depression symptoms assessed with Beck Depressive Inventory (BDI), and frequency of admission were gathered from the medical records of patients hospitalized for major depressive disorders. Statistical parametric mapping was used to evaluate the global differences in FA values between the two groups. Results: There were no significant differences in age, intelligence, and BDI score between nlTFT-MD and abnTFT-MD. Compared to nlTFT-MDD, abnTFT-MD showed decreased FA values in both anterior cingulated cortecies (x,y,z 20, -6, 26, ?e=69, t=4.13, p<0.001; x,y,z -20, -2, 26, ?e=199, t=4.85, p<0.001). In abnTFT-MD, FA values of anterior cingulated cortex were negatively correlated with BDI scores (r=-0.42, p=0.03) and frequency of admission (r=0.47, p=0.02). Discussion: Current results suggested that abnormal thyroid indices would be associated with lower tissue organization of white matter in DLPFC and anterior cingulate cortex in patients with major depression. Moreover, lower tissue organization of white matter in anterior cingulate would be associated with unstable course of illness in MDD patients.

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NR4-25

CLINICAL CORRELATES OF EATING DISORDERS COMORBIDITY IN WOMEN WITH BIPOLAR DISORDER TYPE 1

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SUMMARY:
Objective: Report the presence of current and lifetime eating disorders (Adler et al.) in a well-defined sample of 137 female patients with bipolar disorder (Conus et al.) type I. Methods: Patients were interviewed by trained psychiatrists with the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, Axis I Disorders. Clinical and demographic characteristics of both groups (group with ED vs. group without ED) were compared.
Results: Female patients with ED had an earlier onset of BD and an increased number of mood episodes, especially of depressive polarity. Women in the ED group also showed a high degree of comorbidity with substance use disorders and anxiety disorders and more frequently reported a history of suicide attempt when compared with women without ED.
Conclusion: Presence of ED is a correlate of severity of BD type 1 and development of interventions that may minimize distress, suicide risk and improve treatment outcome is necessary.

NR4-26

EFFICACY OF ADJUNCTIVE ARIPIPRAZOLE IN MAJOR DEPRESSIVE DISORDER PATIENTS WITH MINIMAL OR PARTIAL RESPONSE TO ANTIDEPRESSANT THERAPY

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SUMMARY:

Background: Traditionally, augmentation strategies have been employed in major depressive disorder (MDD) patients with partial response to antidepressant therapy (ADT), while patients with minimal response are often switched to another ADT. Methods: Data from three studies (1,2) were pooled to assess the efficacy of adjunctive aripiprazole in MDD patients with minimal and partial response to 8-week prospective ADT. Trial design has been described in detail (1). Minimal Responders were patients exhibiting <25% improvement on the Montgomery Åsberg Depression Rating Scale (MADRS) during the prospective phase. Partial responders exhibited 25-49% improvement. Change on the MADRS, response (=>50% reduction in MADRS), and remission (MADRS =<10 and =>50% reduction) during the 6-week double-blind adjunctive trial were examined using analysis of covariance and Cochrane Mantel Haenzel tests. Results: 72% (748/1041) and 28% (293/1041) of patients met criteria for minimal and partial response, respectively. ADT Minimal responders on adjunctive aripiprazole (ARI) showed significantly greater improvement in MADRS score at endpoint compared with placebo (-10.26 ARI vs. 6.49 PBO, p<0.001). They also exhibited higher endpoint response rates (35.6% ARI, 18.5% PBO, p<0.05) and remission rates (24.1% ARI, 11.6% PBO, p<0.05). For the ADT partial responders, endpoint MADRS change was -7.85 for ARI and -6.09 for PBO. Endpoint response rates were 42.5% for ARI and 34.4% for PBO, and remission rates were 40.7% for ARI and 31.2% for PBO. Partial responder results were not significant. Adverse event rates =>5% and twice PBO were akathisia, dizziness, somnolence, restlessness, insomnia, constipation, fatigue and blurred vision. Conclusion: Contrary to traditional beliefs, adjunctive ARI had a more robust effect in patients with minimal response to initial ADT than in partial responders. ARI was well tolerated in both responder subgroups.

Supported by Bristol-Myers Squibb and Otsuka Pharmaceuticals Co., Ltd.

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NR4-27

EFFECTS ON COGNITION OF ADJUNCTIVE ZIPRASIDONE VERSUS PLACEBO IN A LONG-TERM RANDOMIZED, DOUBLE BLIND TRIAL IN SUBJECTS WITH BIPOLAR I DISORDER

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SUMMARY:

Background: In clinical practice, antipsychotic agents are frequently combined with mood stabilizers or anticonvulsants for long-term symptom management in bipolar disorder. Ziprasidone has recently been approved for the long-term treatment of bipolar disorder as an adjunctive treatment with lithium or valproate. The impact of medication treatments for the long-term management of bipolar disorder is an important clinical concern. Cognitive side effects may impact long-term function and adversely affect treatment adherence. Here we discuss the impact of ziprasidone when added to lithium or valproate on cognitive performance in maintenance treatment of bipolar disorder. Methods: This phase 3 clinical study had an open-label stabilization period (10-16 weeks) and a double-blind, placebo-controlled randomization period (24 weeks). Subjects with a recent or current manic or mixed episode who remained symptomatic (Mania Rating Scale [MRS] score = 14 at baseline) despite therapeutic blood levels of either lithium (0.6–1.2 mEq/L) or valproate (50–125 µg/ml) had ziprasidone added (80–160 mg/d) in an open-label fashion. Subjects who achieved stabilization (Clinical Global Impression [CGI] score = 3 for 8 consecutive weeks with fixed medication doses for at least the last 4 weeks) were randomized 1:1 to either continue on ziprasidone plus lithium or valproate or to have ziprasidone replaced by placebo and observed over 6 months for recurrence of a mood episode. Cognition was assessed via a computerized cognitive test battery (CNS Vital Signs) screening at baseline and weeks 8 and 16 during stabilization, and weeks 4, 8, 16 and 24 of the maintenance phase. Results: 584 subjects were treated in

the open-label phase; 240 subjects were randomized and 127 were treated with ziprasidone and 112 with placebo in the double-blind period. The LS mean differences from placebo at week 24 of the double blind period (± Standard Error) were: verbal memory: -1.14 (2.56), processing speed: 1.93 (3.17), reasoning: 1.30 (1.63), executive functioning: -2.52 (2.66), working memory: 4.56 (3.75), sustained attention: 3.87 (3.96), and neurocognitive index: 0.49 (1.76). There were no significant differences between placebo and ziprasidone treatment groups on CNS Vital Signs endpoints. Conclusion: Long-term treatment with ziprasidone plus either lithium or valproate had no greater impact on cognitive function than treatment with either mood stabilizer alone.
Supported by Pfizer

NR4-28

HEALTHCARE UTILIZATION AND COSTS IN A COMMERCIAL POPULATION OF PATIENTS WITH TYPE I BIPOLAR DISORDER WHO RELAPSE FREQUENTLY

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SUMMARY:
Objective: To compare healthcare utilization and expenditures of patients with type I bipolar disorder who relapse frequently versus those who do not. Methods: A retrospective cohort design using claims from a large commercial managed care database (MarketScan) was used to examine patients ages 18-64 diagnosed with type I bipolar disorder between January 1, 2004 and June 30, 2006, with at least 24 months of continuous enrollment. Frequent relapsers (FRs) were defined as having =2 clinically significant events (CSEs) during a 12-month period beginning with initial CSE (if any) or bipolar I diagnosis. Infrequent relapsers (IFRs) were those with <2 CSEs. CSEs included emergency room (ER) visits or inpatient hospitalizations (IHs) with a principal diagnosis of type I bipolar disorder or a change in bipolar medication(s). Patients were followed for a subsequent 12-month period to evaluate healthcare utilization and costs. Data were analyzed using chi-square and t-tests for categorical and continuous variables, respectively. Results: 7620 FRs and 11,571 IFRs were identified. Sixty-seven percent of FRs were female (P<0.001). FRs had more comorbid psychiatric diagnoses (mean 2 versus 1, P<0.001) than IFRs. Twenty-two point two percent of FRs in the identification period were FRs in the follow-up period. FRs were more likely to have a mental health–related IH (15% vs 3%, P<0.001) and an ER visit (12% vs 3%, P<0.001) in the follow-up period. Length of mental health–related IH was longer (mean 12 versus 8 days, P<0.001), annual mental health–related healthcare cost was greater (adjusted mean $6617 versus $3276, P<0.001), and total annual healthcare cost was greater (adjusted mean $14,091 versus $9357, P<0.001) for FRs compared with IFRs, respectively. Conclusions: Twenty-two point two percent of type I bipolar patients with FR continued to be FRs in the following year. FRs had nearly twice the mental health–related cost and nearly 1.5 times the total healthcare cost observed with IFRs.
Supported by funding from Ortho-McNeil Janssen Scientific Affairs, LLC

NR4-29

COST-EFFECTIVENESS OF ADJUNCTIVE QUETIAPINE EXTENDED-RELEASE TABLETS WITH MOOD STABILIZERS IN THE MAINTENANCE TREATMENT OF BIPOLAR I DISORDER

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SUMMARY:
Introduction: Bipolar I disorder (BPD I) is a recurrent illness that affects 1% of the US population and constitutes a large economic burden. Methods: The cost-effectiveness of maintenance treatment with quetiapine extended-release tablets (QTP XR) in combination with mood stabilizers (lithium [Li] or divalproex [DVP]) was compared with: placebo (PBO) in combination with Li or DVP, no maintenance treatment, Li monotherapy, lamotrigine, olanzapine, and aripiprazole. Analysis was conducted with a societal and payer perspective using a Markov model. The model simulated a cohort of 1,000 stabilized BPD I patients and estimated the quarterly risk in 3 health states: euthymia, mania, and depression. Efficacy data were derived from 2 randomized, double-blind trials comparing quetiapine in combination with Li or DVP (QTP+Li/DVP) with PBO+Li/DVP for up to 2 years and other published randomized controlled trials. Resource data were extracted from published literature. Drug costs, hospitalizations, and physician visits were among the direct costs. Indirect costs included absenteeism, and mortality rates included suicide. Endpoints included number of acute mood events, hospitalizations due to

acute mood events, and costs per quality-adjusted life-years (QALY). Probabilistic sensitivity analysis (PSA) evaluated uncertainty in the model inputs. Results: QTP XR+Li/DVP was associated with reductions in acute mania (46%), acute depression events (41%), and related hospitalizations (44%) compared with PBO+Li/DVP; similar reductions in events were observed relative to Li monotherapy In the base-case analysis, the discounted incremental cost per QALY for QTP XR+Li/DVP compared with PBO+Li/DVP was USD$22,959, and $100,235 compared with Li monotherapy, while all other comparators were dominated. PSA showed these results to be robust. Conclusion: QTP XR+Li/DVP is a cost-effective maintenance treatment option for patients with BPD I.

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NR4-30

QUALITY OF LIFE IN SUBGROUPS OF BIPOLAR I PATIENTS WHO HAD CHILDHOOD TRAUMA

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SUMMARY:

Introduction: The impact of childhood trauma and domains of childhood abuse in bipolar disorder are rarely evaluated in the literature. The aim of this study is to research the impact of childhood trauma on clinical course and quality of life of bipolar I disorder patients. Methods: Between the dates of January and April 2009, 116 euthymic bipolar I patients who met DSM-IV-TR criteria were included in the study. A structured form designed for the long term and follow-up evaluation of mood disorders (SKIP-TURK), Young Mania Rating Scale, Hamilton Depression Scale, SF-36 and Childhood Trauma Questionnaire were used. Results: In this study it was found that 61.2% of the bipolar patients had any childhood abuse. The subscales scores of SF-36 (physical functioning, role-physical, pain, vitality, social functioning, role-emotion, general health, mental health) of the patients with childhood abuse was significantly lower ($p<0.05$) than the patients without childhood abuse. There was found significantly lower ($p<0.05$) five subscales scores (role-physical, vitality, social functioning, general health and mental health) of SF-36 in the mixed plus rapid cycling and mixed groups than the other group. Conclusion: The patients with the rapid cycling and mixed episodes who had a childhood abuse could have poor clinical course and poor quality of life. This group of patients needs to be more carefully followed-up by means of psychoeducation and psychotherapy.

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NR4-31

HPA AXIS DYSFUNCTION IN REMITTED BIPOLAR PATIENTS

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SUMMARY:

Background: A number of studies have shown that successful resolution of depressive symptoms normalizes the hypothalamic-pituitary-adrenal (HPA) axis. However, it has been suggested that abnormal function of the HPA axis may be a trait marker in bipolar disorder. The aim of the study was to test the hypothesis that the HPA axis dysfunction persists in remitted bipolar depressed patients. Method: We studied 45 DSM-IV major depressed patients (bipolar [BD], n=20 ; unipolar [UD], n=25) who 1) showed highest post-DST cortisol level > 80 nmol/l at baseline (before treatment), and 2) fulfilled stringent criteria for remission. A second DST was carried out in these remitted patients. Responses to DST were compared between patients and 27 healthy hospitalized controls. Results: At baseline, post-DST cortisol levels did not differ between UDs and BDs. While DST response was comparable between remitted UDs and controls, remitted BDs showed higher post-DST cortisol levels than controls ($p<0.002$) and remitted UDs ($p<0.01$). Conclusions: Our results suggest that the HPA axis activity—as evaluated by the DST—remains abnormal in remitted BDs. This abnormality may underlie the vulnerability to subsequent mood episodes and could be a potential trait marker in bipolar disorder.

NR4-32

EXTENDED RELEASE QUETIAPINE FUMARATE IN PATIENTS WITH MDD STRATIFIED BY BASELINE ANXIETY LEVEL: POOLED ANALYSIS OF DATA FROM TWO MONOTHERAPY STUDIES

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SUMMARY:
Objective: Around 50% of patients with MDD have clinically relevant anxiety levels, which may delay remission. Once-daily extended release quetiapine fumarate (QTP XR) monotherapy was evaluated in patients with MDD with high or low baseline anxiety levels. Methods: Data are pooled from two 6-week, double-blind, placebo (PBO)-controlled studies of QTP XR (D1448C00001, D1448C00002). Post hoc analyses: change at Week 6 in MADRS total score (primary variable) according to baseline HAM-A total score >=20 and <20; Pearson correlation analysis (r; 0 indicates no linear relationship between the variables) evaluating correlation between baseline anxiety and outcome at Week 6. Reported AEs were determined for each cohort.
Results: For patients with a baseline HAM-A total score >=20 (n=403), mean baseline MADRS total scores were 33.1 (n=131) for QTP XR 150mg/day, 32.5 (n=137) for QTP XR 300mg/day, and 32.8 (n=135) for PBO. At Week 6, QTP XR 150mg/day (-14.8, p<0.05) and 300mg/day (-15.0, p<0.05) significantly reduced MADRS total scores vs PBO (-11.8). For patients with a baseline HAM-A total score <20 (n=564), mean baseline MADRS total scores were 28.4 (n=183), 28.9 (n=186), and 28.7 (n=195) in the QTP XR 150mg/day, 300mg/day, and PBO groups, respectively. At Week 6, QTP XR 150mg/day (-14.2, p<0.001) and 300mg/day (-14.3, p<0.001) significantly improved MADRS total scores vs PBO (-10.4). In the correlation analysis, r values between baseline HAM-A total score and MADRS total score change from randomization to Week 6 were -0.031 for QTP XR 150mg/day, -0.057 for QTP XR 300mg/day, and 0.053 for PBO. AEs reported for patients with high and low baseline anxiety levels were similar in both groups and consistent with the known tolerability profile of QTP. Conclusions: In these secondary analyses, QTP XR (150 and 300mg/day) was effective in patients with MDD with high or low baseline anxiety levels; there was no correlation between baseline anxiety level and outcome.
Research funded by AstraZeneca.

NR4-33

VILAZODONE PHARMACOKINETICS IN SUBJECTS WITH MILD TO MODERATE RENAL IMPAIRMENT

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NR4-34

TREATMENT-EMERGENT SEXUAL DYSFUNCTION IN OUTPATIENTS WITH MAJOR DEPRESSIVE DISORDER: 6- MONTH TREATMENT AND FUNCTIONAL OUTCOMES

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SUMMARY:
Objective: To describe clinical and functional outcomes for patients receiving treatment for major depressive disorder (MDD), with an emphasis on the impact of treatment-emergent sexual dysfunction (TESD). Methods: This observational study enrolled sexually active outpatients (=18 years old) without SD, who were initiating selective serotonin reuptake inhibitor (SSRI) or serotonin and norephinephrine reuptake inhibitor (SNRI) treatment for MDD. Assessments included the Arizona Sexual Experience Scale (ASEX), Quick Inventory of Depressive Symptomatology-Self Report: Sixteen items (QIDS-SR16), treatment adherence and the EuroQol questionnaire (EQ-5D). Treatment decisions were made according to the usual standard of care; patients were assessed at study entry, and weeks 8, 16 and 24, with ongoing ASEX and medication records. The primary study objective was to compare TESD rates in outpatients receiving duloxetine or SSRI monotherapy over 8 weeks. Cochran-Mantel-Haenszel tests stratified by propensity score were used to compare TESD incidence between cohorts. Logistic regression with covariate adjustment (including propensity score) was conducted to compare remission rates. Factors related to TESD were identified using a generalized linear mixed effects model. Results: Of 1647 patients enrolled from 12 countries, 1549 were included in the analysis cohort (620 in the duloxetine cohort and 860 in the SSRI cohort);

67% of patients remained in their baseline cohorts at 24 weeks. The incidence of physician-rated TESD (based on the ASEX) at 8, 16 and 24 weeks was similar irrespective of treatment: duloxetine 23% versus 29% SSRI monotherapy (adjusted odds ratio, OR [95% CI] 0.77 [0.57, 1.03] at 24 weeks). Overall, 85% of patients achieved remission (QIDS-SR16 total score <5) within 24 weeks; patients on duloxetine were more likely to remit than those on SSRI monotherapy (90% vs 80%, adjusted OR 2.23 [1.43, 3.49]). Other secondary outcomes such as quality of life measures were in favour of duloxetine. Factors related to TESD incidence included country, previous SD with antidepressants, and remission of depression in the past 24 weeks. Conclusions: The pragmatic design and naturalistic setting of this multi-country study provide real-life context to clinical data, and insight into the outcomes of MDD and TESD in actual clinical practice, highlighting the importance of recognising and addressing these symptoms. This study was funded by Eli Lilly

NR4-35

LONG-TERM SAFETY, TOLERABILITY, AND EFFICACY OF EXTENDED RELEASE CARBAMAZEPINE IN A LARGE CLINICAL PRACTICE: A CHART REVIEW STUDY

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SUMMARY:

Background. Recent development of beaded CBZ extended-release capsules (CBZ-ERC) provided a new formulation with potential advantages. The present study examines the long-term tolerability and efficacy of CBZ-ERC in a population that has received long-term treatment with CBZ-ERC in a single private practice setting with exposure up to a maximum of 105 months. The population included children, adolescents, and adults. Methods. The present study assesses these parameters in patients of various bipolar subtypes (mixed/manic, bipolar I depression, and bipolar II), in a single-site private practice setting. Data was obtained from the charts of 300 patients who met DSM-IV criteria for bipolar disorder. Clinical response to CBZ-ERC therapy was defined as a Clinical Global Impression-Improvement (CGI-I) scale score < 3, while relapse was defined as CGI-I of >4 in those subjects who had previously achieved clinical response. Results. Mean age for the overall population was 29.4 years (SD 14.3). Level of severity as measured by a CGI-S at the time of initiation of treatment was 5.3 across all groups. The majority of subjects in the adult and adolescent populations met criteria for type I bipolar disorder (67.5% adults, 49.4% adolescents). In contrast, the majority of children (59.3%) met diagnostic criteria for bipolar disorder NOS. The most common presentation across all three groups consisted of mixed episodes. The most common comorbid diagnosis in the adolescent and child groups was attention deficit disorder (35.6% adolescents, 57.1% children). CBZ-ERC dosing during initial titration differed slightly across groups: adult average 494.2 mg; adolescent average 459.8 mg; child average 373.1 mg. However, at the end of the long-term study, all three groups were titrated to similar levels with an average dose of 765.1 mg (SD 305.1). Overall tolerability was similar in all groups. Overall treatment response rates (CGI-I < 3) were slightly higher in children and adolescents than in adults (adult 75%, adolescents 80.2%, children 80.0%). Rates of relapse were lowest in adolescents and highest in adults (adults 35%, adolescents 26.4%, children 30.8%). Conclusions. Carbamazepine extended-release capsules appear safe and efficacious for the treatment of bipolar disorder when employed in long-term treatment paradigms.

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NR4-36

ASSOCIATION OF THE SEROTONIN TRANSPORTER INTRON 2 VNTR POLYMORPHISM WITH TREATMENT RESPONSE TO MIRTAZAPINE IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

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SUMMARY:

Background: Polymorphisms of the serotonin transporter (5-HTT) gene appear to be associated with treatment response to antidepressants. Our objective was to determine whether the serotonin transporter intron 2 VNTR polymorphism (5-HTTVNTR) is associated with

treatment response to mirtazapine in patients with major depressive disorder (MDD). Methods: The 5-HTTVNTR polymorphism was analyzed in 309 MDD patients between 2005 and 2007 by the Pharmacogenomic Research Center for Psychotropic Drugs at the Department of Psychiatry, Korea University College of Medicine. All subjects were evaluated using the Hamilton Depression Rating Scale (HAMD21) at the beginning of the study and after 1, 2, 4, and 8 weeks of mirtazapine treatment. Results: Baseline HAMD21 scores did not differ according to 5-HTTVNTR genotype. Responder and non-responder groups differed significantly according to genotype, and responses at 8 weeks were significantly better for the 12/12 than for the 10/10 genotype. 5-HTTVNTR genotype and percent decline in HAMD21 score at 8 weeks were significantly associated. Conclusions: The 5-HTTVNTR polymorphism appears to predict response to mirtazapine treatment for MDD in a Korean population.

NR4-37

VILAZODONE PHARMACOKINETICS IN SUBJECTS WITH MILD TO MODERATE HEPATIC IMPAIRMENT

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SUMMARY:

Objective: Vilazodone HCl (VLZ) is a dual-acting SSRI and 5-HT1A receptor partial agonist in development for the treatment of major depressive disorder. The primary objective of this study was to assess the pharmacokinetics (PK) of VLZ in subjects with mild or moderate hepatic impairment. Method: 32 subjects aged 29-65 completed this phase 1, open-label, single-dose study: 8 with mild hepatic impairment (Child-Pugh 5-6 points), 8 with moderate impairment (7-9 points), and 16 with normal hepatic function individually matched for age, sex, and BMI. Subjects received a 20-mg dose of VLZ. PK and safety measures were performed predose to 7 days postdose. Results: Mean Cmax and AUC were similar among groups. Terminal elimination half-lives (30.6 and 29.4 h for mild and moderate impaired subjects vs 25.9 and 25.4 h for healthy control groups) and total drug clearance (25.5 and 29.4 vs 21.7 and 26.8 L/h) were similar for hepatically impaired and healthy subjects, as was mean recovery of VLZ in urine over 96 h (1.30%-0.92% vs 0.84%-1.13% of administered dose). VLZ was extensively bound to plasma proteins, with mean free fraction of 1.59% and 1.64% in mild and moderate hepatically impaired and 0.99% in subgroups of healthy subjects. Due to the observed high variability (CV, 22%-65%) there was no substantial difference in protein binding and total drug clearance was not affected. Mean serum albumin was within normal range for all groups. No differences in safety outcomes were observed. Conclusions: Vilazodone PK are similar in healthy and mild or moderate hepatically impaired subjects. Observed differences are small and of no clinical relevance. Peak exposure and drug accumulation with chronic dosing are not expected to be affected by mild or moderate hepatic impairment. Safety and tolerability of vilazodone were comparable in all groups. Thus, in mild or moderate hepatically impaired subjects no dosage adjustment seems to be required.

PGxHealth, LLC funded the study.

NR4-38

LONG-TERM OUTCOME OF FIRST MANIC EPISODES: A RETROSPECTIVE REVIEW OF 354 INPATIENT CASES

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SUMMARY:

Background: Although our understanding of the psychopathology of bipolar disorder has been greatly improved over the past decade, the Long-Term Outcome (LTO) of the First Manic Episodes (FME) remains controversial. The first aim of this naturalistic study was to assess the LTO of FME following an initial hospitalization. The second aim was to examine the difference in long-term course of FME as opposed to First Major Depressive Episodes (FMDE). Methods: Data was compiled from the separation sheets (ICD-9 format) of 6178 (14+ years) first admitted patients to a Quebec regional psychiatric hospital, from 1980 to 2008. These included 354 FME and 1234 FMDE cases. A subgroup of 166 multiple admission cases provided data on LTO of FME. Results: The observed rate of FME was 5.7% among first admitted subjects. Over a median period of five years the longitudinal diagnostic stability for bipolar disorder was 76.5%. By the 10th year of retrospective follow-up, all multi-admission cases (46.9% of the FME group) had developed at least one depressive episode (predominant polarity). The LTO of the FME patients was significantly different from that of FMDE patients with respect to age, gender, comorbid personality disorders, comorbid drug abuse and chronicity.

Conclusions: In everyday clinical practice, these results and those of other studies indicate that major depressive episodes are overwhelmingly common after the FME and deserve close attention. Furthermore, our long-term naturalistic data upholds DSM-IV classification of "Unipolar Mania" under the heading of "Bipolar I Disorder."

NR4-39

PLACEBO RESPONSE IN TRIALS OF ANTIDEPRESSANTS IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER

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SUMMARY:
Introduction: The degree of placebo response provides a pivotal context for defining antidepressant efficacy in clinical trials. Evidence suggests an increase in the placebo response in the past decades. A variety of factors such as baseline severity of symptoms and attention paid to subjects during clinical trials have been proposed as explanations. The objective of this analysis is to examine the placebo response in Wyeth-sponsored antidepressant trials and explore factors that may be associated with changes in placebo response. Methods: The analysis included data from all Wyeth-sponsored, randomized, double-blind, placebo-controlled studies of venlafaxine and desvenlafaxine completed as of August 2009 involving adult patients with Diagnostic and Statistical Manual of Mental Disorders (DSM) defined MDD. Data from 22 studies in which patients received venlafaxine (25 to 375 mg/d) or placebo for up to 8 weeks and from 9 studies in which patients received desvenlafaxine (50 to 400 mg/d) or placebo for up to 8 weeks were summarized. Effect sizes (using Cohen's d) were calculated based on the 17-item Hamilton Rating Scale for Depression (HAM-D17) total score. Effect sizes were plotted against study start date, mean baseline HAM-D score, minimum baseline HAM-D score, and mean number of assessments per visit. Results: In venlafaxine and desvenlafaxine studies, effect sizes generally decreased over time, suggesting an increase in placebo response. Mean baseline HAM-D17 scores did not appear to substantially influence effect size, although effect sizes tended to be lower as minimum baseline HAM-D17 scores increased. The mean number of assessments per visit increased over time. Effect sizes tended to decrease as the number of assessments per visit increased. Conclusions: Further investigation and analysis of these and other factors that may influence placebo response in antidepressant studies is necessary. Future studies of antidepressants should be designed with such factors in mind. The demonstration of the efficacy of novel medications with potential antidepressant efficacy is jeopardized by the increase in placebo response in clinical trials.
Research supported by Pfizer, formerly Wyeth Research

NR4-40

INCIDENCE OF HEADACHE, NAUSEA, AND MYALGIA AFTER ECT IN ADOLESCENTS AND ADULTS: RELATION TO TREATMENT NUMBER AND PATIENT AGE

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SUMMARY:
Objective: Reports of the incidence of common somatic complaints immediately following electroconvulsive therapy (ECT) vary widely. Headache (HA), nausea (NA) and myalgia (MY) may have a detrimental effect on treatment compliance. This study reports the incidence and severity of these side effects related to patient age group (AG) and treatment number (TN) within a first series of ECT in a large patient population. Method: Data from a university associated neuropsychiatric hospital QA database were extracted for 1002 sequential patients receiving ECT from November 1999 to October 2009. Severity scores from the physician evaluation following each ECT were categorized as: None, Mild: easily treated, Moderate: effectively treated with two or more medications, Severe: not responsive to repeated therapy. Incidence and severity of HA, NA and MY were calculated for AG and TN in the series. Results: Median age was 47 (range 13 to 97), 64% female. Overall incidence of HA, NA and MY were 39.9, 15.6 and 13.3% respectively. The overall incidence of side effects ranged by age and TN: for HA 79% (AG 30-39, TN1) to 18% (AG>59, TN6); NA 45% (AG<30, TN1) to 11% (AG<30, TN7); MY 50% (age 30-39, TN1) to 2% (age > 59, TN7). The incidence of severe side effects decreased for HA, NA, and MY following TN1 to TN3 from 6.8 to 2.3%, 1.8 to 0.5%, and 5.2 to 0.1% respectively. The incidence of severe HA, NA and MY varied for AG 30-39 vs AG > 59 from 3.7 to 0.3%, 1.0 to 0.3%, and 1.1 to 0.5% respectively. Conclusions: This large retrospective study describes the

longitudinal course and the relation of age to systemic side effects after ECT. Young patients had a higher incidence of physical complaints and more severe symptoms compared to older age groups. Somatic side effects were most intense after the first ECT and diminished rapidly with subsequent treatments. These results should be helpful when discussing somatic side effects with patients who are considering ECT.

NR4-41

HIGH LEVELS OF COMORBID PERSONALITY DISORDER PREDICT NON-RESPONSE TO METHYLPHENIDATE FOR ADULTS WITH ADHD

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SUMMARY:

Introduction: This study explored the influence of personality disorder (PD) in a trial of methylphenidate transdermal system (MTS) in adult ADHD and assessed attention-disorganization, hyperactivity-impulsivity, emotional dysregulation (ED) and oppositional defiant symptoms (ODD), symptoms found in this disorder. Methods: This placebo-controlled crossover trial enrolled adults who met the Utah and/or DSM-IV-TR criteria for ADHD. No attempt was made to include or exclude patients with personality disorder. Outcome was measured by the Wender-Reimherr Adult Attention Deficit Disorder Scale (WRAADDS), Connors' Adult ADHD Rating Scale (CAARS) and Clinical Global Impression – Improvement (CGI-I). Personality Disorder was assessed by the clinician using all available information including the SCID-II and two self-report questionnaires. Subjects were categorized into 3 groups: those with no PD (PDnegative), those with one PD (PDpositive) and those with 2 or more PDs (PDplus). An ANOVA assessed treatment effects on WRAADDS and CAARS. Chi-square assessed categorical response defined as CGI-I =2. Results: Sixty-seven subjects entered the trial. 5 subjects had a PD in cluster A, 19 in cluster B, 27 in cluster C and 7 had other PDs. 24 were PDnegative, 25 were PDpositive and 18 were PDplus. Treatment (placebo versus MTS) was significant for WRAADDS and CAARS scores for PDnegative and PDpositive subjects but not for PDplus subjects. Thirty-eight percent of PDplus subjects were responders in the MTS arm versus 71% of PDpositive and PDnegative subjects (CGI-I). Compared with other subjects, PDplus subjects had higher levels of ED (p=.004) and ODD (p=.007). Conclusions: PDplus subjects exhibited no MTS treatment effect for their ADHD symptoms while PDpositive and PDnegative subjects responded positively. PD status influenced treatment across all ADHD symptoms. Assessment for personality disorder as a predicting variable should be considered when developing clinical trials.

NR4-42

ASENAPINE AS ADJUNCTIVE TREATMENT FOR BIPOLAR MANIA: RESULTS OF A PLACEBO-CONTROLLED 12-WEEK STUDY AND 40-WEEK EXTENSION

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SUMMARY:

Objectives: Asenapine is indicated in adults for the acute treatment of schizophrenia and manic or mixed episodes of bipolar I disorder with or without psychotic features. We describe the efficacy and tolerability of adjunctive asenapine in patients with manic episodes associated with bipolar I disorder showing incomplete response to lithium or valproate monotherapy. Methods: A 12-week, randomized, placebo-controlled core study tested the efficacy of flexible-dose sublingual asenapine (5 or 10 mg BID) as an adjunct to continued mood stabilizer therapy. Patients who completed the core study without protocol violations could enter a 40-week extension and continue on their current treatment regimen. Changes from core study baseline on the Young Mania Rating Scale (YMRS) and Montgomery-Asberg Depression Rating Scale (MADRS) total scores were assessed at week 3 of the core study and at week 52 at the end of the extension. Efficacy in the core study was assessed using analysis of covariance in the intent-to-treat (ITT) population, with last observations carried forward to impute missing data. Analysis of efficacy during the extension included the core study data of those entering the extension; descriptive statistics only were employed for the extension. Results: The ITT population comprised 318 patients (asenapine, 155; placebo, 163) in the core study and 71 (38; 33) in the extension. A total of 116 patients (asenapine, 61; placebo, 55) completed the core study and 34 (19; 15) completed the extension. Mean ± SD changes at week 3 with asenapine and placebo,

respectively, were –9.7±10.1 versus –7.7±9.6 (P=0.0257) on YMRS total score and –2.8±7.2 versus –2.2±6.8 (P=0.3684) on MADRS total score. Changes at week 52 with asenapine and placebo were –17.2±13.7 versus –19.7±11.8 on YMRS and –3.3±9.8 versus –3.9±7.7 on MADRS. The incidence of treatment-emergent AEs with asenapine and placebo, respectively, was 73% and 69% in the core study and 78% and 69% in the extension. AEs reported by >=10% of patients and at twice the incidence of placebo in the core study included sedation (asenapine, 13.3%; placebo, 6.0%) and somnolence (11.4%; 4.2%); in the extension study, only sedation (asenapine, 14.6%; placebo, 5.6%) met these criteria. Conclusions: Asenapine was effective and well tolerated as an adjunct to mood stabilizers for up to 1 year in patients with manic episodes associated with bipolar I disorder.

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NR4-43

HIGHER SCORES ON MOTOR IMPULSIVITY AND LOWER SCORES ON COOPERATIVENESS ARE ASSOCIATED WITH HISTORY OF SUICIDE ATTEMPTS IN BRAZILIAN OUTPATIENTS WITH BIPOLAR DISORDER

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SUMMARY:

Objective: To investigate the relationship between personality characteristics and suicide attempts in outpatients with bipolar disorder (BD). Methods: Sixty-one euthymic outpatients with BD type I (DSM- IV) were evaluated. Participants were divided into two groups: suicide attempters (n=27; mean age 38.3 SD 9.7) and non-attempters (n=34; mean age: 40.6 SD 9.3). We used the Barrat Impulsiveness Scale (BIS) to measure impulsivity and the Temperament and Character Inventory (TCI) to assess personality traits. Results: Attempters showed higher scores of impulsivity on the attentional and motor subscales (21.0 versus 19.0, p = 0.043 and 24.8 versus 20.6, p = 0.002; respectively), as well as on the BIS total (73.5 versus 65.5, p = 0.009) in comparison to non-attempters. Regarding the TCI, attempters presented higher scores on Harm Avoidance (22.1 versus 17.8, p = 0.021), and lower scores on Self-Directedness (24.8 versus 29.8, p = 0.020) and Cooperativeness (27.3 vs. 32.6, p < 0.000). Stepwise multiple logistic regression showed that history of suicide attempts was significantly associated with female gender (p = 0.010), motor impulsivity (p = 0.026) and cooperativeness (p = 0.005). Conclusion: History of suicide attempts is associated with higher motor impulsivity and lower cooperativeness in euthymic outpatients with BD type I. Our results may contribute to further improve suicide prevention strategies in this population.

NR4-44

COMPARISON BETWEEN CLINICAL CHARACTERISTICS OF SUICIDE ATTEMPTERS AND NON-ATTEMPTERS IN A SAMPLE OF BIPOLAR DISORDER PATIENTS WITH MANIA AS FIRST EPISODE

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SUMMARY:

Objective: Little attention has been drawn to mania as first episode polarity and suicide attempts in bipolar disorder (BD). Our aim is to compare clinical characteristics between suicide attempters and non-attempters in a sample of BD patients with mania as first related episode. Methods: We selected 247 outpatients with mania as first episode polarity from a sample of 552 patients with DSM-IV BD type I (DSM-IV) from the Brazilian Research Consortium for Bipolar Disorders. Participants were divided in two groups: suicide attempters (N=93, mean age: 43.0±12.9, males:30%) and non-attempters (N=154, mean age:39.8± 9.8, males:70%), according to the presence of lifetime suicide attempts. We compared these two groups regarding demographic and clinical variables. Results: Attempters had more rapid cycling (p= 0.002), more SUD (substance use disorders, p=0.020), more anxiety disorders (p=0.002), eating disorders (p= 0.014), and early onset of mania (age of onset <=19) (p=0.001). Stepwise logistic regression revealed that the following variables are associated with suicide attempts: early onset of mania (Wald = 6.56; OR 2.2; 95% CI= 1.20-4.12, p=0.010), SUD (Wald= 4.48; OR 1.9; 95% CI= 1.04 -3.44; p=0.034) and anxiety disorders (Wald= 6.38; OR 2.0; 95% CI = 1.17 – 3.64; p=0.012). This model predicts 67% of suicide attempts status. Conclusion: In our sample of BD patients with mania as first episode polarity, early age of onset of mania, SUD and anxiety disorders are associated with suicide attempts during lifetime. Our results suggest that these

characteristics might be markers of suicidal behavior in this subgroup of patients.

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NR4-45

ASSOCIATION OF MEDICATION ADHERENCE WITH THERAPEUTIC ALLIANCE IN INDIVIDUALS WITH BIPOLAR DISORDER

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SUMMARY:

Objective: Despite low medication adherence rates for bipolar disorder and the impact of adherence on outcomes, little is known about the association of adherence with specific aspects of the therapeutic alliance. Our aim is to understand aspects that may affect medication adherence among patients with bipolar disorder. Methods: We examined data from 3,640 patients with a DSM-IV diagnosis for bipolar disorder I, II or NOS, cyclothymia, or schizoaffective disorder bipolar type who participated in the multicenter Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). Logistic regression models were utilized to investigate the association between self-reported medication adherence and participants' perceptions of their relationship with their provider and quality of psychiatric care, as assessed by the Helping Alliance Questionnaire at baseline and Care Satisfaction Questionnaire over the study duration. Results: Factors endorsed by participants, such as degree of collaboration, empathy, compassion and accessibility, were significantly associated with treatment adherence (uncorrected $p<0.05$). Conversely, some factors, such as patients' perceptions of their providers' experience as well as of their degree of discussing medication risks and benefits, were not significantly associated with adherence. Conclusions: Patients' perception of a collaborative therapeutic alliance and an efficient, yet respectful, treatment environment were positively associated with medication adherence, with some notable exceptions. This study informs strategies which may positively impact medication adherence.

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NR4-46

CORRELATION BETWEEN FUNCTIONALITY AND SUBJECTIVE WELL-BEING IN UNIPOLAR DEPRESSIVE PATIENTS IN REMISSION

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SUMMARY:

Introduction: In treatment studies of unipolar depression, remission is defined by the score achieved in symptomatic rating scales. Many patients in symptomatic remission cannot regain the functionality they had prior to getting sick and achieving an incomplete recovery. Improvement in functionality is rarely included in efficacy studies. The aim of this study is to evaluate whether a correlation exists between the symptoms remission scores, the functionality scores and subjective perception of improvement. Materials and methods: Forty-eight outpatients in two public hospitals were included in this cross-sectional study. After verifying the diagnosis of unipolar depression with mood disorders module of the structured interview MINI 500, patients were administered the HAM-D scale to determine the presence of symptomatic remission (less or equal to 7 points) and FAST scale as a measure of functionality. All the patients completed the Beck scale, a self-administered

inventory of depressive symptoms as a way of assessing the subjective perception of improvement. We analyzed the correlation between the scale's scores. Results: The scores on the FAST scale showed a statistically significant positive correlation with the Beck Inventory scores (Spearman's rho = 0.79, p <0.001) and HAM-D scale (rho = 0.43, p = 0.004). A linear regression analysis with the FAST as the dependent variable and age, sex, number of episodes, education , treatment time and BDI as independent variable revealed that BDI was the variable that better predicted the functionality (standardized Beta 0,7 p < 0,001; R2 = 0.501 p = 0.001).
Conclusions: In this study achieving remission scores was not accompanied with complete functionality or subjective well-being. High scores on the Beck scale in patients with scores of remission in the HAM correlated significantly with low functionality. Future studies are needed to evaluate the predictive value of function recovery in unipolar patients in remission.

NR4-47

COMPARISON OF HOSPITALIZATIONS AND COSTS AMONG BIPOLAR PATIENTS WHO SWITCHED TO EXTENDED-RELEASE QUETIAPINE FROM IMMEDIATE-RELEASE QUETIAPINE

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SUMMARY:
Introduction: Immediate-release quetiapine (QTP IR) and extended-release quetiapine (QTP XR) are both indicated in the US for the treatment of bipolar I disorder (BPD). This analysis compares all-cause and mental health hospitalizations and associated costs among patients who switch from QTP IR to QTP XR. Methods: Retrospective analysis of commercial managed care pharmacy and medical claims. Patients with prescription claims for QTP XR between June 1, 2007 and June 30, 2008 with ICD-9-CM codes for BPD who were continuously enrolled in their health plan for at least 6 months prior to and 6 months after the index date, and were prescribed QTP IR during the pre-index period, were included in the analysis. The index date was the date of the first QTP XR prescription claim, which indicated a switch from QTP IR to QTP XR. Differences in hospitalizations and costs during the 6-month pre-index and post-index periods were compared using nonparametric and parametric statistical tests. Results: In total, 190 patients met the inclusion/exclusion criteria for the analysis. The proportion of patients with at least 1 hospitalization for any cause during the pre-index period was 25.8% versus 14.7% in the post-index period (P=0.0033). The proportion of patients with at least one mental health hospitalization during the pre-index period was 22.1% versus 8.9% in the post-index period (P<0.0001). Mean all-cause hospitalization cost per patient during the pre-index period was USD3679 versus USD1422 in the post-index period (P=0.0036). Mean mental health hospitalization cost per patient during the pre-index period was USD2835 versus USD776 in the post-index period (P=0.0019). Conclusion: This analysis suggests that the rates of all-cause and mental health hospitalizations and associated per patient costs decrease significantly among BPD patients who switch from QTP IR to QTP XR.
Supported by funding from AstraZeneca Pharmaceuticals LP

NR4-48

A WEB-BASED SYSTEM FOR MEASURING OUTCOME IN THE TREATMENT OF DEPRESSION: RELIABILITY, VALIDITY, AND PATIENT ACCEPTANCE

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SUMMARY:
Background: There have been increasing calls for the use of standardized assessments in clinical practice. A web-based administration of outcome assessments offers several advantages over paper-and-pencil assessments such as patient convenience, reduced missing data, reduced costs, automatic scoring, and generation of large data bases. The present study evaluates the acceptability, reliability, and validity of a web based administration of a depression scale. Methods: Forty depressed outpatients completed a web-based and paper version of the Clinically Useful Depression Outcome Scale (CUDOS). Patients were also asked to complete a brief 6-question survey of the acceptability of the two modes of scale administration asking which of the two approaches took less time to complete, was less burdensome to complete, perceived as more confidential and secure, and preferred to complete at follow-up appointments. At the time of the visit, the patients' psychiatrist completed the Montgomery-Asberg

Depression Rating Scale (MADRS), and rated patients on the Clinical Global Index of severity (CGI) and Global Assessment of Functioning (GAF). Results: The correlation between the web-administered and paper versions of the CUDOS was high. The mean scores were similar on the paper and internet administrations. The internal consistency of the paper and internet administrations of the CUDOS was high and all item-scale correlations for the paper and internet versions were significant. The paper and internet versions of the CUDOS were equally correlated with clinicians' ratings on the MADRS, CGI, and GAF. Patients reported high levels of satisfaction with internet administration, and preferred this method of monitoring outcome to paper administration in the office. Conclusions: The results of this first study of the use of a web-based system of monitoring outcome in routine clinical practice supported the reliability and validity of internet administration of the CUDOS, and patients clearly preferred internet administration of the scale.

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NR4-49

DEPRESSED PATIENTS' PERSPECTIVES OF TWO MEASURES OF OUTCOME: THE QUICK INVENTORY OF DEPRESSIVE SYMPTOMATOLOGY & REMISSION FROM DEPRESSION QUESTIONNAIRE

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SUMMARY:

Background: Current standards for treating major depressive disorder (MDD) recommend that achieving remission should be considered the ultimate treatment goal. Despite its emphasis as the primary goal of MDD treatment, however, remission has proven to be an elusive construct to capture and apply. There have been differences in current operational definitions of remission, and at their root, the current definitions are exclusively symptom-based and are thus limited in scope. A recent report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project suggested that ameliorating or eliminating depression symptoms, while an important goal, is not necessarily the primary outcome that patients wish to achieve from treatment. In the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project we examined the patient acceptability of a new measure, the Remission from Depression Questionnaire (RDQ), a scale designed to capture a broader array of domains considered by patients to be relevant to the construct of remission. The acceptability of the RDQ was compared to that of the Quick Inventory of Depressive Symptomatology (QIDS), the instrument used to measure outcome in the STAR*D study. Methods: One hundred two depressed outpatients in ongoing outpatient psychiatric treatment completed the RDQ and QIDS and a 9-item measure of patient preference. Results: Patients did not report differences between the scales in completion time, burden to complete, and understandability of the items. The patients indicated that the RDQ was a better indicator of their overall state and their goals in treatment. Consistent with this, the patients judged the RDQ to be a more accurate and preferred measure to determine the outcome of treatment, and a more accurate indicator of remission. Conclusions: Patients considered the multifactorial RDQ a more accurate indicator of their goals of treatment than a purely symptom measure such as the QIDS.

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NR4-50

THE RELATIONSHIP BETWEEN CONTINUED USE OF ANTIDEPRESSANTS AND ACUTE PSYCHIATRIC EVENTS AMONG PATIENTS WITH MANIC OR MIXED BIPOLAR DISORDER EPISODES

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SUMMARY:
Objective: Bipolar disorder (BD) treatment guidelines state that antidepressants (ADs) may precipitate or exacerbate manic or mixed episodes and recommend tapering or discontinuing ADs for patients with a recent acute manic or mixed episode. This study assessed patterns of continued AD use among patients with BD, and the relationship between such use and acute psychiatric events in clinical practice. Methods: This retrospective analysis identified patients based on a BD I mania or BD I mixed diagnosis and an acute psychiatric event ("index event") from the PharMetrics database over the period January 1, 2004 through June 30, 2007. Patients with a schizophrenia diagnosis were excluded, and all patients were required to be at least 18 years of age at index and eligible for 12 months prior to and following the index event. An acute psychiatric event was defined as: (1) hospitalization or ER visit with primary listed diagnosis of BD; or (2) office visit with primary listed diagnosis of BD with a prescription for a new BD medication. Study measures included the likelihood of continued AD use (defined as 30+ days of available antidepressant therapy at any time during the post-index period) and secondary acute events post-index period.
Results: 5378 patients met study criteria (mean age, 43 years; 60% female). Of these, 59% met the definition of continued AD use. Patients with such use were more likely to experience a post-index acute event than those without continuing AD use (overall: 41% vs 25%, P<.001; BD I mixed: 39% vs 25%, P<.001; BD I mania: 45% vs 25%, P<.001). Conclusions: Our findings suggest that over half of BD patients in clinical practice with BD I mixed and BD I mania may continue to receive ADs, and such continued use is associated with a greater likelihood of acute psychiatric events compared with patients not taking ADs. Ensuring more appropriate use of ADs may alleviate this clinical burden.
Supported by funding from AstraZeneca Pharmaceuticals LP.

NR4-51

EFFICACY OF ARIPIPRAZOLE IN THE TREATMENT OF IRRITABILITY IN PEDIATRIC PATIENTS (6–17 YEARS) WITH AUTISTIC DISORDER: RESULTS FROM A 52-WEEK STUDY

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SUMMARY:
Background: Two 8-week, randomized, placebo-controlled trials evaluated aripiprazole (ARI) in the treatment of irritability associated with autistic disorder. Here we report efficacy results from a longer-term study. Methods: 52-week, open label, flexibly dosed (2–15 mg/day) study of ARI in the treatment of irritability in pediatric patients (6–17 years) with autistic disorder. Subjects either completed one of the 8-week randomized trials and had received either ARI (prior ARI [PA]) or placebo (prior placebo [PP]), or were de novo (DN). Safety and tolerability were the primary outcomes; efficacy was a secondary outcome and included the Aberrant Behavior Checklist-Irritability (ABC-I) subscale, Clinical Global Impression - Severity (CGI-S) and Improvement (CGI-I) scores, and other efficacy measures.
Results: Three hundred thirty subjects entered the treatment phase: 174 PA, 70 PP and 86 DN. One hundred and ninety nine subjects completed 52 weeks of treatment. Mean changes from baseline to endpoint in the ABC-I subscale score (LOCF) were: PA +0.7, PP –6.1, and DN –6.5. Mean changes in CGI-S (LOCF) scores at endpoint were: PA 0.0, PP –0.4, and DN –0.8. For CGI-I (LOCF), using as baseline the start of the parent study for rollover subjects and the start of the open-label study for DN subjects, 19.6% were considered "very much improved" and 38.2% were "much improved." All groups demonstrated improvement in measures of health-related quality of life; improvement in caregiver strain was observed in PP and DN groups; no change from the antecedent trials was seen for PA subjects.
Conclusions: Improvements in symptoms were most evident in DN and PP subjects; efficacy observed in the antecedent trials was maintained in PA subjects, and endpoint scores for all subgroups were similar. Interpretation of the results is limited by the open-label nature of the study, but were consistent with longer-term improvements in symptoms of irritability associated with autistic disorder.
Supported by Bristol-Myers Squibb and Otsuka Pharmaceutical Co, Ltd.

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NR4-52

ASSOCIATION OF AGE OF ONSET AND MOOD IN BIPOLAR DISORDER: COMPARING SUBGROUPS IDENTIFIED BY CLUSTER ANALYSIS AND CLINICAL OBSERVATION

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SUMMARY:

Objective: Patients with an early age of onset of bipolar disorder may experience a more severe clinical course. This analysis examined the association between self-reported mood ratings and the age of onset, comparing the results using subgroups identified by cluster analysis and by clinical observation. Methods: 270 patients residing in the US used ChronoRecord software to rate mood daily for about 6 months. The age of onset subgroups were determined using two approaches: model-based cluster analysis and with previously defined cutoff values based upon clinical observation (= 12 years, 13-19 years, 20-29 years, >29 years). Univariate general linear models (GLM) were used to estimate if the age of onset subgroups were associated with the percent of days depressed, euthymic and manic, controlling for demographic differences between the subgroups. Results: Model-based cluster analysis found a mixture of 2 distributions with peaks at age 15.1 ± 4.7 years and 27.5 ± 10.2 years. Analysis of these two subgroups detected no significant differences in demographic characteristics or mood ratings. In contrast, using the subgroups arising from clinical observation, demographic differences were found between the four subgroups in the diagnosis of bipolar I/II, years of illness, age and use of lamotrigine. Post-hoc pairwise comparison found that patients with an age of onset less <= 12 years spent about twice as many days manic as those with an age of onset between 13 and 19 years (16.4 percent versus 8.0 percent, p=0.006), and twice as many days manic as those with an age of onset between 20 and 29 years (16.4 percent versus 8.2 percent, p=0.031). The majority of the additional days of mania occurred outside of an episode. Conclusion: The age of onset subgroups arising from clinical observation may be more useful than those determined by cluster analysis.

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NR4-53

EFFECTS OF ADJUNCTIVE EXTENDED RELEASE QUETIAPINE FUMARATE ON SLEEP DISTURBANCE AND QUALITY IN PATIENTS WITH MDD: A POOLED ANALYSIS

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SUMMARY:

Objectives: Disrupted sleep is a common feature of depression and a risk factor for recurrence and suicide. The effects of once-daily extended release quetiapine fumarate (QTP XR) adjunct to ongoing antidepressant (AD) therapy on restoration of sleep and sleep quality in patients with MDD and an inadequate response to prior AD treatment was investigated. Methods: Pooled data from 2 (D1448C00006 and D1448C00007) 6-week, multicenter, double-blind, randomized, placebo (PBO+AD)-controlled studies of adjunctive QTP XR (150 and 300 mg/day) were analyzed. Primary endpoint (both studies): change in depressive symptoms (MADRS total score). This post hoc analysis is based on secondary endpoints: change in MADRS item 4 (reduced sleep), HAM-D items 4 (insomnia-early), 5 (insomnia-middle) and 6 (insomnia-late), and sleep disturbance factor (items 4+5+6), and sleep quality (PSQI total score). Change in MADRS total score in patients with high/low levels of sleep disturbance (baseline HAM-D sleep disturbance factor score >=4 and <4, respectively) was evaluated. Results: Nine hundred nineteen patients (MITT) were randomized (QTP XR 150 mg/day [n=309]; 300 mg/day [n=307]; PBO+AD [n=303]). At Week 6, QTP XR significantly reduced MADRS item 4, HAM-D sleep disturbance factor and items 4, 5, and 6 and PSQI total scores from baseline (p<0.001, both doses vs PBO+AD). In patients with high sleep disturbance (n=226, QTP XR 150mg/day; n=215, 300mg/day; n=210, PBO+AD),

QTP XR significantly (p<0.01) improved MADRS total score versus PBO+AD from Week 1 onwards. In patients with low sleep disturbance (n=83, QTP XR 150mg/day; n=92, 300mg/day; n=93, PBO+AD), QTP XR improved MADRS total score vs PBO+AD at Weeks 1 (p<0.01) and 2 (p<0.05) only. Conclusions: Adjunctive QTP XR showed significant restoration of sleep and improvement in sleep quality in patients with MDD and an inadequate response to prior AD treatment. In patients with high levels of sleep disturbance, adjunctive QTP XR improved depressive symptoms from Week 1 onwards.
Research funded by AstraZeneca.

NR4-54

EFFICACY OF EXTENDED RELEASE QUETIAPINE FUMARATE MONOTHERAPY ACCORDING TO MDD SEVERITY: POOLED ANALYSIS OF DATA FROM FOUR ACUTE STUDIES

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SUMMARY:
Objectives: Major depressive disorder (MDD) is a principal cause of disability associated with neuropsychiatric disorders and patients (pts) with severe depression are at a greater risk of complications such as treatment resistance. The effects of once-daily extended release quetiapine fumarate (QTP XR) monotherapy in pts with MDD were evaluated across various levels of disease severity. Methods: Pooled data from 4 acute (QTP XR 50, 150, and 300 mg/day doses combined) 6- or 8-week placebo (PBO)-controlled QTP XR monotherapy studies (D1448C00001/D1448C00002/D1448C00003/D1448C00004) were analyzed. Key inclusion criterion for all 4 studies: HAM-D total score >=22. Primary endpoint: change from randomization in Montgomery-Åsberg Depression Rating Scale (MADRS) total score. A post hoc analysis assessed change from randomization in MADRS total score and MADRS response (>=50% reduction in MADRS total score) at endpoint (Week 6 or Week 8) in 6 severity cohorts (defined by a MADRS total score at randomization >=24, >=26, >=28, >=30, >=32, or >=34). Results: In total, 1,752 patients (the 'all pts' group) were evaluated (MADRS score >=24 at randomization, n=1601; >=26, n=1467; >=28, n=1269; >=30, n=1038; >=32, n=745; >=34, n=500). At endpoint, QTP XR significantly reduced mean MADRS total score in 'all pts' (p<0.001 versus PBO) and in all 6 severity cohorts (>=24, >=26, >=28, >=30, and >=32, p<0.001 vs PBO; >=34, p<0.01 vs PBO). MADRS response rates were significantly higher in the QTP XR group vs PBO in the 'all pts' group (p<0.001 vs PBO) and in all 6 severity cohorts (>=24, >=26, >=28, >=30, and >=32, p<0.001 versus PBO; >=34, p=0.001 vs PBO). Safety and tolerability results were consistent with the known tolerability profile of quetiapine. Conclusions: In patients with MDD, QTP XR monotherapy significantly improved depressive symptoms in patients with various levels of disease severity, including patients with severe levels of depression.
Research funded by AstraZeneca.

NR4-55

ASSESSING THE TRUE TREATMENT EFFECT OF ACTIVE TREATMENT VERSUS PLACEBO THERAPY IN PATIENTS WITH MAJOR DEPRESSIVE DISORDER (MDD)

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SUMMARY:
Background: Based on grouped data, it is sometimes stated that antidepressants have only a small benefit compared to placebo. Using a novel statistical approach, the aim of this investigation is to assess whether antidepressant therapy does indeed result in a small specific effect for all patients. Methods: The latent class mixture model was used to identify patient subgroups to directly model the skewness of the MADRS scores at Week 8 from randomized placebo-controlled 8-week escitalopram trials in adults with MDD. It was assumed that there were two subgroups, one of patients who benefited from treatment, and the other comprising those patients who did not. Results: A total of 1,357 patients were included in the analyses. While the overall treatment difference between escitalopram and placebo was 3.2 MADRS points in favor of escitalopram, the difference between patients benefiting from either placebo or escitalopram compared to patients who did not was 15.9 MADRS points (95% CI: [15.1 to 16.6]). The percentage of patients who benefitted from placebo treatment was 41.9% compared to 61.3% with escitalopram (difference of 19.5%, 95%CI: [13.2 to 25.7]), corresponding to a number-needed-to-treat of 6.

Patients who benefited from placebo treatment (41.9%) can be regarded as responding to the nonspecific aspects of care. Similarly, patients who did not benefit from escitalopram treatment (38.7%) were considered to be people who also would not have responded to placebo. For severely depressed patients (baseline MADRS =30), the treatment difference for those that benefitted from any study intervention was 17.7 MADRS points (95%CI: [16.7 to 18.7]). Specifically, the percentage of severely depressed patients who benefitted from escitalopram versus placebo was 23.3%. For moderately depressed patients (baseline MADRS <30), the treatment difference for all responders was 14.4 MADRS points (95%CI: [13.4 to 15.4]), and the percentage of patients who benefitted from escitalopram versus placebo treatment was 14.4%. Conclusion: Latent class mixture model analyses indicate that the proportion of patients who respond to an active antidepressant is clinically meaningful and that these depressed individuals obtain a large and clinically relevant improvement from baseline of 16 points on the MADRS scale. This model gives a considerably better fit to the data than one in which all patients are assumed to benefit from treatment.

This study was funded by H Lundbeck A/S

NR4-56

RISK FOR VIOLENCE AND ARREST IN BIPOLAR DISORDER: RESULTS FROM THE STEP-BD COHORT

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SUMMARY:

Objective: Bipolar disorder has been associated with an elevated risk for violent behavior compared to individuals without serious mental illness. The clinical and sociodemographic features which may contribute to an elevated risk for violent behavior in individuals with bipolar disorder, however, are not well established. Therefore, we investigated the prevalence of self-reported lifetime violence in subjects with BD, and sought to confirm and extend previously-reported predictors of lifetime violent behavior in a large cohort of patients with BD. Methods: The Systematic Treatment Enhancement for Bipolar Disorder (STEP-BD) is a multicenter prospective cohort study of bipolar disorder (BD) conducted in the United States between 1999 and 2005. All 4,107 subjects were assessed at study entry with a structured diagnostic evaluation, including the SCID and MINI and were asked about lifetime history of violent behavior. Results: Of the 3,936 subjects with a diagnosis of Bipolar Disorder (I, II, NOS) for whom history of violence was available, 957 (23.4%) reported a history of violent behavior. Clinical features independently associated with risk of violence included bipolar I subtype, lifetime substance abuse, earlier onset of manic episodes, history of anger attacks, and history of PTSD or ADHD. The median time between onset of first mood episode and first reported violence was 5 years. Conclusions: Approximately 1 in 4 individuals with bipolar disorder reported a history of violent behavior. The findings are limited by being retrospective and by the absence of detail about the behavior and its severity.

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NR4-57

A 52-WEEK SAFETY AND TOLERABILITY STUDY OF ARIPIPRAZOLE FOR THE TREATMENT OF IRRITABILITY IN PEDIATRIC PATIENTS (6–17 YEARS) WITH AUTISTIC DISORDER

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SUMMARY:

Background: Two 8-week, randomized, placebo-controlled trials evaluated the efficacy and safety of aripiprazole for the treatment of irritability in children and adolescents with autistic disorder. The present study provides longer-

term safety data. Methods: Fifty-two-week, open label, flexibly dosed (2–15 mg/day) study of aripiprazole for the treatment of irritability associated with autistic disorder. Subjects included those who had either completed one of the two 8-week randomized trials (prior aripiprazole [PA] or prior placebo [PP]) and de novo (DN) subjects. Results: Three hundred thirty subjects enrolled: 174 PA, 70 PP and 86 DN. Most were male and 6–12 years old. One hundred and ninety-nine subjects completed 52 weeks of treatment. Completion rates: PA=62%, PP=53%, DN=64%. Adverse events (AEs) in =>5% of patients in any group were: increased appetite PA 10.9%, PP 11.4%, DN 18.6%; sedation PA 5.2%, PP 14.3%, DN 9.3%; somnolence PA 1.7%, PP 8.6%, DN 4.7%; lethargy PA 1.1%, PP 1.4%, DN 8.1%; fatigue PA 5.2%, PP 10.0%; DN 8.1%; nasopharyngitis PA 12.6%, PP 14.3%, DN 14.0%; URI PA 9.2%, PP 15.7%; DN 12.8%; constipation PA 4.0%, PP 5.7%, DN 7.0%. Incidence of EPS-related AEs were: DN 18.6%, PA 14.9%, and PP 8.6%. Discontinuation rates due to AEs = 10.6%, most commonly aggression and weight increase. Nine subjects experienced serious AEs, most frequently aggression. Mean change from baseline (baseline of antecedent study for PA) in body weight z-score by time period was: =<3 months = 0.15; 3 to 6 months = 0.26; 6 to 9 months = 0.32; >9 months = 0.33. The percentage of subjects with clinically significant fasting metabolic abnormalities at >9 months were: glucose 2%; total cholesterol 5%; LDL 7%; low HDL 30%; and triglycerides 5%. Conclusion: Aripiprazole was generally safe and well-tolerated in the treatment of irritability associated with autistic disorder. There are few discontinuations due to AEs. Increased weight gain, though present, appears to plateau over time. Supported by Bristol-Myers Squibb and Otsuka Pharmaceutical Co, Ltd.

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NR4-58

NEURAL CORRELATES OF CLINICAL IMPROVEMENT IN MAJOR DEPRESSIVE DISORDER: A PAIN-INDUCTION FUNCTIONAL MAGNETIC RESONANCE IMAGING STUDY

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SUMMARY:

Objective: The purpose of this study was to use functional magnetic resonance imaging (fMRI) during thermal pain induction to investigate the neural correlates of clinical improvement in major depressive disorder (MDD) after antidepressant treatment. Method: Thirteen patients with MDD and 20 healthy subjects were scanned 3 times: before (basal) and after 1 and 8 weeks of treatment with duloxetine, using fMRI and a block-design experimental thermal pain paradigm. Painful stimulation was applied to the right volar forearm. Severity of MDD was evaluated at each time-point using HAM-17. Imaging data were analyzed by means of SPM5. We performed a series of correlation analyses between treatment-related variations in clinical scores and fMRI brain activation reductions after 1 and 8 weeks of treatment. Results: First week of treatment: We found that reductions in Somatic subscale of HAM-17 were significantly correlated with activation reductions in the right prefrontal cortex, whereas reductions in Core Subscale scores of HAM-17 were significantly correlated with activation decrements in the ventromedial and subgenual frontal cortices. Eighth week of treatment: The improvement in Core Subscale correlated with the magnitude of activation reduction in the right prefrontal cortex and left insulo-opercular region, whereas the improvement in Somatic subscale was associated with activation reductions in the pons. Response predictors: We performed an analysis to specifically assess regional activations in basal fMRI able to predict response (50% reductions in the baseline HAM-17 score) to 8 weeks of treatment. We found that greater activity in the subgenual and right prefrontal cortices during pain-induction were significantly associated with positive responses to duloxetine treatment. Conclusions: In our study, depression clinical improvement was related to reductions of abnormally enhanced basal responses to pain in a network including frontal, limbic, paralimbic and brainstem structures. Basal activations within part of this network predicts treatment outcome. These structures have been consistently involved in mood regulation, neural models of MDD as well as treatment response (1, 2). In addition, our results suggest a specific involment of these structures in distinct depressive symptoms modulation.

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NR4-59

DESCRIPTIVE EPIDEMIOLOGY AND COMORBIDITY OF BIPOLAR DISORDER IN THE NATIONAL HOSPITAL DISCHARGE SURVEY (NHDS)

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SUMMARY:
Objective: Forty to sixty-five percent of patients with bipolar disorder have been diagnosed with one or more comorbid conditions. The purpose of this study was to identify comorbid disorders and compare their prevalence between hospitalizations with and without bipolar disorder. Methods: The 1979-2006 National Hospital Discharge Survey (NHDS) data were analyzed to examine temporal trends in the proportional morbidity (PM) of bipolar disorder, demographic characteristics, and the most frequent comorbid conditions among hospitalizations with and without bipolar disorder. The demographic characteristics are presented for the NHDS sample of 6,379,347 records. For discharges of patients aged 13 to 64 with at least one comorbid condition, the conditions of those with a primary diagnosis of bipolar disorder (N=27,054) were compared to those with other primary diagnoses (N=2,325,247). Proportional Morbidity Ratios (PMRs) were calculated. Results: There was an average 10% ($p<0.001$) increase per year in the proportion of discharges with bipolar disorder and a significant reduction in their mean length of hospital stay. Proportions of discharge records with bipolar disorder were higher among males (PMR=1.1), whites (2.0), and highest among ages 13 to 19 (18.0) and those from the Northeast (1.7). Discharge records with primary diagnosis of bipolar disorder showed higher proportions of the majority of psychiatric and some general medical conditions including acquired hypothyroidism (2.6), viral hepatitis (1.6), obesity (1.3), various diseases of the skin and subcutaneous tissue (range 2.6-4.2) and of the nervous (1.4-3.8), respiratory (1.4-2.3), and musculoskeletal (1.2-1.9) systems. Discussion: Knowledge of the risks of comorbid psychiatric and general medical conditions is critical both for clinicians and for patients with bipolar disorder. Closer attention to prevention, early diagnosis, and treatment of comorbid conditions may decrease medical morbidity and mortality, and improve the prognosis of patients with bipolar disorder.

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NR4-60

TREATMENT-EMERGENT SEXUAL DYSFUNCTION IN OUTPATIENTS WITH MAJOR DEPRESSIVE DISORDER: 6- MONTH TREATMENT AND FUNCTIONAL OUTCOMES

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SUMMARY:
Objective: To describe clinical and functional outcomes for patients receiving treatment for major depressive disorder (MDD), with an emphasis on the impact of treatment-emergent sexual dysfunction (TESD). Methods: This observational study enrolled sexually active outpatients (=18 years old) without SD, who were initiating selective serotonin reuptake inhibitor (SSRI) or serotonin and norephinephrine reuptake inhibitor (SNRI) treatment for MDD. Assessments included the Arizona Sexual Experience Scale (ASEX), Quick Inventory of Depressive Symptomatology-Self Report: 16 items (QIDS-SR16), treatment adherence and the EuroQol questionnaire (EQ-5D). Treatment decisions were made according to the usual standard of care; patients were assessed at study entry, and weeks 8, 16 and 24, with ongoing ASEX and medication records. The primary study objective was to compare TESD rates in outpatients receiving duloxetine or SSRI monotherapy over 8 weeks. Cochran-Mantel-Haenszel tests stratified by propensity score were used to compare TESD incidence between cohorts. Logistic regression with covariate adjustment (including propensity score) was conducted to compare remission rates. Factors related to TESD were identified using a generalized linear mixed effects model. Results: Of 1647 patients enrolled from 12

countries , 1549 were included in the analysis cohort (620 in the duloxetine cohort and 860 in the SSRI cohort); 67% of patients remained in their baseline cohorts at 24 weeks. The incidence of physician-rated TESD (based on the ASEX) at 8, 16 and 24 weeks was similar irrespective of treatment: duloxetine 23% versus 29% SSRI monotherapy (adjusted odds ratio, OR [95% CI] 0.77 [0.57, 1.03] at 24 weeks). Overall, 85% of patients achieved remission (QIDS-SR16 total score <5) within 24 weeks; patients on duloxetine were more likely to remit than those on SSRI monotherapy (90% versus 80%, adjusted OR 2.23 [1.43, 3.49]). Other secondary outcomes such as quality of life measures were in favour of duloxetine. Factors related to TESD incidence included country, previous SD with antidepressants, and remission of depression in the past 24 weeks. Conclusions: The pragmatic design and naturalistic setting of this multi-country study provide real-life context to clinical data, and insight into the outcomes of MDD and TESD in actual clinical practice, highlighting the importance of recognising and addressing these symptoms. This study was funded by Eli Lilly.

NR4-61

BRIEF BEHAVIORAL THERAPY FOR INSOMNIA FOR OUTPATIENTS WITH RESIDUAL DEPRESSION WITH COMORBID INSOMNIA: ASSESSOR-BLIND, RANDOMIZED CONTROLLED TRIAL

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SUMMARY:

Context: It is unclear whether psychotherapy targeted for insomnia can improve clinical outcomes for patients with residual depression and treatment refractory insomnia. Objectives: To evaluate the added value of brief Behavioral Therapy for insomnia (bBTi) over treatment as usual (TAU) for residual depression and refractory insomnia. Design, Setting and Patients: Randomized controlled trial in 37 adults (62% female; average age of 50.5 years old) at three psychiatric outpatient departments. Interventions: Participants received either TAU alone or TAU plus bBTi, consisting of 4 weekly 1-hour individual sessions, administered by psychiatrists or nurses who had received a 2-day training and monthly supervision. Main Outcome Measures: The Insomnia Severity Index (ISI) scores at 8 weeks (primary outcome). Sleep parameters from the Pittsburgh Sleep Questionnaire Index (PSQI), the Hamilton Rating Scale for Depression (HAMD) scores assessed by blind raters, and remission rates for both insomnia and depression at 4 and 8 weeks (secondary outcomes). Results: Controlling for the baseline scores, the bBTi plus TAU resulted in significantly lower ISI scores than TAU alone at 8 weeks (P<.0005). The sleep efficiency for the combination was also significantly better than that for TAU alone (P=.015). Significant differences were observed in favor of the combination group for both on the total HAMD scores (P=.013) and on the HAMD scores after removing the three sleep items (P=.008). The combination treatment produced higher rates of remission than TAU alone, both in terms of insomnia (50% [10/20] versus 0% [0/17]) with a number-needed-to-treat (NNT) of 2 (95% confidence intervals, 1 to 4), and in terms of depression (50% [10/20] versus 6% [1/17]) with an NNT of 2 (1 to 5). Conclusion: In patients with residual depression and treatment refractory insomnia, adding bBTi to usual clinical care produced added benefits.

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NR4-62

THE PROPHYLACTIC EFFICACY OF SSRIS

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SUMMARY:

Introduction: Depression is associated with significant morbidity and mortality, especially when it is recurrent. The importance of continued use of antidepressants in the long-term treatment of depression has been suggested in double-blind studies but these studies are of limited

duration. The purpose of this evaluation is to evaluate in a naturalistic clinical setting the long-term course of patients who continued on one of 4 SSRI's following recovery from a depressive episode, and to see if there are any variables associated with longer stability. Methods: 363 patients who recovered from a Major Depressive episode and then remained stable for 6 months were subsequently followed on 1 of 4 SSRI's (Fluoxetine, Escitalopram, Paroxetine or Sertraline from four classes until they either terminated well or relapsed. The patients involved in this study either exhibited symptom remission with a Montgomery-Asberg Depression Rating Scale (MADRS) of 8 or less, or they had a 50% reduction of MADRS score whereby the score was in the 9-14 range. After clinical response was achieved, personality disorders were assessed using the Structured Interview for DSM-IV Personality Disorder, and the Dysfunctional Attitude Scale was administered. All patients included in this analysis maintained their improvement over a subsequent six month course, and were then followed regularly for maintenance antidepressant treatment. Results: The probability of remaining well on maintenance therapy was 82.7% at 1 year, 71.5% at 2 years, 60.2% at 3 years, 51.4% at 4 years, 44.0% at 5 years, 38.3 % at 6 years, 32.3% at 7 years and 26.5% at 8 years. A Univariate Analysis of Variance showed no statistically significant differences in long-term stability when comparing the months remaining stable for the 4 different drugs (F=1.398, df=8,479, p=.195). A second Univariate Analysis of Variance was used to determine whether there were significant differences in efficacy among the different classes of drugs. No significant differences were found when comparing the months remaining stable for the 4 SSRI's. A Backward Regression Analysis identified which variables predict the length of time for which a patient may remain stable. These are, in order of importance: a lower score on the MADRS (positively correlated with stability), psychotherapy in addition to pharmacotherapy (positively correlated with stability), and a personality disorder diagnosis (negatively correlated with stability).

NR4-63

TREATMENT OUTCOMES BASED ON DISEASE SEVERITY FOR SUBJECTS WITH BIPOLAR I DISORDER TREATED WITH ZIPRASIDONE PLUS A MOOD STABILIZER

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SUMMARY:
Background: In a 6-month, randomized, placebo-controlled, double-blind trial enrolling subjects with bipolar I disorder and a Mania Rating Scale (MRS) score = 14, ziprasidone was found to be an effective and well-tolerated treatment in combination with a mood stabilizer. To elucidate the profile of subjects who received the most benefit from ziprasidone, treatment outcomes across a spectrum of illness severity were determined. Methods: We compared the proportion of subjects who were randomized to double-blind treatment (subjects achieving = 8 consecutive weeks of stability with open-label ziprasidone [80–160 mg/d] and lithium or valproate) and the proportion who relapsed during double-blind treatment for the most severely ill quartile (baseline MRS = 26) and decile (baseline MRS = 30). All p values were calculated using the Fisher exact test. Results: Rates of stabilization were similar for patients with an MRS score < 30 (209/512, 40.8%) when compared with rates for patients with baseline MRS = 30 (30/71, 42.2%), p = 0.90; stabilization rates were 175/420 (41.7%) and 64/163 (39.3%) for subjects with MRS scores < 26 and MRS = 26, respectively (p = 0.64). Among subjects with MRS scores < 30, relapse rates were lower for those randomized to ziprasidone (21/114, 18.4%) compared with those randomized to placebo (30/95, 31.6%), p = 0.04; the same was true for subjects with MRS scores = 30 (relapse rates: ziprasidone: 4/13, 30.8%; placebo: 6/15, 40.0%), but this difference was not statistically significant (p = 0.71). Among subjects with MRS score < 26, relapse rates were lower for those randomized to ziprasidone (14/93, 15.1%) compared with those randomized to placebo (28/82, 34.1%), p < 0.01; for subjects with MRS scores = 26, relapse rates were 11/34 (32.4%) and 8/28 (28.6%) for ziprasidone and placebo, respectively (p = 0.79). Conclusion: These analyses indicate that ziprasidone, when added to lithium or valproate, was equally effective in stabilizing both mild to moderately ill subjects and severely ill subjects. Mild to moderately ill subjects randomized to continue on ziprasidone were significantly less likely to relapse compared with placebo subjects. With the much smaller sample size of the severely ill group, separation was not demonstrated.
Study supported by Pfizer Inc.

NR4-64

ALLERGEN-SPECIFIC IGE AND ALLERGY SYMPTOMS ARE ASSOCIATED WITH DEPRESSION SCORES IN PATIENTS WITH

MOOD DISORDERS EXPOSED TO SEASONAL POLLEN-PEAKS

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SUMMARY:

Introduction: Allergic rhinitis and depression are commonly co-occurring and underdiagnosed illnesses. Is this association at a trait (vulnerability) or state (trigger) level, biologically driven or merely psychological? We now examine a hypothesized relationship between allergen specific Immunoglobulin E (IgE), changes in allergy symptoms, and changes in depression scores (typical and atypical) in patients with recurrent mood disorders exposed to natural peaks of tree or ragweed pollen. Method: One hundred participants from Baltimore or Washington, D.C. (age 43.8 +10.5, 60 men and 40 women; 53 IgE negative and 47 IgE positive for trees and/or ragweed pollen) with diagnoses of recurrent mood disorder were evaluated blindly, once during a low-pollen period and once during the preceding or subsequent peak high-pollen period. Individuals with any active substance related or psychotic disorders were excluded. Those subjects taking antihistamines and decongestants (not affecting cytokines and inflammatory mediators) were included while subjects taking on montelukast or intranasal corticosteroid were excluded. Volumetric sampling for pollen, reported in Grains/m3, was conducted as recommended by National Allergy Bureau guidelines. This model allowed matching sensitization to exposure to seasonal allergens. We compared the difference between the Structured Interview Guide for the Hamilton Depression Rating Scale- Seasonal Affective Disorder Version (SIGH-SAD) scores off- and on- allergy seasons. Sensitization was defined at 0.35kUa/L allergen-specific IgE levels using ImmunoCAP 250. Data were analyzed with ANCOVAs with adjustment for CRP level (as a nonspecific inflammation marker). Results: Typical-depression changes were significantly related to changes in allergy symptoms ($p<0.008$), while atypical-depression changes were significantly related to allergen-specific IgE positivity ($p<0.045$). Conclusion: To our knowledge, this is the first report of a biological marker of allergic sensitization (allergen-specific IgE) predicting worsening in depressive symptoms during the high pollen season in patients with recurrent mood disorders. Our preliminary findings argue for a "state" level connection between allergy and worsening of mood disorders. Our results also suggest that the link is biologically driven, beyond the mere psychological impact of allergic symptoms, being conducive to research on new preventative and therapeutic targets in the management of mood disorders.

NR4-65

PRESCRIBING PATTERNS AND PATIENT OUT-OF-POCKET EXPENSES AMONG BIPOLAR DISORDER PATIENTS RECEIVING EXTENDED-RELEASE QUETIAPINE OR ARIPIPRAZOLE

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SUMMARY:

Objectives: To examine prescribing patterns and out-of-pocket (OOP) expenses for extended-release quetiapine (QTP XR) and aripiprazole (ARP) among patients with bipolar disorder (BPD). Method: Retrospective analysis of administrative claims data from commercial managed care plans was conducted. Adult BPD patients were assigned to QTP XR or ARP groups based on the first prescription filled between June 2007 and June 2008. Prescribing patterns were described by rates of monotherapy and combination therapies with 1, 2, or 3 agents (antidepressants [AD], mood stabilizers [MS], or other antipsychotics [AP]). Patient OOP expenses were calculated by subtracting the amount paid by the plan from the amount allowed for an agent (paid amount plus any member liability). Results: QTP XR was prescribed as monotherapy for 74.2% of patients compared with 46.7% of ARP patients. The proportion of patients receiving QTP XR concomitantly with 1, 2, or 3 other agents was 16.5%, 8.7%, and 0.6%, respectively, compared with 36.5%, 15%, and 1.7% for ARP patients. 11% of QTP XR versus 27.8% of ARP patients received combination therapy with only AD, while 7.1% of QTP XR versus 9.7% of ARP patients received combination therapy with both a MS and an AD. Eight point two percent of ARP patients used additional AP in single- or multiple-agent combinations compared with 2.3% of QTP XR patients. Median per patient OOP expenses for monotherapy were USD20 for QTP XR and USD26 for ARP. Median per patient OOP expenses for combinations were 2 to 4 times higher than for monotherapy (USD40 with AD, USD50 with MS, and USD40 with AP). The median OOP expenses for combinations with >2 agents ranged between USD59-92 per patient. Conclusion: QTP XR was prescribed predominantly as monotherapy whereas

ARP was prescribed predominantly as combination therapy. Patients receiving combination therapies incurred 2 to 4 times higher OOP expenses than patients receiving monotherapy.

Supported by funding from AstraZeneca Pharmaceuticals LP.

NR4-66

LEFT DORSOLATERAL PREFRONTAL TRANSCRANIAL MAGNETIC STIMULATION (TMS): EFFECT ON SLEEP IN PATIENTS WITH PHARMACORESISTANT MAJOR DEPRESSIVE DISORDER

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SUMMARY:

Introduction: Sleep difficulties during major depressive episodes range from 50-90% of patients. Apart from alleviating major depression (MDD), many antidepressant therapies have inherent sedating or activating properties, which may either simplify or complicate management of associated insomnia. While TMS has been associated with insomnia as an adverse effect at a rate of 10% in two small uncontrolled trials (1), effects upon sleep in MDD have not been systematically studied. We examined changes in sleep during an industry-sponsored (Neuronetics, Inc.), multicenter, sham-controlled, trial of TMS therapy for pharmacoresistant MDD (2). Methods: Three hundred and one patients were randomized to receive active (N=165) or sham (N=158) TMS over the 6-week trial. Depression severity was rated with the 24-item Hamilton Depression Scale (HAMD), and the Inventory of Depressive Symptoms (IDS-SR) at baseline, and at 2, 4, and 6 week time points. Insomnia was assessed using the HAMD sleep disturbance factor, which consists of item 4 (difficulty falling asleep), item 5 (middle insomnia), and item 6 (early morning awakening). The IDS-SR sleep factor consists of similar insomnia items plus hypersomnia. Results: There were no significant differences between the active and sham groups in the HAMD or IDS-SR sleep factor analyses at any time point during the six weeks of treatment. However, a statistically significant result was observed for the active/responder vs. active/non-responder comparison at week 2, week 4 and week 6 for the HAMD sleep factor ($p=0.0186$, $p=0.0001$, and $p<0.0001$) and at week 4 and week 6 for the IDS-SR sleep factor ($p<.0001$ at both time points). The proportion of participants reporting sleep difficulty as an adverse event over the length of the study did not differ between active treatment (24.2% insomnia, 0.6% somnolence) and sham (25.3% insomnia, 1.3% somnolence). Conclusion: TMS does not appear to have any direct effect upon sleep in MDD, but insomnia does improve as MDD improves, whether receiving real or sham TMS.

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NR4-67

GLOBAL FUNCTIONING OF BIPOLAR PATIENTS IS INFLUENCED BY IMPULSIVITY AND TEMPERAMENT

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SUMMARY:

Introduction: It has been shown that social functioning and adjustment is reduced in bipolar patients (BP). However, less is known about the impact of the disorder on the lifestyle and social functioning during the maintenance phases. Objectives: The aim of the present study was to evaluate global functioning and adjustment of euthymic BP using the Functioning Assessment Short Test (FAST) and its relationship with both impulsivity (Barratt Impulsiveness Scale, BIS-11) and affective temperament-profiles (Temperament Evaluation of Memphis, Pisa, Paris and San Diego-Autoquestionnaire, TEMPS-A). Methods: Seventy-one euthymic BP (35 females and 36 males; 55 type I and 16 type II) were assessed by a semi-structured interview to obtain socio-demographical and clinical data. The patients agreed to participate in our study by signing a written informed consent and the protocol was approved by the Research Ethics Committee of our Hospital. Global functioning was evaluated with the FAST, and the BIS-11 was used to measure trait-like impulsivity. At the same time, the TEMPS-A was used to evaluate affective temperament-profiles. Measures were compared using ANOVA and analysis of correlation. SPSS

16 was used for this purpose. Results: Our results showed that there is a positive correlation between the total score of the FAST and the score of the Attentional/Cognitive Impulsivity subscale of the BIS-11 (r=.279, p<.05). Moreover, we analysed the total score of the FAST and the affective temperament-profiles scores (using TEMPS-A) and we found significant correlations. There is a directly proportional relationship between global functioning impairment and the following temperament-profiles: Depressive (r=.337,p<.01), Cyclothymic (r=.361,p<.01), Irritable (r=.333,p<.01) and Anxious (r=.301,p<.05); but the Hyperthymic profile reported an inversely proportional relationship (r=-.327,p<.01). We also found a significant relationship between suicidal behaviour and attentional/cognitive impulsivity (F=5,768, p<.019). Conclusions: Our findings support the idea that euthymic BP with high scores in the attentional/cognitive impulsivity subscale have a poor global functioning level. Patients with high scores in temperament-profiles also have a poor global functioning, except for the hyperthymic group. Our study also showed that high scores of attentional/cognitive impulsivity increase the risk of suicide attempts.

NR4-68

THE COMPARATIVE EFFICACY AND SAFETY OF ADJUNCTIVE ANTIPSYCHOTICS IN MAJOR DEPRESSIVE DISORDER PATIENTS WHO FAIL ANTIDEPRESSANT THERAPY

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SUMMARY:

Background: Augmentation with atypical antipsychotics is effective in treating patients suffering from major depressive disorder (MDD) who respond insufficiently to conventional antidepressants. Direct head-to-head trials comparing these agents are lacking. Objective: An indirect comparison was conducted to assess the comparative efficacy and safety of augmentation with atypical antipsychotics in MDD. Methods: A systematic literature search was conducted of Medline/PubMed (1966-Sept 2009). Eligible trials enrolled patients diagnosed with unipolar major depressive disorder with resistance to at least one prior antidepressant. Trials had to be double-blind placebo-controlled assessing the efficacy and/or safety of augmentation therapy with aripiprazole, quetiapine, or olanzapine during an acute depressive episode. Response rates, remission rates and discontinuation rates due to adverse events were extracted and compared in a Bayesian meta-analysis. Results: Three aripiprazole, two quetiapine and five olanzapine trials were identified together reporting on 2979 patients. Aripiprazole augmentation showed numerically higher efficacy rates compared to quetiapine and olanzapine. Response odds ratios (95% CI) compared to quetiapine and olanzapine were 1.34 (0.82-2.06) and 1.52 (1.00-2.19) respectively. Remission odds ratios compared to quetiapine and olanzapine were 1.3 (0.78 – 2.07) and 1.26 (0.77-1.92) respectively. Aripiprazole augmentation showed numerically lower discontinuation rates due to adverse events compared to quetiapine and olanzapine (OR = 0.99(0.24-2.62) and 0.77(0.23-1.89)). Conclusions: Among augmentation treatments with atypical antipsychotics in MDD, aripiprazole shows a tendency towards higher efficacy rates and lower discontinuation rates due to adverse events compared to quetiapine and olanzapine. More direct head-to-head trials are needed to assess the comparative efficacy and safety of adjunctive antipsychotics in MDD.

NR4-69

EFFICACY OF ADJUNCTIVE ARIPIPRAZOLE TO LITHIUM OR VALPROATE IN THE LONG-TERM TREATMENT OF MANIA IN SUBJECTS WITH BIPOLAR I DISORDER (CN138-189)

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SUMMARY:

Objective: To evaluate the long-term safety and efficacy of aripiprazole (ARI) in combination with lithium (Li) or valproate (VPL) in delaying time to relapse in bipolar I disorder subjects with mania. Methods: Bipolar I disorder subjects with a current manic or mixed episode received Li or VPL for at least 2 weeks. Subjects with an inadequate response (Young Mania Rating Scale [YMRS] =16 and =35% decrease from baseline) to mood stabilizer monotherapy received single-blind ARI in combination with a mood stabilizer. Subjects who maintained mood stability (YMRS and Montgomery Asberg Depression Rating Scale =12) for 12 consecutive weeks were randomly assigned to double-blind ARI (10 to 30 mg/day) or placebo (Pbo) in combination with Li or VPL. Relapse was monitored up to 52 weeks. The incidence of treatment-emergent adverse events (TEAEs) and weight changes were

also evaluated during double-blind treatment. Results: A total of 337 patients (169 Pbo, 168 ARI) were randomized to either continuation of adjunctive ARI or Pbo with Li or VPL. Completers included 52.7% Pbo, 61.3% ARI. A total of 34 subjects (15 Pbo, 19 ARI) discontinued due to adverse events. The overall relapse rate at 52 weeks was 25.4% of adjunctive Pbo- and 14.9% of adjunctive ARI-treated subjects. Adjunctive ARI significantly delayed the time to any relapse as compared to Pbo plus mood stabilizer, hazard ratio = 0.544 (95% CI: 0.33, 0.89, log-rank p=0.014). The most frequent TEAEs (=5% and greater than Pbo) were headache (10.8% Pbo, 13.2% ARI), weight increase (6.6% Pbo, 9.0% ARI), and tremor (2.4% Pbo, 6.0% ARI). Mean changes in body weight during long-term therapy were similar (p=0.49) between adjunctive Pbo (0.60 kg) versus adjunctive ARI (1.07 kg) (Week 52, last observation carried forward [LOCF]). Conclusion: These findings suggest that there is a long-term benefit to continue combination of aripiprazole with a mood stabilizer after sustained remission is attained.

Supported by Bristol-Myers Squibb and Otsuka Pharmaceuticals Co., Ltd.

NR4-70

YMRS LINE ITEM ANALYSIS IN PEDIATRIC PATIENTS WITH BIPOLAR I DISORDER TREATED WITH ARIPIPRAZOLE

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SUMMARY:

Background: Aripiprazole demonstrated efficacy for the treatment of pediatric patients (10–17 years) with bipolar I disorder in a clinical trial that utilized the Young Mania Rating Scale (YMRS) Total score as the primary outcome measure. This analysis evaluated the profile of discrete symptom response. Methods: Post-hoc analysis of the 11 individual items of the YMRS (last observation carried forward) using data from a 4-week, double-blind, randomized trial (including a 26-week placebo-controlled extension phase) that compared aripiprazole (10 or 30 mg/day, n=197) with placebo (n=99) for the treatment of an acute manic or mixed episode of bipolar I disorder in pediatric patients (10–17 years). Results: 296 patients were randomized; 80% completed the study. Subjects receiving aripiprazole had a significantly greater reduction than subjects receiving placebo (p<0.05) in the YMRS Total score as early as Week 1; this was maintained through Week 4 and Week 30. Significant decreases at Week 4 were seen in eight YMRS items: elevated mood, increased motor activity/energy, need for sleep, irritability, speech (rate and amount), language/thought disorder, abnormal thought content and disruptive/aggressive behavior. Improvement in these items was also significant at Week 30, with the exception of abnormal thought content (p=0.12). There were no statistically significant differences in appearance, sexual interest, or insight; except for insight at Week 30 (p<0.05). Conclusions: Aripiprazole demonstrated acute and sustained improvements in symptoms that are among the most common and troublesome in pediatric patients with bipolar I disorder experiencing an acute manic or mixed episode.

Supported by Bristol-Myers Squibb and Otsuka Pharmaceutical Co, Ltd.

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NR4-71

ATTRIBUTES OF RESPONSE IN DEPRESSED PATIENTS SWITCHED TO TREATMENT WITH DULOXETINE

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SUMMARY:

Purpose: To assess the clinical outcomes associated with response in depressed patients with pain switched to duloxetine. Methods: This 8-week, multicenter, single arm, open-label clinical trial included outpatients from Brazil, Canada, China and Korea (N=242) with major depressive disorder switched to duloxetine 60 mg/day after failing selective serotonin reuptake inhibitor (SSRI) or serotonin and norepinephrine reuptake inhibitor (SNRI) treatment. The primary analysis compared mean change from baseline in Brief Pain Inventory – Modified Short Form (BPI-SF) interference score between responders (=50% reduction from baseline on the 17-item Hamilton Depression Rating Scale [HAMD17] Maier subscale) and non-responders after 4 weeks of duloxetine treatment.

Responders and non-responders (received duloxetine 120 mg/day for the final 4 weeks) were also compared on depression, anxiety, pain and functional outcomes after 8 weeks. Longitudinal outcomes were analyzed using mixed-effect models with repeated measures. Results: Pain interference improved from baseline in responders (N=108) and non-responders (N=85) after 4 weeks of duloxetine treatment, with greater reductions in responders (BPI-SF mean difference 1.01 [95% CI 0.42 to 1.61]; p<0.001). Reductions in pain interference remained greater in responders versus non-responders after 8 weeks, albeit with a smaller mean difference between groups (0.68 [95% CI 0.03 to 1.33]; p=0.042). Greater improvements in depression, anxiety and function were observed in responders versus non-responders after 8 weeks via HAMD17 total, Hamilton Anxiety Rating Scale total, Clinical Global Impressions of Severity and Sheehan Disability Scale scores (all p<0.001). Conclusion: In patients switched from SSRIs/SNRIs to duloxetine 60 mg/day for 4 weeks, Maier subscale responders showed greater improvement in pain interference than non-responders. Both groups had clinically significant improvements in pain, depression, anxiety and function over 8 weeks.

This study (F1J-CR-S022) was supported by Eli Lilly and Company.

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NR4-72

DEPRESSION IN WOMEN: CHARACTERISTICS OF A SAMPLE OF OUTPATIENTS OLDER THAN 40 YEARS WITH DEPRESSIVE DISORDER

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SUMMARY:

Objective: The aim of this study is to determine the characteristics and quality of life of women older than 40 years with major depressive disorder treated in psychiatric outpatient centers. Method. Epidemiological, cross-sectional study, with a sample of 1069 women attending 437 outpatient psychiatry centers in Spain. Major depressive disorder was diagnosed using DSM-IV criteria. Quality of life was assessed with the Q-LES-Q questionnaire (Quality of Life Enjoyment and Satisfaction Questionnaire). Results: Data from 942 women were analyzed, mean age of 52.46 years (ranging from 41 to 84 years). Of them, 63.3% were married, 31.6% housewives, 25.4% employees and 46.0% had completed primary education. Overall, 62.9% of patients had medical conditions; 52.5% were overweight or obese, 53.8% with menopausal status, 79.7% had a history of psychiatric disease, 79.4% had taken psychopharmacological treatment previously, 73.8 % had consulted a general practitioner once or twice during the last month, and 29% had consulted with a specialist in that period. Mean score on the Q-LES-Q was higher than 50% in two areas: school/class tasks and treatment satisfaction. Conclusion: These results suggest that depressed women older than 40 attending psychiatry centres show: history of physical and psychiatric illness, previous psychopharmacological treatment, and an important impairment of their quality of life.

Study funded by Wyeth Farma, now a part of Pfizer.

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NR4-73

BRAIN IMAGING CORRELATES OF ANTIDEPRESSANT RESPONSE TO REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (RTMS) IN DEPRESSED PATIENTS

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SUMMARY:

Objectives: To evaluate functional and structural magnetic resonance imaging data as predictors of clinical response to rTMS in a group of patients with major depressive disorder (MDD). Method: Randomized double-blind

design. At Tertiary University Hospital in Barcelona, a group of 21 MDD patients selected from consecutive subjects who were referred to Affective Disorders Unit and 13 healthy control (HC) subjects were evaluated. Severity of depression was assessed with the Hamilton Rating Scale for depression (HAM-D). rTMS was administered over the left dorsolateral prefrontal cortex using a Magstim Rapid stimulator with a figure-eight coil (5 sessions per week for 3 weeks). Ten subjects received active rTMS and 11 sham treatment. A fMRI assessment was performed before treatment initiation. Images were acquired in a 1.5-T MRI scanner. We used a six-minute, phonologically-guided, word-generation task (COWAT using F-A-S) with a block design (alternating 30-second on/off blocks). Processing and analysis was performed with Statistical Parametric Mapping, with a significance threshold of $p<0.05$, uncorrected. Clinical data were analyzed using SPSS v15.0. Results: At the end of treatment, the proportion of patients with a HAM-D reduction greater than 50% was larger in the active rTMS group (70% active and 27.3% sham). A positive correlation was observed between clinical response and activity at baseline in the left medial orbitofrontal (BA 11), the anterior cingulate (BA 24/32) and the right middle frontal (BA 46). During F-A-S performance these areas were deactivated. A positive correlation was observed between clinical response and activity at baseline and the left ventral putamen which was activated during F-A-S. In an analysis focused on these regions we obtained a positive correlation between clinical response and grey matter volume in the left medial orbitofrontal cortex. Only the activity in the right middle frontal cortex was significantly different in MDD vs HC. Conclusions: Activity of some fronto-limbic areas during F-A-S performance could be considered as a useful predictor of rTMS-induced clinical response. As most of these regions were deactivated during FAS performance, differences in the resting pattern of activity between responders and non-responders may be suspected.

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NR4-74

DEVELOPMENT OF IN VITRO DIAGNOSTIC TEST FOR LITHIUM-SENSITIVE BIPOLAR DISORDER

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SUMMARY:

Purpose: To determine the impact of lithium treatment on circadian rhythm expression in human primary fibroblasts. Background: There is need to develop a simple, rapid and reliable assay to predict which patients will show a therapeutic response to lithium treatment. Since sleep and activity rhythms can influence the effectiveness of lithium and course of the illness, and vice versa, it has been proposed there is a close correlation between cause of illness and regulation of circadian rhythm expression. Recent studies have shown the feasibility of using peripheral cells to determine human circadian rhythm expression. Therefore, we established an assay system by which circadian rhythms can be monitored to test our hypothesis that clinical response to lithium can be predicted using human peripheral cells. Methods: As an initial approach six healthy subjects were recruited to establish the in vitro circadian rhythm recording method. In vitro measurements of circadian rhythm were performed in human primary skin fibroblasts with the Bmal1 promoter-driven luciferase gene as a reporter. Results: We successfully expanded fibroblast cultures and established Bmal1-luciferase cell lines for each subject. Robust and stable circadian rhythms were recorded in fibroblasts obtained from all six healthy subjects. The period length was significantly longer in the presence of lithium at 7 mM and 10 mM but not at 3 mM. Conclusion: Our data obtained using healthy subjects indicate that we are able to record circadian rhythms and determine the effects of lithium stimulation. We are now processing lithium responsive and non-responsive bipolar disorder patients' samples to test our hypothesis, and we have collected samples from 3 lithium naïve study subjects.

NR4-75

NATURAL KILLER T CELL IN DEPRESSED PATIENTS TREATED WITH SSRIS

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SUMMARY:

Objective: An association between depression and altered immunity has been suggested by many studies, although the findings have not appeared fully consistent. The present investigation examined the effect of selective

serotonin reuptake inhibitors (SSRIs) on immune system in patients with major depressive disorder (MDD) during acute depressive state and continuation treatment. Methods: Fifty-eight patients with MDD were evaluated with Hamilton Rating Scale for Depression (HRDS) and Montgomery-Åsberg Depression Rating Scale (MADRS). ACTH, cortisol, CD4, CD8, CD19, CD56 and natural killer cell activity (NKCA) were measured at baseline and after 4 week treatment with SSRIs. After treatment with SSRIs, plasma hormones and immune variables in responder group were compared with those in non-responder group. Significance is indicated by a P value of less than 0.05. Data were analyzed using Statistica (version 6.0). Results: CD56 (NK-T) cell in responder group was more increased than that in non-responder group at baseline. NKCA in responders was more increased than that in non-responders after 4-week treatment. For NK cell, there was a significant interaction between responder/non -responder groups and treatment with SSRIs. Conclusion: The longitudinal effects related to treatment with SSRIs on NK cell number and NKCA appeared with concurrent clinical improvement. Increase in the number of NK-T cell and NK cell function with short-term clinical improvement by treatment with SSRIs might provide the evidence as immunologic response in patients with MDD.

NR4-76

AN OPEN LABEL STUDY OF TRANSCRANIAL MAGNETIC STIMULATION COMBINED WITH ANTIDEPRESSANT MEDICATION FOR THE TREATMENT OF MAJOR DEPRESSIVE DISORDER

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SUMMARY:
Transcranial magnetic stimulation (TMS) was approved by the FDA in 2008 as a treatment for depression based on results using TMS as monotherapy when one agent failed in the current episode. The utility of this novel therapy is only beginning to be explored. Collecting data in open label and blinded studies in a variety of treatment paradigms will help determine the effectiveness of this intervention. This open label study reports the results of the use of TMS in the first 19 clinical patients treated at Sheppard Pratt Health System (SPHS). Method: Patients coming to SPHS for TMS were evaluated clinically for current diagnosis, current and past medication and were administered the Montgomery Asberg Depression Rating Scale (MADRS) before the start of treatment and at the end of treatment. Study Population: Of the 19 patients, data was evaluable for 13 (three patients had primary diagnoses other than MDD, two completed their course at other TMS locations, and one stopped treatment due to treatment intolerance). All patients met criteria for treatment resistant depression (TRD) having failed two to six treatments of adequate dose and duration in the current episode. All patients were on adjunctive antidepressant medication. Results: The average MADRS at treatment onset was 33.8. Eight patients (62%) met response criteria (50% decline in MADRS) and 2 patients (15%) met remission criteria (final MADRS less than 10). Percent drop in MADRS scores ranged from 30 to 88% with an average of 55%. Conclusions: TMS shows promise as adjunctive treatment for TRD in a more chronically ill population than has been previously studied. This needs to be explored in larger blinded trials.
This study did not have any industry support.

NR4-77

CHARACTERISTICS OF EMOTIONAL RESPONSE AND ITS RELATIONSHIP WITH EARLY-LIFE STRESS AND RESILIENCE IN MAJOR DEPRESSIVE DISORDER

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SUMMARY:
Objectives: Early-life stress (ELS) including abuse, neglect and exposure to parental conflict has been known to contribute to develop major depressive disorder. Meanwhile, resilience may play a protective role against ELS. In the present study, we investigated the relationship of depressive symptom severity with ELS, resilience, and emotional responses in the patients with major depressive disorder. Methods: Twenty-six patients with major depressive disorder and 26 healthy controls were recruited for this study and informed consents were taken from all participants. Every subject was assessed about ELS (Oh 2004), resilience (Reivich and Shatter 2002), and depressive symptom severity with self-report questionnaires. Emotional response was measured about valence and arousal levels of each subject after they viewed five emotional faces including angry, sad, fear, disgust, and happy and neutral faces using modified self-assessment manikin scale. Independent sample t-test, Mann-Whitney test and Spearman correlation analyses

were conducted. Results: In the major depressive disorder patient group, total ELS score and exposure to parental conflict were significantly higher than in the healthy control group. Mean resilience score of the patient group was significantly lower than those of the control group. In the comparison of emotional responses, the patient group showed significantly lower valence score to happy face and significantly higher arousal score to the neutral face compared to the control group. In the patient group, neglect score was positively correlated with arousal score to neutral face and inversely correlated with valence score to happy face. Conclusion: Higher ELS, lower resilience and abnormal emotional response to happy and neutral faces were found in the major depressive disorder group in this study. Especially, neglect experience might have association with abnormal emotional responses. Changes in lower resilience and abnormal emotional response after treatment of depression will be needed. Keywords: early-life stress, resilience, neglect, major depressive disorder.

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NR4-78

RELATIONSHIP OF PSYCHOPATHOLOGY WITH EARLY-LIFE STRESS AND RESILIENCE IN A YOUNG ADULTHOOD POPULATION

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SUMMARY:
Objectives: Early-life stress (ELS) including abuse, neglect and exposure to parental conflict may mediate long-lasting psychological complications during adulthood and individual resilience may protect mental health from these stressors. We investigated the relationship of psychopathology with ELS and resilience in young adult people who underwent screening procedures before military service. Methods: Four hundred and sixty one subjects waiting to enter the army gave written informed consent and participated in this study. Psychopathology was assessed with Korean Military Personality Inventory (KMPI). ELS and resilience were assessed using Childhood Abuse Experience Scale (Oh, 2004) and Resilience Scale (Reivich and Shatte, 2002), respectively. Data were analyzed using correlation analyses and multiple linear regression analyses. Total psychopathology score in KMPI were dependent variable and demographic variable, ELS and resilience factor scores were independent variables. Results: Final regression model explained 31% of total variances in total psychopathology scale score. Job status, emotional abuse and neglect were positively related with psychopathology and emotional control, while impulse control and optimism scores among resilience factors were inversely associated with psychopathology in this study. Conclusion: ELS and resilience may be important modulating factors in developing psychopathology. In this study, we suggest that emotional abuse and neglect might be provocative factors and capacity to control emotion and impulse and optimistic attitude may be protective factors for psychopathology in young adulthood. Psychological intervention targeting these provocative and protective factors should be considered and investigated. Keywords: emotional abuse, neglect, resilience, psychopathology, young adulthood.

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NR4-79

CLOSE CORRELATION OF THE PHQ-9 AND BDI-II FOR DEPRESSION MEASUREMENT IN THE MOOD DISORDERS OUTPATIENT AND INPATIENT SETTINGS

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SUMMARY:
Objective: To directly compare the Patient Health Questionnaire (PHQ-9) and Beck Depression Inventory II (BDI-II) for symptom severity measurement in a tertiary subspecialized outpatient mood clinic and inpatient mood disorders unit. Methods: We conducted a retrospective study of patients who completed both a PHQ-9 and BDI-II as part of routine clinical care (1) during their initial outpatient mood disorders subspecialty clinic evaluation between August 2008 and November 2009, and (2) on

admission to an inpatient mood disorders unit between April 2006 and August 2009. The PHQ-9 and BDI-II scores were compared using the intraclass correlation coefficient (ICC) for the (1) outpatients, (2) inpatients, and (3) the combined group. Results: The mean PHQ-9 and BDI scores for these outpatients (n=299) were 14.8 (SD 7.4) and 27.5 (SD 14.2) corresponding to mild and high moderate/severe categorical ratings respectively; for inpatients (n=368), 18.9 (SD 5.7) and 33.9 (SD 11.6) corresponding to the severe category for both instruments respectively. The ICC for the outpatient and inpatient settings were 0.895 [95% CI 0.825,0.965] and 0.795 [95% CI 0.586,0.990], respectively. For the combined outpatient and inpatient settings, the ICC was 0.864 [95% CI 0.764,0.964]. Statistically, ICC > 0.75 indicates that the two comparison items are essentially the same. Conclusions: The PHQ-9 and BDI-II scores in an outpatient and inpatient mood disorders subspecialty setting are closely correlated and essentially interchangeable. In milder cases, the categorical distinction may not be as interchangeable. There are practical applications to our findings, as the PHQ-9 is a shorter measure and is free compared to the BDI-II, suggesting it can reasonably replace the BDI-II in such settings.

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NR4-80

EFFICACY OF LEVOMILNACIPRAN IN IMPROVING SYMPTOMS AND FUNCTIONAL IMPAIRMENT ASSOCIATED WITH MAJOR DEPRESSIVE DISORDER

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SUMMARY:

Objective: Levomilnacipran (1S, 2R-milnacipran) is a potent and selective norepinephrine and serotonin reuptake inhibitor in clinical development for the treatment of major depressive disorder (MDD). Post hoc analyses of rating scale single items and subscales from a placebo-controlled clinical trial were performed to characterize the effects of levomilnacipran on symptoms and functional impairment in MDD.

Methods: A 10-week, randomized, controlled flexible-dose international, multicenter study evaluated efficacy and safety of levomilnacipran sustained release (SR) 75-100 mg/day (n=276) versus placebo (n=277) in patients (18-70 years) with DSM-IV–defined MDD. Primary efficacy outcome was Montgomery-Asberg Depression Rating Scale (MADRS) total score change from baseline to Week 10. Post hoc analyses compared the effect of levomilnacipran to placebo on MADRS and Hamilton Rating Scale for Depression (HAMD17) single items and Sheehan Disability Scale (SDS) work, social life, and family life subscales (MMRM; full analysis set). Results: Levomilnacipran showed significantly greater adjusted mean total score improvement relative to placebo on the MADRS and HAMD17 (MMRM; both P<.0001). Single-item analyses showed that levomilnacipran was superior to placebo on every MADRS item (P<.01 to <.0001) and most HAMD17 items, including early, middle, and late insomnia (P=.0004, P=.0062, and P=.015, respectively), work/activities (P<.0001), psychomotor retardation (P<.0066), general somatic symptoms (P<.0001), and psychic anxiety (P=.0009). Significantly greater improvements for levomilnacipran were also seen on each SDS subscale (P<.0001). Conclusions: Levomilnacipran demonstrated superiority over placebo on all MADRS and most HAMD17 items and on all subscale analyses; improvement in functional impairment and MDD symptoms related to fatigue and energy were noted. Levomilnacipran development is ongoing.

Supported by Forest Research Institute, Inc and Pierre-Fabre Médicament.

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NR4-81

ASSOCIATION BETWEEN MEDIAN FAMILY INCOME AND SELF-REPORTED MOOD IN

BIPOLAR DISORDER

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SUMMARY:
Objective: A wide range of diseases and populations have shown that lower socioeconomic status (SES) is related to poorer health. In the US, economic parameters were found to be the most useful indicator of SES. The purpose of this study was to analyze if income was associated with daily self-reported mood in patients with bipolar disorder. Methods: Two hundred eighty-four patients with bipolar disorder residing in the US self-reported mood ratings daily for about 6 months, returning 50,054 days of data. All patients were treated by a psychiatrist, took psychotropic medications and used the self-monitoring tool throughout the study period. Median family income was obtained from US census tract data, and ranged between between $14,100 and $257,200. The association between income and mood was analyzed using income as both a continuous and categorical variable (three income groups). Education level was included in the analysis a priori. Results: Both the continuous and categorical approaches found a positive association between income and euthymia, a negative association between income and mania, and no association between income and depression. Using post-hoc pairwise comparison, patients in the lower income group spent 12.4% fewer days euthymic than those in the upper income group (p=.0.008), and 9.7% (p=0.024) fewer days euthymic than those in the middle income group. Patients in the lower income group spent 7.1% more days manic than those in the upper income group (p=0.006). There was no association between education and income. Conclusion: Median family income is associated with mood in patients with bipolar disorder and should be included in long-term studies of outcome.

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NR4-82

ANXIETY AS PREDICTOR OR MODERATOR FOR EFFECT OF ZIPRASIDONE COMBINED WITH MOOD STABILIZER IN MAINTENANCE TREATMENT OF BIPOLAR I DISORDER

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SUMMARY:
Objectives: We conducted a post-hoc analysis to investigate anxiety as a predictor or moderator of the therapeutic effects of ziprasidone combined with a mood stabilizer (lithium or valproic acid). Methods: In the stabilization phase, 584 patients with bipolar I disorder received up to 4 months of ziprasidone (80-160 mg/d) combined with lithium or valproic acid (ZIP+MS). Patients who achieved at least 8 weeks of clinical stability were subsequently randomized to double-blind (DB) treatment (up to 6 months) of ziprasidone + MS (ZIP+Li, N=57; ZIP+VAL, N=70) versus placebo + MS (PBO+Li, N=49; PBO+VAL, N=63). Baseline severity of anxiety was evaluated by a SADS-C anxiety score (sum of the worry, somatic anxiety, psychotic anxiety, phobia, and obsessions/compulsions items). Results: During the open-label stabilization phase, change in MRS (-13.5, SD 9.6) was significantly associated with the severity of pre-existing anxiety symptoms (p<0.01). Among the 330 patients with lower pre-treatment anxiety level (score < 2 on all 5 SADS-C anxiety items), 262 attained remission (79%), as compared to 155 of 220 (70%) patients in the higher pre-treatment anxiety level (score >= 3 on at least 1 SADS-C anxiety item) group (p<0.05). Among subjects with higher anxiety levels, remission rate was 77% (93/121) in the ZIP+VAL group compared to 62% (57/92) in the ZIP+Li group (p = 0.03). Remission rate was similar between ZIP+VAL (77%) and ZIP+Li (82%) in the lower anxiety group (p = 0.30). During the DB phase, the effect of ZIP+Li/Val (vs. placebo) differed between lower vs. higher baseline anxiety, and adjunctive MS used (Li n=106 vs. VAL n=133) (p<0.05). In the lower anxiety subgroup, Li alone had a higher rate of intervention for mood episode (45%, 20/44) compared to ZIP+Li (18%, 9/49), ZIP+VAL (19%, 12/62) and VAL alone (22%, 13/59) (p<0.001), whereas in the higher anxiety subgroup, Li/VAL alone had a higher rate of intervention for mood episode (44%, 4/9) compared to ZIP+Li/VAL (25%, 4/16) (p = 0.37). Conclusions: Ziprasidone combined with mood stabilizers is more effective than mood stabilizer alone in preventing

interventions for mood episode, in both high and low baseline anxiety levels. Our findings suggest that baseline co-morbid anxiety can have predictive or moderating influence on the efficacy of adjunctive ziprasidone treatment for bipolar disorder.
Supported by funding from Pfizer Inc.

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NR4-83

THE EFFECTS OF QUETIAPINE XR MONOTHERAPY ON SLEEP DISTURBANCE: POOLED DATA FROM FOUR ACUTE STUDIES IN PATIENTS WITH MDD

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SUMMARY:
Objectives: Sleep disturbance is a core symptom of major depressive disorder (MDD). Additionally, patients with insomnia have greater levels of depression than those without. The effect of once-daily extended release quetiapine fumarate (QTP XR) monotherapy on sleep quality in pts with MDD was analyzed. Methods: Pooled data from 4 acute (6- or 8-week) placebo (PBO)-controlled QTP XR (50-300 mg/day, administered in the evening) monotherapy studies (Study 1, Study 2, Study 3, Study 4) were analyzed. Primary endpoint: change from baseline in MADRS scores. Post hoc analyses based on secondary endpoints: changes in MADRS item 4 (reduced sleep), HAM-D items 4 (insomnia early), 5 (insomnia middle) and 6 (insomnia late), and sleep disturbance factor (HAM-D items 4+5+6), Pittsburgh Sleep Quality Index (PSQI) total score. MADRS total score change was analyzed in patients with high (baseline HAM-D sleep disturbance factor score >=4) and low (baseline HAM-D sleep disturbance factor score <4) sleep disturbance. Results: Two thousand one hundred sixteen patients randomized. QTP XR (all doses combined) significantly reduced ($p<0.001$) MADRS item 4, HAM-D sleep disturbance factor and items 4, 5, and 6, and PSQI total scores vs PBO (baseline to last assessment). In pts with high levels of sleep disturbance, QTP XR (n=865) significantly improved MADRS total score from baseline vs PBO (n=514) from Wk 1 onwards ($p<0.001$). In patients with low levels of sleep disturbance, improvements in MADRS total score were seen with QTP XR (n=252): significant versus PBO (n=121) only at Wks 2 ($p<0.001$), 4 ($p<0.05$), and 6 ($p<0.05$). Safety and tolerability results were consistent with known tolerability profile of quetiapine. Conclusions: In patients with MDD, QTP XR monotherapy significantly improved sleep quality. Significant improvement in depressive symptoms was demonstrated in MDD patients with high levels of sleep disturbance, improvements were less consistent in patients with low levels of sleep disturbance.
Research funded by AstraZeneca.

NR4-84

A LARGE SCALE DTI STUDY IN MAJOR DEPRESSIVE DISORDER: UTILITY OF LEGACY DATA

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SUMMARY:
Background: Previous reports revealed frontal and temporal white matter (WM) abnormalities in major depressive disorder (MDD), but the number of large scale diffusion tensor imaging (DTI) studies is limited. The present study examines whether DTI data collected as part of routine clinical treatment can be re-analyzed to test white matter integrity in MDD. Method: Billing codes and automated systems were used to screen approximately 4 million electronic medical records to collect subjects with a diagnosis of major depression and non-pathological brain MRIs which included DTI data. We also selected age and gender-matched controls (HC) with no history of neurological or psychiatric illness. A hand-segmented white matter map (ICBM DTI-81) was used for automated white matter segmentation of the whole brain. ROIs were co-registered for each subject's DTI space using linear and non-linear registration procedures, and fractional anisotropy (FA) between groups was compared. Results: We found 402 individuals (MDD=320, HC=82) with brain MRIs defined as pathology-free by the original neuroradiology report. From this pool 297 subjects (74%) had DTI data on file, and 213 (53%) were eligible for our study based on clinical and imaging quality criteria. We

were able to recover the neuroimaging data for 171 subjects (43%) with eligible DTI that were subsequently used in the DTI processing pipeline. Only good registration results (75% of cases) were included in this study, comprising 128 subjects (MDD=95, HC=33). Compared to controls, depressed patients showed significantly reduced FA of the body and column of the fornix (p=.045) and patients had numerically lower FA on 19/23 WM tracts (p=.002, chi-sq=9.8 for the group analysis). Conclusion: Our study demonstrates the feasibility of investigating white matter integrity in psychiatric populations using diffusion data collected as part of routine clinical treatment. Our findings suggest both regional and global white matter abnormalities in major depressive disorder. Funding: This study was supported by a subcontract (PI: Dan Iosifescu) to NIH grant U54 LM008748 (PI: Isaac Kohane).

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NR4-85

BASELINE CHARACTERISTICS OF PATIENTS WITH MAJOR DEPRESSIVE DISORDER FROM THE CLINICAL OUTCOMES IN MEASUREMENT-BASED TREATMENT (COMET) STUDY

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SUMMARY:

Introduction: Primary care physicians (PCPs) treat the majority of patients with major depressive disorder (MDD), however, only a minority of PCPs currently use measurement-based treatment (MBT) to monitor and optimize therapy. The impact of MBT on outcomes in patients with MDD is currently being studied in the COMET trial, the results of which will be available by 2011. Objective: To describe baseline characteristics and severity level of the initial cohort of MDD patients enrolled into the COMET trial. All patients enrolled had a primary care physician visit and were newly prescribed an antidepressant medication. Method: After approximately 3 months from initiation of enrollment, baseline data for all patients enrolled to date (n=416) was analyzed. All patients completed a baseline survey that included current depression severity based on Patient Global Impression - Severity (PGI-S) and Patient Health Questionnaire (PHQ)-9, depression history, and healthcare utilization in the past 3 months. Seventy-four treating PCPs completed a baseline case report form for each of the 416 patients that included current depression severity based on Clinical Global Impression - Severity (CGI-S), comorbidities, and healthcare utilization during the past 3 months. Patient depression was categorized as either None/Mild/Moderate (NMM) or Moderately Severe/Severe (MSS) based on the PHQ-9. Results: Of the 416 patients (66% female, mean age 47 years), 75% (n=308) reported feeling chronically tired or having little energy more than half the days over the previous 2 weeks. A total of 52% (n=217) of patients diagnosed as having MDD and prescribed antidepressive therapy were rated as MSS by PHQ-9. More MSS patients than NMM patients reported =>3 episodes of depression (72% vs. 48%, p<0.0001) in their lifetime and MSS patients rated higher than NMM patients on the PGI-S (4.4 vs. 3.0, p<0.0001) and the CGI-S (4.5 vs. 3.6, p<0.0001). Only 20% of MSS patients (n=44) and 10% of NMM patients (n=20) reported using antidepressant medication in the 12 months prior to enrollment. Of these, 75% (n=33) of MSS patients and 75% (n=15) of NMM patients reported less than a 50% improvement in symptoms. Conclusions: COMET is a randomized study that will investigate the effect of MBT on outcomes in a cohort of MDD patients.

NR4-86

LONG-TERM SAFETY AND TOLERABILITY OF ADJUNCTIVE ARIPIPRAZOLE IN THE TREATMENT OF PATIENTS WITH MAJOR DEPRESSIVE DISORDER

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SUMMARY:

Objective: To evaluate the long-term adverse event (AE) profile of aripiprazole adjunctive to standard antidepressant therapy (ADT) in patients with major depressive disorder (MDD). Methods: This post-hoc analysis of a 52-week open-label trial of aripiprazole adjunctive to ADT included patients with MDD who had an inadequate response

to standard ADT. Patients with previous aripiprazole exposure were excluded. Aripiprazole was initiated at 5 mg/day and titrated to 10 mg/day at the end of Week 1, if well tolerated. AEs were evaluated by overall incidence, time of first onset, percent resolution and median time to resolution. Metabolic parameters and median time to all-cause discontinuation were also assessed. Results: Seven hundred twenty patients received open-label aripiprazole adjunctive to ADT. Median time to discontinuation was 192 days; approximately 34% of patients completed the 52-week trial. The most commonly reported AEs were akathisia (n=173; 24%), fatigue (n=135; 18.8%), weight gain (n=131; 18.2%), somnolence (n=103; 4.3%), and restlessness (n=98; 13.6%). Peak incidence of first onset of somnolence occurred at Week 1. Peak incidence of first onset of akathisia, fatigue and restlessness occurred between Weeks 2 and 4 and coincided with the dose titration to 10 mg/day. Peak incidence of first onset of weight gain occurred between Weeks 5 and 8 and declined to <1% by Week 52. Akathisia and restlessness resolved in >80% of cases with median times to resolution of 37 and 29 days, respectively. Fatigue and somnolence resolved in >70% of cases with median times to resolution of 59 and 32 days, respectively. Mean body weight increased by 4.3 kg and total cholesterol decreased by 2 mg/dL. Conclusions: The long-term AE profile of aripiprazole adjunctive to ADT was consistent with the findings of short-term trials in patients with MDD.

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NR4-87

CLINICAL FEATURES OF OLFACTORY REFERENCE SYNDROME

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SUMMARY:

Background: Olfactory reference syndrome (ORS), a false belief that one emits a foul or offensive body odor, has been described around the world for the past century. However, only a few small studies have systematically assessed ORS's clinical features. We examined clinical features of ORS, including some that have not previously been studied; we also used standardized measures that have not been used in prior studies. Methods: Twenty patients with ORS were systematically assessed using semi-structured measures, including the SCID to assess comorbidity, Brown Assessment of Beliefs Scale to assess insight/delusionality and referential thinking, and a slightly modified version of the Yale-Brown Obsessive-Compulsive Scale to assess ORS severity. Results: Subjects' mean age was 33.4 ± 14.1 years; 60% were female. Mean age of ORS onset was 15.6 ± 5.7. Subjects reported lifetime preoccupation with 2.9 ± 1.4 sources of body odor, most often the mouth (75%), armpits (60%), and genitals (35%); bad breath (75%) and sweat (65%) were the most common odor descriptions. On average, preoccupations occurred for 3 to 8 hours a day. Eighty-five percent of subjects currently had delusional ORS beliefs (i.e., complete conviction that they smelled bad), and 77% had current ideas or delusions of reference. Eighty-five percent reported actually smelling the odor (an olfactory hallucination). Nearly all subjects (95%) performed at least one ORS-related compulsive behavior, most commonly smelling themselves (80%), excessively showering (68%), and excessively changing clothes (50%). All subjects attempted to mask the perceived odor, most often with perfume/powder (90%), gum (60%), deodorant (55%), or mints (55%). Seventy-four percent had avoided social interactions, and 40% had been housebound for at least one week, because of ORS symptoms. Sixty-eight percent had a history of suicidal ideation, 32% had attempted suicide, and 53% had been psychiatrically hospitalized. The most common lifetime comorbid disorders were major depressive disorder (85%), social phobia (65%), and substance use disorders (50%). Nearly half (44%) of patients had sought non-psychiatric medical treatment for the perceived odor, and one third had received it. Such treatment was reported to be ineffective in all cases. Conclusion: ORS appears to be characterized by high morbidity and seeking of non-psychiatric treatment, which appears ineffective. Further research is needed on this understudied disorder.

NR4-88

AGE AT ONSET AND CLINICAL CORRELATES IN BODY DYSMORPHIC DISORDER

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SUMMARY:
Objective: Across a number of disorders, early age of disorder onset is associated with greater illness severity and greater comorbidity with other disorders. However, clinical correlates of age at onset have not been studied in body dysmorphic disorder (BDD). We predicted that early age at onset would be associated with greater BDD severity, more comorbidity, and poorer functioning and quality of life. Methods: Age at onset and other variables of interest were assessed at intake in 200 participants with DSM-IV BDD in a study of the course of BDD. Reliable and valid measures were used. Subjects with early onset BDD (age 17 or younger) were compared to those with late onset BDD, controlling for gender and racial/ethnic minority status. Results: BDD had a mean age at onset of 16.4 (SD=7.03). 69% of participants had onset of BDD by age 17. Earlier age of BDD onset was found for females (p=.005) and members of minority groups (p=.049). Severity of BDD was not associated with age of onset. However, individuals with early onset BDD were more likely to have a history of suicidal ideation (p=.047), a history of attempted suicide (p=.034), and a history of physical violence (p=.042). As predicted, participants with early onset BDD had a greater number of lifetime comorbid disorders on both Axis I (p=.005) and Axis II (p=.006). More specifically, those with early onset BDD were more likely to have a lifetime eating disorder (p=.038), lifetime substance use disorder (p<.001), and borderline personality disorder (p=.037); significant differences were not found for any other individual Axis I or Axis II disorders. Functioning and quality of life were markedly poor in both groups, but contrary to our hypothesis, they were not significantly poorer in those with early onset BDD. Conclusions: These findings suggest that clinicians should be aware that BDD appears to often onset during childhood or adolescence, and that onset during this period is associated with greater morbidity and with more Axis I and Axis II comorbidity. It is interesting that BDD had earlier onset in females than in males, unlike obsessive compulsive disorder (where males are more likely to experience early onset), a disorder with which BDD has important similarities. Further research is needed to confirm these findings and to increase understanding of early onset BDD.

NR5-01

EXTENDED-RELEASE DEXMETHYLPHENIDATE IMPROVES PERMP MATH TEST PERFORMANCE THROUGHOUT THE LABORATORY-CLASSROOM DAY IN CHILDREN WITH ADHD

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SUMMARY:
Methods: Children 6 to 12 years old with attention-deficit/hyperactivity disorder (ADHD) stabilized on MPH 40-60 mg/d or d-MPH 20-30 mg/d were randomized to receive d-MPH-ER 20 mg/d, 30 mg/d, and placebo for 7 days each in this double-blind, 3 periods x 3 treatments, crossover study. The final dose of each treatment period was administered in the laboratory classroom. Patients completed the PERMP, a paper-and-pencil math test, at baseline and 3, 6, 9, 10, 11, and 12 hours postdose. Adverse events (AEs) were noted. Results: A total of 165 children (94 boys; mean age: 9.6±1.8 years) were randomized; 162 were included in intent-to-treat analyses. PERMP math test-attempted and -correct scores (change from predose) were significantly higher than placebo for both d-MPH-ER 20-mg and -30 mg doses at 3, 6, 9, 10, 11, and 12 hours postdose (P<0.001 for all). Both attempted and correct scores were significantly higher with d-MPH-ER 30 mg than with d-MPH-ER 20 mg at 10, 11, and 12 hours postdose (attempted: 10 hours, P=0.008; 11 hours, P=0.019; and 12 hours, P=0.028; correct: 10 hours, P=0.013; 11 hours, P=0.007; and 12 hours, P=0.003). Tolerability was comparable between doses. The most common AEs (=3%) were decreased appetite, headache, upper abdominal pain, and tachycardia. Conclusion: Significant improvement versus placebo in math test performance was observed with both d-MPH-ER 20-mg and 30-mg doses. Furthermore, d-MPH-ER 30 mg was superior to d-MPH-ER 20 mg at later time points in the day. These results suggest that when tolerated, higher doses of d-MPH-ER may have a longer duration of effect.
This study was supported by Novartis Pharmaceuticals Corporation.

NR5-02

ADHD IN TURKISH ELEMENTARY SCHOOL STUDENTS: A TWO YEAR LONGITUDINAL STUDY OF PREVALENCE

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SUMMARY:
Objective: Despite the extensive data on the epidemiology of ADHD, there is still continuing concern for overestimation of ADHD prevalence. Some clinicians and researchers suggest that ADHD is largely an American disorder and is much less prevalent elsewhere. Other experts have argued that the variability of ADHD prevalence estimates may be explained by the use of different methodologies. For better understanding of ADHD prevalence, large scale epidemiological studies of ADHD are needed from the countries where ADHD epidemiology has been less studied. The aim of this study is to evaluate the prevalence of ADHD in Turkish elementary school students in a longitudinal design. Method: Fifteen hundred 2nd grade students from Izmir, Turkey have been screened for the presence of ADHD by using teacher and parent versions of DSM-IV-based ADHD Scale. Students with at least 5 symptoms of inattention on teacher and parent scales were considered to have positive screening for ADHD inattention subtype. Similarly, at least 5 symptoms of hyperactivity-impulsivity on teacher and parent scales were considered to have positive screening for ADHD hyperactivity-impulsivity subtype. All positive screened students (86) and one-to-one matched controls were evaluated with a semistructured interview (Schedule for Affective Disorders and Schizophrenia for School-Age Children- Epidemiologic Version [K-SADS-E]), and all diagnostic decisions made by using best estimate procedure. The next wave of study was conducted one year after the first wave with the same study sample and methodology, when children were attending 3rd grade. Results: The prevalence of ADHD was estimated to be 13.38% (95% confidence interval=11.75-15.43), male/female ratio of 3.2:1 and the comorbidity with other disruptive behavior disorders was high (70.35%). The prevalence of ADHD in the second wave was decreased to 12.64% with male/female ratio of 3.4:1. Conclusion: Like children of many different countries worldwide, ADHD is also a common disorder in Turkish elementary school students and tends to persist over the course of one year.

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NR5-03
SAFETY PROFILE OF LISDEXAMFETAMINE DIMESYLATE IN CLINICAL TRIALS IN CHILDREN, ADOLESCENTS, AND ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

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SUMMARY:
Objective: To assess the safety profile of lisdexamfetamine dimesylate (LDX) across age groups in studies of children, adolescents, and adults. Method: Safety data from 3 randomized, 4-week, double-blind, placebo-controlled, forced dose-titration studies in children (6-12 years), adolescents (13-17 years), and adults (18-55 years) with ADHD receiving placebo or LDX 30, 50, or 70 mg/d were assessed. Data included adverse events (AEs), systolic blood pressure (SBP), diastolic blood pressure (DBP), pulse, weight, and ECG. Results: Safety was evaluated in 290 children, 310 adolescents, and 420 adults. Common AEs (% reporting: >=10% in >=1 group) with placebo vs LDX (all doses) each in children, adolescents, and adults, respectively, were upper abdominal pain (5.6 versus 11.9), (3.9 versus 0.9), and (1.6 versus 2.5); decreased appetite (4.2 versus 39.0), (2.6 versus 33.9), and (1.6 versus 26.5); dry mouth (0.0 versus 4.6), (1.3 versus 4.3), and (3.2 versus 25.7); headache (9.7 versus 11.9), (13.0 versus 14.6), and (12.9 versus 20.7); insomnia (2.8 versus 18.8), (3.9 versus 11.2), and (4.8 versus 19.3). Nine point two percent, 3.9%, and 5.9% of children, adolescents, and adults receiving LDX discontinued due to AEs. Most AEs were mild to moderate; no deaths occurred; 2 adults reported serious AEs unrelated to LDX. For placebo, 30, 50, and 70 mg/d LDX, respectively, in children LS mean (SE) change from baseline to endpoint for SBP was 1.3 (1.05), 0.4 (1.08), 1.8 (1.06), 2.6 (1.05) mmHg; DBP was 0.6 (0.91), 0.6 (0.93), 1.9 (0.92), 2.3 (0.91) mmHg; pulse was -0.7 (1.17), 0.3 (1.20), 2.0 (1.18), 4.1 (1.17) bpm. In adolescents, mean (SE) change in SBP was 2.2 (1.04), -0.8 (1.22), 0.3 (1.01), 1.7 (1.21) mmHg; DBP was 0.5 (0.97), -0.5 (1.05), 0.4 (0.84), 3.4 (0.80) mmHg; pulse was 0.8 (1.36), 5.0 (1.18), 3.8 (1.37), 5.4 (1.27) bpm. In adults, LS mean (SE) change in SBP was -0.6 (1.05), 0.8 (0.77), 0.3 (0.77), 1.3 (0.75) mmHg; DBP was 1.1 (0.83),

0.8 (0.61), 1.1 (0.60), 1.6 (0.60) mmHg; pulse was -0.0 (1.14), 2.8 (0.83), 4.2 (0.83), 5.2 (0.82) bpm. Mean (SD) changes in body weight with LDX were <=-2.5 (3.37), -4.8 (3.48), and -4.3 (4.49) lb for children, adolescents, and adults, respectively. Conclusion: With LDX, incidence of upper abdominal pain and decreased appetite was higher in children versus adults while dry mouth and headache were higher in adults versus children. AEs were otherwise similar across age groups. LDX demonstrated a safety profile on these parameters consistent with long-acting stimulant use.

Supported by funding from Shire Development Inc.

NR5-04

COMPARATIVE EFFECTS OF LISDEXAMFETAMINE DIMESYLATE AND MIXED AMPHETAMINE SALTS EXTENDED RELEASE IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

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SUMMARY:

Objectives: To assess the efficacy and safety of lisdexamfetamine dimesylate (LDX) and mixed amphetamine salts extended release (MAS XR) using data from 2 studies with similar designs. Methods: Both studies were 4-week, parallel group, forced-dose escalation trials in adults with attention-deficit/hyperactivity disorder (ADHD). The ADHD Rating Scale IV with adult prompts (ADHD-RS-IV) was the primary efficacy measure. Both studies included screening and washout, then a forced-dose escalation to randomly assigned dosages (30 to 70 mg/d LDX or 20 to 60 mg/d MAS XR) or placebo. Dosage groups for this post hoc analysis were chosen because 20 and 40 mg/d MAS XR have amphetamine base approximately equal to 50 and 70 mg/d LDX, respectively. Safety was assessed by monitoring treatment-emergent adverse events (TEAEs), vital signs, and electrocardiograms. Results: In the MAS XR study (128 adults), the mean (SD) ADHD-RS-IV scores at baseline were 36.9 (7.06), 37.2 (6.92), and 35.7 (5.98) for the placebo, 20-mg/d, and 40-mg/d groups, respectively. Baseline ADHD-RS-IV scores were higher in the LDX study (301 adults); mean (SD) ADHD-RS-IV scores at baseline were 39.4 (6.42), 40.8 (7.30), and 41.0 (6.02) for the placebo, 50-mg/d, and 70-mg/d groups, respectively. For MAS XR, the difference in least squares mean change from baseline (vs placebo) in ADHD-RS-IV was -5.56 (P=.047) for 20 mg/d and -8.80 (P=.001) for 40 mg/d; with LDX it was -9.2 (P<.0001) for 50 mg/d and -10.4 (P<.0001) for 70 mg/d. Common TEAEs were dry mouth (33.7%), anorexia (30.1%), insomnia (27.7%), headache (20.5%), and weight loss (14.5%) for MAS XR and dry mouth (28%), decreased appetite and anorexia (31.4%), and insomnia/initial insomnia/middle insomnia (27.6%) for LDX. Conclusions: In approximately equivalent amphetamine doses, LDX resulted in a numerically larger improvement in ADHD-RS-IV than MAS XR. LDX and MAS XR demonstrated safety profiles consistent with long-acting stimulant use in these studies. Prospective comparison studies are needed to confirm results.

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NR5-05

RELIABILITY AND VALIDITY OF TURGAY DSM-IV-BASED DISRUPTIVE BEHAVIOR DISORDERS RATING SCALE TEACHER AND PARENT FORMS

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SUMMARY:

Objective: The aim of the study is to evaluate the reliability and validity of Turgay DSM-IV Disruptive Behavior Disorders Rating Scale in an epidemiologic sample of Turkish elementary school children. Method: Fifteen hundred 2nd grade students from Izmir, Turkey have been screened for the presence of ADHD by using DSM-IV based ADHD Scale. All positive screened students (86) and one-to-one matched controls (except one missing case) were evaluated with a semistructured interview (Schedule for Affective Disorders and Schizophrenia for School-Age Children- Epidemiologic Version ([K-SADS-E]), and all diagnostic decisions made by using best estimate procedure. The validity and reliability of the Turgay DSM-IV Disruptive Behavior Disorders Rating Scale Parent and Teacher Forms was evaluated in this study sample of 171 subjects. Item-total correlations and Cronbach-alpha coefficient were calculated to evaluate the item quality and the internal consistency reliability of the scales. Confirmatory Factor analysis was conducted for studying validity of the scales. The internal consistency reliability of the scales was found to be quite high (.92 and .91 for parent form; .97 and .96 for teacher form). Logistic Regression Analysis of Turgay DSM-IV Based Disruptive Behavior Disorders Rating Scale Teacher and Parent Forms revealed

that 87.6% correctly classified the diagnostic group, and 91.5% correctly classified the control group. Conclusion: These results suggest that the Turgay DSM-IV Disruptive Behavior Disorders Rating Scale Teacher and Parent forms are reliable and valid for diagnostic and scanning purposes. Key Words: Attention Deficit Hyperactivity Disorder, child, validity.

NR5-06

IS DSM-IV-BASED ADHD SELF-REPORT SCALE A VALID AND RELIABLE TOOL FOR 8 YEAR-OLD CHILDREN? DEVELOPMENT OF A RELIABLE AND VALID SELF REPORT QUESTIONNAIRE

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SUMMARY:
Objective: The current study investigates whether self-reports of children provide reliable and valid information concerning ADHD. For this purpose, we developed a DSM-IV-Based ADHD Self-Report Scale for elementary school children based on the 18 DSM-VI ADHD symptoms. Method: The validity and reliability of the Ercan DSM-IV-Based ADHD Self Report Scale was evaluated in an epidemiologic sample of 171 second grade students (89 ADHD; 82 controls). In the first stage of the study, 1500 2nd grade students had been screened for the presence of ADHD by using DSM-IV-based ADHD Scale. All positive screened students (86) and one-to-one matched controls (except one missing case) were evaluated with a semistructured interview (Schedule for Affective Disorders and Schizophrenia for School-Age Children-Epidemiologic Version (K-SADS-E), and all diagnostic decisions made by using best estimate procedure. After the diagnostic evaluation, 89 subjets were classified as ADHD and 82 non-ADHD. Ercan DSM-IV Based ADHD Self Report Scale scores of diagnostic group and the control group were compared and the significant difference was found between the groups. Item-total correlations and Cronbach-alpha coefficient of the Ercan DSM-IV-based ADHD Self-Report Scale were calculated to evaluate the item quality and the internal reliability. Confirmatory Factor analysis was conducted for studying validity of the scales. A logistic regression analysis was performed using scales on the Ercan DSM-IV-Based ADHD Self-Report Scale as predictors of membership in the two groups (ADHD vs. non- ADHD). Logistic Regression showed that attention deficit subscale classification percentage is 69.4 and the hyperactivity subscale classification percentage is 64. The internal consistency reliability of the scales was found to be quite high (.85 for attention deficit and .84 for hyperactivity -impulsivity subscale). Conclusion: These results suggest that the Ercan DSM-IV-Based ADHD Self-Report Scale is a reliable and valid tool for diagnostic and screening purposes.

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NR5-07

ADOLESCENTS WITH CHILDHOOD DIAGNOSIS OF ADHD: COMORBIDITY, EXECUTIVE FUNCTIONS, ATTACHMENT AND IDENTITY

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SUMMARY:
Objective: To examine the comorbidity, executive function, attachment styles and identity status in adolescents with ADHD. Method: This retrospective cohort (year 2000) study includes the evaluation (in 2006) of 45 adolescents with ADHD in comparison with 28 adolescents without ADHD. All participants were given K-SADS-L, WISC-R, Stroop test, Adolescent Symptom Inventory, Identity Assessment Form and Relationship Questionnaire. ANOVA with posthocs, Chi-square, t-test and Pearson correlation analyses were performed by SPSS 13.0. Results: 75.6% of the cohort had ongoing ADHD in adolescence. Comorbid psychiatric disorders were significantly higher, most common being anxiety disorders (37.5%), ODD (11.1%) and CD (8.8%), in the ADHD group with a RR of 3.3 (95% CI). No difference was found for continuity within subtypes (p=1.00) and remission wasn't associated with subtype (p=0.063). Gender was not associated with remision, subtype or comorbidity. Stroop scores were higher for adolescents with ADHD (t=2.227, p=0.029). In WISC-R digit span and matrix reasoning subtest scores were lower in the study group (F=0.881, p=0.019). There were no differences regarding attachment

styles and identity status. Conclusion: Adolescents with ADHD are under greater risk for comorbidity and they have more difficulties in executive functions. There is no difference of attachment styles or identity status.

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NR5-08

EFFECT OF OROS METHYLPHENIDATE (MPH) TREATMENT ON BEHAVIOR AND PERFORMANCE IN CHILDREN WITH ADHD WITH AND WITHOUT COMORBID LEARNING DISABILITIES

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SUMMARY:
Introduction: Learning disabilities (LD) are more common in children with ADHD than without ADHD. We evaluated effects of OROS MPH on performance in children with ADHD with and without LD. Methods: We analyzed 2 double-blind, randomized, placebo-controlled, crossover, analog classroom studies evaluating OROS MPH in 9–12 year olds with ADHD (NCT00799409, NCT00799487). Subjects had Wechsler Abbreviated Scale of Intelligence score >80 with or without mild/moderate math LD (Wechsler Individual Achievement Test®—2nd Edition Numerical Operations score >=71 and <=85) and/or language LD (Gray Oral Reading Test fluency or Comprehensive Test of Phonological Processing standard score >4 and <8). Subjects took individually determined doses of OROS MPH for 6 weeks, except on 2 laboratory school days when randomized to OROS MPH on day 1/placebo on day 2 or the reverse. Permanent Product Math Test number attempted (PERMP-a) and correct (PERMP-c) and Swanson, Kotkin, Alger, M-Flynn, and Pelham (SKAMP) scores were measured on both days. Results: Of 139 subjects, 89 (64%) had no LD, 46 (33%) had LD, and 4 (3%) were undetermined. Subjects had greater LS mean PERMP-a and -c scores with OROS MPH than pbo. Treatment effects for PERMP-a occurred in subjects without LD (OROS MPH, 114.6; pbo, 82.2) and with LD (OROS MPH, 100.9; pbo, 81.6), P<0.0001. Treatment effects for SKAMP composite scores: subjects without LD (OROS MPH, 8.4; pbo, 19.5) and with LD (OROS MPH, 10.4; pbo, 19.2), P<0.0001. Similar patterns were seen in SKAMP attention and deportment scores. AEs in =10% of subjects: headache, upper abdominal pain, decreased appetite, irritability, and initial insomnia. Two subjects discontinued due to AEs. No serious AEs or deaths were reported. Conclusion: Behavior and performance improved during treatment with OROS MPH in children with ADHD with and without comorbid LD. Sponsored by Ortho-McNeil Janssen Scientific Affairs, LLC, Raritan, NJ. Medical writing assistance provided by Ellen Stoltzfus, PhD, JK Associates, Inc.

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NR5-09

AGE AND GENDER CHARACTERISTICS OF ADHD COMORBIDITIES IN A LARGE CLINICAL SAMPLE

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SUMMARY:
Objective: To assess comorbidity types and frequencies, and the presence of identifying age and gender characteristics in a large sample of 1000 patients with ADHD. Method: Subjects were evaluated by structured clinical interview according to DSM-IV criteria, and utilizing the DuPaul ADHD Rating Scale and the Offord and Boyle Child Health Study parent and teacher rating scales. Sample: A clinical outpatient group of 792 males and 208 females between the ages of 3 and 18 years. Results: All results are statistically significant, p< 0.05. Across age groups over 80% of patients received a diagnosis of ADHD comorbid with at least one other Axis I DSM-IV psychiatric disorder. Across age groups, oppositional defiant disorder (ODD)

and conduct disorder (CD) were most common. In the preschool age group, communication disorders were common, but decreased with age. CD was most common in ADHD Combined type and rare in Inattentive type. Anxiety disorders showed no gender bias. In preschool aged males, ODD was more common. Mood disorder frequency increased with age, and was more prevalent in females. Conclusions: ADHD is highly comorbid and exhibits specific age and gender characteristics that evolve across the lifespan. Knowledge of these features aids in the formulation of differential diagnoses and in the selection of medications as they are influenced by changing comorbidity considerations in ADHD.

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NR5-10

DIFFERENCES IN THE DIAGNOSIS AND TREATMENT OF CHILDHOOD ATTENTION-DEFICIT/HYPERACTIVITY DISORDER PATIENTS WITH OR WITHOUT OPPOSITIONAL SYMPTOMS

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SUMMARY:

Objective: To evaluate differences in diagnosis and treatment of patients with attention-deficit/hyperactivity disorder (ADHD) with oppositional symptoms (OS). Methods: This national study comprised a physicians' Awareness, Trial, and Usage (ATU) survey, a patient chart review, and a parent survey involving patients aged 6–17 years with ADHD. 1) Physicians randomly enrolled patients with ADHD with and without OS. The patient case report form gathered demographic, diagnostic, and treatment data. The parent survey and patient chart review used the oppositional scale of the Conners' Rating Scales – Revised. 2) Statistical significance testing at the 95% confidence level was conducted between and among analytic subgroups. Results: Three hundred sixty-five physicians completed the ATU, yielding 1122 patient chart reviews and 713 parent surveys. Physicians estimated that 42% of patients with ADHD (6–17 years) had OS. Of these, oppositional defiant disorder was diagnosed in 23% aged 6–12 years and 26% aged 13–17 years. Parents reported that 93% of patients exhibited =1 of 10 prespecified OS at diagnosis and many did not discuss these symptoms with their child's physician. Patients without OS (parent-determined) had a mean of 5.3 symptoms (mean CPRS-R:L score 6.0), and patients with OS had a mean of 8.7 symptoms (mean CPRS-R:L score 20.4). Of 281 patients classified as OS by parents, 185 (66%) were classified as OS based on physician perception. However, physicians reported a mean oppositional score of 10.6 for a child with OS, while the parent score was 20.4 of 30; also, physicians believed children with OS had fewer symptoms than parents believed them to have (7.2 vs 8.7, respectively; $P<0.05$ for both comparisons). A total of 34% of patients classified as OS by parents were reported as non-OS by the physician. The majority of parents (=62%) reported more behavioral problems in children they identified with OS, regardless of physicians' perception. These behaviors were underestimated by physicians regardless of whether they agreed with parents on the presence/absence of OS. Conclusions: Differences in identification exist between physician perceptions of ADHD with OS and results obtained from standardized parent surveys. Parents may not discuss OS with their child's physician, who may not then fully grasp the extent of OS. Physicians may therefore be underdiagnosing ADHD with OS, and may not recognize the severity and adverse impact of OS on the patient, their families and the health-care system.

NR5-11

EARLY IMPROVEMENTS WITH ATOMOXETINE THERAPY PREDICT FINAL TREATMENT OUTCOME: A CLASSIFICATION AND REGRESSION TREE (CART) ANALYSIS OF ADULT ADHD DATA

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SUMMARY:

Objectives: Identify incremental symptomatic improvements (imps) in adult patients with attention-deficit/hyperactivity disorder (ADHD) following treatment with atomoxetine (ATX) for 2 or 4 weeks (wks), and determine which imps best predict subsequent overall response after 6-10 wks of ATX therapy. Methods:

Data were pooled from patients assigned to ATX therapy in 3 placebo-controlled clinical trials. Early imps were assessed at either 2 or 4 weeks into ATX treatment (first post randomization visit); overall response was assessed following 6 to 10 weeks treatment (last patient visit). Efficacy measures included the Conners' Adult ADHD Rating Scale—Investigator Rated: Screening Version (CAARS). Classification and regression tree (CART) algorithms were applied to individual items or composite scores to develop models of positive predictive value (PPV) for response (defined as CAARS total score reductions ?40% from baseline at last patient visit). Results: Patients with ?1 point imps in at least 3 of 5 selected CAARS items (Items 16, 18, 27, 29, or 30) exhibited a 71% PPV for response. Early improvers (EIs; patients with ?1 point imps in at least 2 or 3 of the 5 selected CAARS items at 2 weeks) had CAARS total scores and subscores (hyperactivity/impulsivity and inattention) that were significantly better than early non improvers (ENIs) throughout the remainder of ATX treatment (p<0.001 at 4, 6, 8, and 10 wks). Of the patients who ultimately showed response (195 out of 440), 60.0% exhibited imp in ?2 CAARS items at 2 and 4 weeks, and an additional 21.5% exhibited imp in ?2 items at 4 weeks. Conclusions: Imps in CAARS 5 item composite scores observed with ATX treatment were predictive of subsequent overall response. EIs demonstrated increased ADHD symptomatic improvement (compared with ENIs) throughout the course of ATX therapy. Over 80% of eventual responders were identified by specific symptomatic improvements after 2 or 4 wks of therapy.
Funding: Lilly USA, LLC funded this analysis in its entirety.

NR5-12

STIMULANT TREATMENT AND ACADEMIC GRADES OF URBAN CHILDREN AND ADOLESCENTS WITH ADHD

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SUMMARY:
Objective: To assess whether stimulant adherence is associated with improved academic performance measured by grade point average (GPA) for children diagnosed and treated for ADHD. Content: Medicaid claims were merged with academic records from Philadelphia public schools. The analysis focused on Medicaid-eligible children in 1st through 8th grades diagnosed with ADHD and who had filled =1 stimulant prescription. Students with a diagnosis of mental retardation, learning disabilities, autism, or speech, hearing, visual, or language impairments were excluded.
Methods: Marking periods were scored for grade point average (range: 0–4.0) based on English, math, social studies, and science grades and stimulant adherence (medication possession ratio =0.70). Random and fixed effects models estimated effects of stimulant adherence on GPA, between all adherent and non-adherent marking periods in aggregate and within individual students' marking periods, respectively. Results: 3,548 students contributed 29,153 marking periods of which 19.3% periods were adherent. The mean GPA was significantly higher during stimulant adherent (2.18) than non-adherent (1.99) marking periods in aggregate (P<.0001). The regression coefficient representing within-student association between stimulant adherence and GPA over time was 0.107 (P<.0001) indicating adherence was associated with a 0.107 increase in GPA. In stratified analyses, analogous coefficients were 0.108 for boys, 0.103 for girls, 0.077 for elementary students, and 0.114 for middle school students (all P<.0001). The association was stronger among students with (0.143) than without (0.083) comorbid disruptive behavior disorders (both P<.0001). Conclusions: Adherence with stimulant therapy is associated with improved GPA of urban elementary and middle school students diagnosed with ADHD, especially among students with comorbid disruptive behavior disorders.
Supported by Ortho-McNeil Janssen Scientific Affairs, LLC, Raritan, NJ

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NR5-13

ADHERENCE AND PERSISTENCE TO MEDICATIONS FOR ATTENTION-DEFICIT/HYPERACTIVITY DISORDER (ADHD) IN CHILDREN AND ADOLESCENTS

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SUMMARY:
Objectives: Pharmacological treatment for ADHD in children and adolescents is common. Adherence to medication is important in the treatment of ADHD since low adherence is associated with poor symptom control. We examined rates of adherence and persistence to long-acting stimulants (LAS), short-acting stimulants (SAS), and atomoxetine (ATX) and the associations between these outcomes and relevant covariates. Methods: This retrospective study used data from a large US managed care claims database (PharMetrics). Children (6 to <12 years old) and adolescents (12 to <18 years old) with a diagnosis of ADHD (ICD-9-CM 314.00 or 314.01) and a claim for a prescription of LAS, SAS, or ATX between August 1, 2006 and October 1, 2006 (start of school year) were included in the study. Patients were excluded if they had a claim for multiple ADHD medications in the index window or any claim for an ADHD medication 4 months prior to the index claim (representing drug naivety dating back to the previous school year). Patients were required to have continuous enrollment for the entire study period. Adherence was assessed using medication possession ratio (MPR) and persistence was assessed using time to discontinuation (TTD) (30-day gap in medication supply). Covariates examined were index medication, age, hyperactivity, gender, region, payer, comorbidities, and median co-pay. Results: Among 2,097 patients who met inclusion criteria, mean age was 12.8 years and 70.5% were male. Mean MPR was 53.5% (n=1,339, SD=.212) for LAS, 48.8% (n=185, SD=.219) for SAS, and 54.7% (n=171, SD=.261) for ATX. LAS and ATX both exhibited a significantly different MPR than SAS (p<.05). Median TTD was 72 days for LAS, 30 days for SAS, and 68 days for ATX. LAS and ATX both exhibited a significantly different TTD than SAS (p<.001). Children were more adherent than adolescents (p<.0001) and ADHD with hyperactivity was associated with better adherence than ADHD without hyperactivity (p<.01). Having a comorbid mood disorder was also associated with better adherence (p<.05). Conclusions: Adherence and persistence to ADHD medications in children and adolescents is low. Patients taking LAS and ATX had higher adherence and longer persistence than patients taking SAS. Further research is needed to evaluate the impact of poor adherence and persistence on health outcomes and costs in the management of ADHD. Adherence improving interventions should be considered.

Research was conducted by Eli Lilly.

NR5-14

EFFICACY OF LISDEXAMFETAMINE DIMESYLATE IN CHILDREN WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER AND SUBOPTIMAL RESPONSE TO METHYLPHENIDATE

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SUMMARY:
Objective: To evaluate the efficacy of lisdexamfetamine dimesylate (LDX) for the treatment of attention-deficit/hyperactivity disorder (ADHD) in children (6–12 years) with suboptimal response to prior methylphenidate (MPH) treatment. Methods: Using the ADHD Rating Scale (ADHD-RS)-IV and the Clinical Global Impressions-Improvement (CGI-I) scale, we assessed the efficacy of LDX for a subset of children who had suboptimal response (ADHD-RS total score >18) to MPH treatment prior to enrollment in a multicenter, placebo-controlled, double-blind, parallel-group, forced-dose outpatient study that randomized 290 children to receive LDX (30, 50, or 70 mg/d) or placebo for 4 weeks. ADHD-RS-IV and CGI-I scores were obtained at screening prior to discontinuing MPH, at baseline following washout, weekly throughout the study, and at end point. Results: Of 290 randomized patients, 28 patients were being treated with MPH when screened and 26 with ADHD-RS total scores >18 while on MPH. The overall study population had mean (SD) baseline ADHD-RS total scores of 42.4 (7.13) and 43.9 (6.78) for the placebo (n=72) and LDX groups (n=213), respectively; end point ADHD-RS total scores were 36.6 (12.64) and 19.5 (14.0). For the 26 prior MPH users, ADHD-RS total screening scores were 36.6 (11.28) and 37.3 (9.60) for placebo (n=7) and LDX (n=19), respectively; baseline scores were 42.6 (6.35) and 43.2 (5.62); and end point scores were 36.1 (14.52) and 19.2 (14.65). Prior MPH users experienced a 57.1% reduction in ADHD-RS total score from baseline, and placebo-adjusted ADHD-RS total score reduction (95% CI) was -17.6 (-29.65, -5.49; P=.0063). In the overall study population, 154 patients on LDX (72.3%) were classified as clinical "responders" who had 30% reduction in ADHD-RS total score and a CGI-I score of =2 (much improved or very much improved); 130 (61%) were classified as "symptomatic remitters," as

defined by having an ADHD-RS total score <18. Of the 19 subjects in the LDX group who were previously treated with MPH, 15 (78.9%) were classified as responders and 12 (63.2%) as remitters. Conclusions: This post hoc analysis indicates that children who had significant clinical symptoms despite concurrent MPH treatment improved when switched to LDX. Their efficacy outcomes were similar to the results of the total population of children assessed in the clinical trial.
Supported by funding from Shire Development Inc.

NR5-15

EXAMINATION OF EFFECTS OF LISDEXAMFETAMINE DIMESYLATE ON SLEEP QUALITY IN STUDIES OF ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

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SUMMARY:

Objective: To assess effects of lisdexamfetamine dimesylate (LDX) on sleep in adults (18-55 years) with attention-deficit/hyperactivity disorder (ADHD). Method: Pittsburgh Sleep Quality Index (PSQI) and sleep-related treatment-emergent adverse events (TEAE) were analyzed post hoc from 2 studies of LDX (30-70mg/d): a 4-week, randomized, parallel-group, double-blind, placebo-controlled, forced dose-titration study and a 12-month, open-label, dose-optimization study. PSQI scores were analyzed by the proportion of adults with categorical changes (improved, no change, worsened) based on standard error of measurement. Subjects were also classified at baseline and endpoint as "good" sleepers (PSQI<=5) or "poor" sleepers (PSQI>5). TEAEs were analyzed by incidence, duration, and category change. Results: At endpoint, for subjects in the parallel-group study receiving placebo (n=61) or LDX (n=339), respectively: 13 (21.3%) and 111 (32.7%) had improved; 41 (67.2%) and 189 (55.8%) had unchanged; and 7 (11.5%) and 39 (11.5%) had worsened PSQI scores. For subjects in the open-label study (n=314): 148 (47.1%), 131 (41.7%), and 35 (11.1%) had improved, unchanged, and worsened PSQI scores, respectively. In the parallel-group study for subjects on LDX, 165 of 339 were classified as poor sleepers at baseline and of these 71 of 339 (20.9%) were good sleepers at endpoint and the rest were unchanged; 174 of 339 were good sleepers at baseline and of these 26 of 339 (7.7%) were poor sleepers at endpoint and the rest were unchanged. In the LDX open-label study, 171 of 314 were poor sleepers at baseline and of these 81 of 314 (25.8%) were good sleepers at endpoint; 143 of 314 were good sleepers at baseline and of these 20 of 314 (6.4%) were poor sleepers at endpoint. Common (>2%) sleep-related AEs with LDX in the parallel-group and open-label studies were insomnia (19.3% and 19.5%), initial insomnia (5.0% and 4.9%), middle insomnia (3.6% and 2.9%), and fatigue (4.7% and 4.3%), respectively. Sleep-related AEs contributed to 9 and 5 withdrawals from the parallel-group and open-label studies, respectively. Conclusion: Despite TEAEs in some subjects, most subjects had unchanged or improved PSQI scores with LDX treatment. In both studies, some subjects showed an improvement in overall sleep quality by change from baseline poor sleeper status, while a smaller proportion of baseline good sleepers changed to endpoint poor sleeper status. Supported by funding from Shire Development Inc.

NR5-16

THE APPLICATION OF A COMPARATIVE EFFECTIVENESS TRIAL CRITERIA TO A COMMERCIALLY-INSURED POPULATION OF CHILDREN WITH ADHD

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SUMMARY:

Objective: Randomized trials have strong internal validity, but generalizing findings must be done with care. This study quantified the percentage of patients in a US managed care database excluded by the NOTA 6-week effectiveness trial exclusion criteria and the percentage of patients who had discontinued initial drug at 12 months. Methods: From the PharMetrics database representing the US managed care population, an overall study population was selected of children aged 6–17 with a diagnosis of ADHD and initiating ADHD medication in April 2007 through March 2008, based on the inclusion criteria for the NOTA trial reported on ClinicalTrials.gov. The percentages of patients excluded by individual and cumulative exclusion criteria were calculated. Differences in demographics and comorbidities between the NOTA-

modeled and the overall population were described. For the overall population, the percentage of patients discontinuing treatment at 12 months post-initiation was calculated, with discontinuation defined as =60 continuous days without drug or no refill by September 30 for gaps in therapy beginning in June through August. Results: An overall study population of 29,468 was identified, with a mean age (SD) of 12.0 (3.3) years and 69% male. Application of the NOTA exclusion criteria eliminated 14.6% of the overall population, including 3.4% with cardiovascular diagnoses excluded in NOTA. Prevalence of diagnoses for depression and anxiety were reduced from 17.9% to 14.4% and 16.8% to 12.3%, respectively, after applying the criteria. At 12 months, 66.3% of overall patients had discontinued their initial ADHD medication. Conclusions: In interpreting results from short-term trials such as NOTA, managed care decision makers should consider issues such as comorbidities and long-term persistence, in order to create appropriate guidelines and policy.

Support: Supported by Ortho-McNeil Janssen Scientific Affairs, LLC, Raritan, NJ.

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NR5-17

PSYCHOPATHOLOGY AND TEMPERAMENT IN PARENTS OF CHILDREN AND ADOLESCENTS WITH ATTENTION DEFICITY HYPERACTIVITY DISORDERS: A CONTROLLED STUDY

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SUMMARY:

Objective: The aim of the present study was to investigate the characteristics of psychopathology and temperament in mothers and fathers of child and adolescents with attention-deficity/hyperactivity disorder (ADHD). We compared the psychiatric diagnoses and temperamental characteristics of parents of children and adolescents with ADHD with parents of children and adolescents without ADHD. Methods: Diagnostic interviews of parents were conducted with Structured Clinical Interview for DSM Non-Patients, Axis I Disorders and Axis II Disorders (SCID-NP, SCID-I and SCID-II). Temperament characteristics were evaluated with Temperament Evaluation of Memphis, Pisa, Paris and San Diego Autoquestionnaire (TEMPS-A). Results: Mood disorders, anxiety disorders and some personality disorders were more frequent in mothers of children and adolescents with ADHD than controls (relatively $p< 0.001$, $p= 0.015$ and $p< 0.001$). The most frequent personality disorders were avoidant, dependent and obsessive compulsive personality disorders. Depressive, cyclothymic and anxious temperaments scores were higher in mothers (relatively $p= 0.011$, $p= 0.02$ and $p= 0.037$), than in the controls, and irritable temperament scores were higher in fathers of children and adolescents with ADHD ($p= 0.045$) than in the controls. Conclusion: Axis I and II disorders and some characteristics of temperament were more frequent in the parents of children and adolescents with ADHD than in the parents of children and adolescents without ADHD. Some thereshold traits have significant etyhologic effects for ADHD such as parental psychopathology.

NR5-18

MENTAL STATUS OF CAREGIVERS AND TREATMENT ADHERENCE: COMPARISON OF CAREGIVERS OF BIPOLAR AND SCHIZOPHRENIC PATIENTS

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SUMMARY:

Objective: Bipolar disorder and schizophrenia were chronic and recurrent disorders. The aim of this study was to compare the depression and anxiety levels of caregivers of bipolar and schizophrenic patients. Methods: 34 caregivers of bipolar patients and 34 caregivers of schizophrenic patients were recruited form consecutive admission and compared crossectionally with HDRS and HARS. Results: Adherence to controls and pharmacological treatment were more frequent in bipolar patients than the schizophrenics ($p= 0.05$ ve $p< 0.001$). Schizophrenic patients caregivers' anxiety scores were higher than bipolar patients caregivers' ($p= 0.017$ and $p= 0.009$). Conclusion: Nonadherence to

treatment was more frequent in schizophrenic patients and nonadherence patients' caregivers' anxiety scores were higher.

NR5-19

EFFECT OF OROS METHYLPHENIDATE TREATMENT ON READING PERFORMANCE IN CHILDREN WITH ADHD

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SUMMARY:

Introduction: Attention problems in early childhood have been implicated in low reading achievement in late adolescence. We evaluated the effect of OROS MPH treatment on reading fluency and reading comprehension in older children with ADHD. Methods: We analyzed data from a double-blind, randomized, placebo-controlled, crossover, analog classroom study evaluating individually determined dose of OROS MPH in children aged 9 to 12 years with ADHD (NCT00799409). Subjects took open-label OROS MPH for 6 weeks, except on two laboratory school assessment days, randomized to OROS MPH on the first day and placebo on the second day, or vice versa. The Dynamic Indicators of Basic Early Literacy Skills (DIBELS) and Gray Silent Reading Test (GSRT) were administered once on each of the 2 laboratory school days. Results: Of 78 subjects, 91% completed the study. Subjects had DIBELS total least squares mean scores of 112.0 with OROS MPH and 106.2 with placebo (P=0.0092), indicating better accuracy and reading rate with OROS MPH. The GSRT Silent Reading Quotient was 92.0 with OROS MPH and 85.5 with placebo (P=0.0038), indicating an improvement with OROS MPH that was consistent with the silent reading comprehension ability of children in a normative population. Adverse events (AEs) reported by >=5% of subjects were decreased appetite, upper abdominal pain, headache, irritability, initial insomnia, dizziness, nasal congestion, and pyrexia. No deaths, serious AEs, or dropouts for AEs were reported. Conclusions: Results suggest that OROS MPH may improve oral reading fluency and reading comprehension in children with ADHD. Additional evaluations are warranted to confirm the effects of treatment on these skills. Study sponsored by Ortho-McNeil Janssen Scientific Affairs, LLC, Raritan, NJ. Editorial assistance provided by Ellen Stoltzfus, PhD, JK Associates, Inc.

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NR5-20

VISUAL MEMORY AS AN ENDOPHENOTYPE IN ADHD: EVIDENCE FROM THE CAMBRIDGE NEUROPSYCHOLOGICAL TEST BATTERY

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SUMMARY:

Objective: Although executive functions have been proposed as endophenotypes for determining genetic pathways contributing to attention-deficit/hyperactivity disorder (ADHD), there is lack of such data regarding visual memory. This work assessed the visual memory performance in adolescent probands with ADHD and their unaffected siblings as compared with the controls. Methods: The sample included 279 adolescents aged 11-17 years, who were clinically diagnosed with DSM-IV ADHD at the mean age of 6.7 (SD = 2.9), 108 unaffected siblings aged 8 years or older, and 173 unaffected school controls. All the participants had IQ greater than 80. Structural psychiatric interviews were administered to the participants and their mothers to confirm clinical diagnosis of ADHD at childhood and current ADHD and other psychiatric diagnoses. All the participants were assessed by using the visual memory tasks of the Cambridge Neuropsychological Test Automated Battery (CANTAB): Delayed Matching to Sample (DMS), Pattern Recognition Memory (PRM), Spatial Recognition Memory (SRM), and Paired Associates Learning (PAL). Results: Compared with the controls, probands with ADHD and their unaffected siblings had significantly poorer performance in the DMS with increased magnitudes of group differences in the DMS increased as the task difficulties increased even after controlling for IQ, comorbidity, use of methylphenidate, and demographics. Probands with ADHD performed worse than controls in the PRM and PAL tasks but there was no significant difference between unaffected siblings and controls. There was no group difference in the SRM. In general, persistent ADHD, current use of and duration of treatment with methylphenidate were associated with

more severe visual memory deficits. Conclusions: Our findings suggest that children and adolescents with ADHD may have impaired visual memory that is associated with the presence of current persistence of ADHD. Decreased performance in the DMS in unaffected siblings indicates that visual memory measured by the DMS may be a useful endophenotype for genetic studies of ADHD.

NR5-21

CLINICAL UTILITY OF ADHD SYMPTOM THRESHOLDS TO ASSESS NORMALIZATION OF EXECUTIVE FUNCTION WITH LISDEXAMFETAMINE DIMESYLATE TREATMENT

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SUMMARY:
Objective: To assess the relation of various cutoff scores of the Attention-Deficit/Hyperactivity Disorder Rating Scale IV (ADHD-RS-IV) to levels of improvement in ADHD-related executive functions (EF) as measured by the Brown ADD Scale (BADDS) and to provide a measure of clinically meaningful EF improvement after ADHD treatment. Method: The BADDS, a validated, normed, self-report measure of EF in ADHD provides a qualitative measure to rate treatment progress ranging from equivocal to optimal response. The ADHD-RS-IV assesses current symptoms based on DSM-IV criteria. Post hoc, these measures were used together to analyze data from a 4-week, open-label, dose-optimization phase in a double-blind, placebo-controlled study of lisdexamfetamine dimesylate (LDX) in adults with ADHD. Postbaseline ADHD-RS-IV scores were categorized according to 4 cutoff criteria of symptom remission: 1.) ADHD-RS-IV total score <=18; 2.) ADHD-RS-IV total score <=10; 3.) no ADHD-RS-IV item scored >1; 4.) ADHD-RS-IV total score <=18 and <=2 items per subscale with a score of 2. Sensitivity and specificity of ADHD-RS-IV criteria for identifying subjects with optimal BADDS scores were assessed using receiver operating characteristics (ROC). Safety evaluation included adverse events (AEs). Results: At the dose-optimization endpoint, 85 of 127 subjects had optimal BADDS scores. Sensitivity was 0.72, 0.96, 0.92, and 0.75; specificity was 0.46, 0.39, 0.39, and 0.42 for criteria 1 to 4, respectively. Criteria 2 and 3 had high sensitivity, but specificity was similar in the 4 criteria. For criterion 2, 22/85 subjects with optimal scores and 1/42 with nonoptimal scores met cutoff criteria (positive predictive value [PPV]=0.26, negative predictive value [NPV]=0.98). For criterion 3, 23/85 subjects with optimal scores and 2/42 with nonoptimal scores met cutoff criteria (PPV=0.27, NPV=0.95). ROC areas under the curve (AUC) were 0.699, 0.776, 0.732, and 0.668 for criteria 1 to 4, respectively. AEs were similar to those in other LDX trials. Conclusion: Criteria 2 and 3 had satisfactorily high sensitivity (those responding at that ADHD-RS-IV threshold have normalization of EF) but none of the criteria had adequate specificity (those not responding at the ADHD-RS-IV threshold lack normalization of EF). AUC comparison indicates that criteria 2 and 3 ADHD-RS-IV thresholds may be more accurate in assessment of EF normalization as measured by the BADDS. Supported by funding from Shire Development Inc.

NR5-22

WHAT PREDICTS SUBSTANCE ABUSE IN ADHD YOUTH?: A 10-YEAR FOLLOW-UP STUDY

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SUMMARY:
Background: High rates of Substance Use Disorders (SUD, including drug or alcohol abuse or dependence) have been found in samples of adolescents and adults with Attention Deficit Hyperactivity Disorder (ADHD). Predictors of ADHD youth who are at risk for the development of SUD remain unclear. As such, the main aims of this study were to identify clinically meaningful characteristics of children that predicted the future development of SUD. Methods: We comprehensively assessed 379 children (268 probands, 111 siblings) with DSM-III-R ADHD (mean age ? SD = 10.6 ? 3.1 years) and 423 controls (229 probands, 194 siblings) (11.3 ? 3.4 years) from a ten-year prospective family case-control study of ADHD youth. Individuals were assessed by structured psychiatric interview for psychopathology and SUD. Results: Over the ten-year follow-up, ADHD was found to be a significant predictor of any SUD (Odds Ratio, (95% Confidence Interval) = 1.66 (1.27, 2.15), p=0.001) and cigarette smoking (2.34 (1.72, 3.19), p<0.001). Within ADHD, comorbid Conduct Disorder at baseline was also found to be a significant

predictor of any SUD (3.22 (1.97, 5.26), p<0.001). We did not find any other significant associations for other comorbidities, for any social or family environment factors nor for any school or cognitive functioning factors (all p values > 0.05). We found similar results for any alcohol use disorders, any drug use disorders, and for cigarette smoking. Conclusions: The results of this 10-year, follow-up derived from an ongoing controlled family study of ADHD demonstrates that ADHD and Conduct Disorder identifiable early in life predict future SUD.

NR5-23

CHANGES OF SLEEP PARAMETERS AFTER TAKING METHYLPHENIDATE IN CHILDREN WITH ADHD

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SUMMARY:
Objective: The primary aim of this study was to evaluate bedtime, wake-up time, total sleep duration (TSD), and sleep latency after taking methylphenidate (MPH) during weekdays and weekends. The secondary aim was to compare the difference of sleep parameters among dose and kinds of MPH and ages. Methods: 30 ADHD children, aged from 7 to 12 years, were enrolled in this study. They were randomly assigned to take one of the two kinds of MPH (Oros-methylphenidate and Metadat-CD). Flexible dosing strategy was applied and the goal dose was 1.0 mg/kg. Baseline evaluation of demographic and lifestyle factors, SNAP-IV for ADHD severity, CGI-S, and WISC-III were performed. Dose of MPH was adjusted every week and the target dose of MPH was 1.0mg/kg. Medication record and sleep diary were checked by the parents every day. Exclusion criteria are as follows: IQ<70, taking any medications that potentially affected their sleep, such as antihistamine, antipsychotics, and antidepressants with the previous week, seizure disorder or other neurological problems, any sleep disorders such as narcolepsy and obstructive sleep apnea. Results: Baseline bedtime, wake-up time, sleep latency and total sleep time (TST) during weekdays were 21:59±0:53, 7:12±0:40, 14:14± 10:38 minutes, and 8.99± 0.87 hours, respectfully. Bedtime was significantly delayed after taking MPH (p<.01). TST was also significantly shortened between baseline and other weeks (p<.01). In assessing weekend sleep parameters, both bedtime and TST were significantly changed after taking MPH. But all of the differences were significant only between baseline and other weeks. TST was not significantly different according to the types and dose of MPH. Conclusions: This study shows that MPH itself reduced TST about 30 minutes mainly due to delay of bedtime regardless of weekdays or weekends. However types and dose of MPH do not affect the sleep parameters.

NR5-24

EFFECTS OF LONG-TERM OPEN-LABEL COADMINISTRATION OF GUANFACINE EXTENDED RELEASE AND STIMULANTS ON CORE SYMPTOMS OF ADHD

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SUMMARY:
Introduction: A short-term (9-week) open-label study of guanfacine extended release (GXR) and stimulant coadministration found statistically significant and clinically meaningful improvements in children and adolescents with attention-deficit/hyperactivity disorder (ADHD) whose symptoms were suboptimally controlled on a stable stimulant dose. This analysis characterizes the long-term effectiveness of GXR and stimulant coadministration in such subjects. Methods: Fifty-three subjects aged 6-17 years with ADHD who participated in the short-term study continued into a 2-year open-label extension study, constituting a portion of the larger nonrandomized long-term study population (some of whom received GXR alone). For this subgroup, doses of GXR (up to 4 mg/d) and stimulant were adjusted for clinical effect and tolerability. Effectiveness measures included ADHD Rating Scale Version IV (ADHD-RS-IV) total, inattentiveness, and hyperactivity/impulsivity subscale scores assessed at monthly visits. Results: Mean (SD) baseline (pretreatment baseline score from the short-term trial) ADHD-RS-IV total score was 29.3 (10.9). Mean (SD) total scores were decreased from baseline at all monthly visits, from -14.7 (11.6) at month 4 to -19.9 (10.3) at month 16. At endpoint (the last postbaseline assessment on treatment), the mean (SD) reduction in ADHD-RS-IV total score from baseline was -16.1 (11.0; P<0.001). Reductions from baseline in mean (SD) inattentiveness subscale scores were observed at month 1 (-10.5 [6.56]) and at all monthly visits thereafter. The mean (SD) reduction in inattentiveness subscale scores from baseline to endpoint was -9.2 (6.4; P<0.001). Reductions

in mean hyperactivity/impulsivity subscale scores were observed at month 1 (-8.0 [5.9]) and persisted throughout the 24-month study. From baseline to endpoint, the mean (SD) decrease in hyperactivity/impulsivity subscale score was -6.9 (6.1; P<0.001). Treatment-emergent adverse events (TEAEs), which included all on-treatment AEs, were reported by 86.8% of subjects and were generally mild or moderate. The most common TEAEs considered possibly or probably related to study drug(s) were decreased appetite (13.2%), headache (13.2%), and irritability (11.3%). Conclusions: GXR and stimulant coadministration in patients with ADHD and a history of suboptimal response to stimulant monotherapy may be associated with sustained effectiveness, with generally mild to moderate AEs.

NR5-25

CHANGES IN PARENTAL STRESS WITH GUANFACINE EXTENDED RELEASE IN CHILDREN WITH ATTENTION-DEFICIT/ HYPERACTIVITY DISORDER AND OPPOSITIONAL SYMPTOMS

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SUMMARY:
Introduction: Guanfacine extended release (GXR), an extended-release formulation of the selective alpha-2a adrenoceptor agonist guanfacine, has been recently approved by the US Food and Drug Administration for the treatment of ADHD in children and adolescents aged 6-17 years. The primary objective of the present trial was to assess the efficacy of GXR in the treatment of children with ADHD and oppositional symptoms. The current analysis examines the effects of treatment with GXR on stress in the parent-child system as measured by the Parenting Stress Index-Short Form (PSI/SF). Methods: Children aged 6 to 12 years with a primary diagnosis of ADHD were eligible to participate in this randomized, double-blind, placebo-controlled, dose-optimization study. Subjects were required to have a baseline ADHD-RS-IV total score =>24 and exhibit oppositional symptoms as assessed by the oppositional subscale of the CPRS-R:L (baseline score =>14 [males] or =>12 [females]). Following washout, 217 subjects were randomized to receive GXR or placebo (2:1 ratio), then began a 5-week dose-optimization period, followed by a 3-week maintenance period at their optimal dose (1-4 mg/d). The PSI/SF is composed of 36 items that are each rated by the parent on a 5-point scale. The PSI/SF, which was administered at baseline and final study evaluation (endpoint), yields a total score, and used 3 subscales: Parental Distress, Parent-Child Dysfunctional Interaction, and Difficult Child. PSI/SF total scores may range from 36 to 180 and, in this study, higher scores represented lower levels of parenting stress. Results: GXR was associated with significantly greater least squares (LS) mean improvement in PSI/SF total scores than placebo (17.0 vs 7.7; P=0.002) at endpoint. GXR was associated with significantly greater LS mean improvement than placebo on the Parental Distress (5.0 vs 2.5; P=0.034) and Difficult Child (8.1 vs 3.3; P<0.001) subscales. GXR produced numerically greater improvement than placebo on the Parent-Child Dysfunctional Interaction subscale and the difference approached statistical significance (LS mean 3.9 vs 2.0; P=0.064). Conclusions: This analysis suggests that once-daily GXR is efficacious in reducing parental stress overall, parental stress from personal factors (as measured by the Parental Distress subscale), and parental perception of a difficult child when used to treat children with ADHD and oppositional symptoms.

NR5-26

SCHOOL-BASED INTERVENTION FOR K-SECOND GRADERS PRESENTING WITH DISRUPTIVE BEHAVIOR

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SUMMARY:
Objective: The aim of the study is to assess changes in pro- and antisocial behaviors in response to an intensive, school-based early intervention for students with classroom disruptive behaviors. Method: Teachers/parents referred kindergarten through second graders due to difficult to manage, disruptive classroom behavior. Students who met criteria for an Attention Deficit/Hyperactivity Disorder, Pervasive Developmental Disorder or Mood Disorder in association with significant disruptive behavior were included. Prior to and at completion of the intervention, teachers scored participants' behavior using the School Social Behavior Scales (2nd Ed). The intervention duration was one school year and consisted of the Dina Dinosaur Child Training Programs (Small Group Therapy) component of The Incredible Years. Data were

analyzed using paired t-tests to examine the differences in mean scores before versus after the intervention. Results: Eighty-eight participants (male = 71), aged five to eight years, completed the study. Scores on all the pro-social scales (Social Competence scale, Peer Relationship, Self-management/Compliance and Academic Behavior subscales) improved significantly (p<.001). Scores on all the antisocial scales decreased significantly with scores on the Antisocial Behavior Scale and the Defiant/Disruptive subscale decreasing to a more significant degree (p<.001) than the Hostile/Irritable and Antisocial/Aggressive subscales (p<.01). Conclusions: The small group module of The Incredible Years program proved effective in reducing disruptive behavior and increasing pro-social behavior in kids K to 2nd grade. Although all measured behaviors improved, those assessed by two of the Antisocial Behavior subscales seems to either benefit less robustly, or possibly need longer intervention to respond. Benefits due to the intervention support its implementation for disruptive behavior in schools.

NR5-27

CLINICAL PREDICTORS OF CARDIOMETABOLIC RISK IN CHILDREN TREATED WITH ANTIPSYCHOTIC MEDICATIONS

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SUMMARY:

Introduction: Youth receiving antipsychotic medications are at risk for adverse changes in adiposity and insulin sensitivity [1], key predictors of long-term cardiometabolic risk. Rates of metabolic screening and monitoring for patients treated with antipsychotics remain low overall, with children having the lowest rates of monitoring compared to other age groups [2]. The aims of this analysis, conducted in a dataset of children undergoing antipsychotic treatment, were to characterize the relationship between 1) commonly-used surrogate measures of adiposity such as body mass index percentile (BMI percentile) versus gold-standard measures of adiposity measured by dual energy X-ray absorptiometry (DEXA) and magnetic resonance imaging (MRI) and 2) clinically available laboratory measures such as fasting plasma insulin versus gold-standard measure of whole body insulin sensitivity derived from hyperinsulinemic-euglycemic clamps. Methods: Antipsychotic-naïve participants ages 6-18 are assessed before and after 3 months of antipsychotic therapy using gold standard and clinical measures of adiposity and insulin sensitivity. Gold-standard measures include DEXA total and percent total fat, abdominal MRI (visceral and subcutaneous fat), and hyperinsulinemic-euglycemic glucose clamps with stable isotope tracing. Clinical measures include anthropomorphic assessment (height, weight, BMI percentile and waist circumference), fasting lipids, glucose, HgbA1c and insulin. For this analysis (N=86), scatterplots were constructed and correlations run comparing clinical versus laboratory measures of adiposity and insulin sensitivity, examining both baseline and change values. Results: Significant correlations were observed between most clinical and surrogate measures of adiposity with somewhat stronger relationships observed at baseline compared to during treatment-induced change. Several laboratory measures (e.g., fasting plasma, triglycerides and insulin) were significantly correlated with insulin sensitivity at baseline but not during change. Overall, however, clinical measures explained only limited proportions of the variance in gold standard measures of both adiposity and insulin sensitivity. Conclusions: Efforts to understand the effect of treatment on changes in adiposity and insulin sensitivity require the use of direct, sensitive measures of cardiometablic risk rather than clinical surrogate measures.

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NR5-28

CONTINUITY OF DEPRESSIVE DISORDERS FROM CHILDHOOD AND ADOLESCENCE TO ADULTHOOD: A NATURALISTIC STUDY AT COMMUNITY MENTAL HEALTH CENTERS IN MADRID, SPAIN

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SUMMARY:

Background: High rate of homotypic continuity of adolescent depression in adulthood has been reported. Depressive disorders in childhood have been associated with increased risk of other psychiatric diagnoses in adulthood such as bipolar disorder, anxiety disorders or substance

abuse disorders. The objective of our investigation was to determine homotypic continuity of depressive disorders in patients with depressive disorders followed in clinical services since childhood or adolescence. Methods: Prospective cohort study of children and adolescents receiving psychiatric care at all Community Mental Health Centers in Madrid, Spain between January 1, 1986 and December 31, 2007. Patients had to receive their first diagnosis of an ICD-10 F32 or ICD-10 F33 depressive disorder between 6 and 17 years old and had to be at least 20 years old at the end of the study period. Subjects whose first diagnosis of depressive disorder was in childhood (6-12 years: DEPRESSED-CHILD group) and subjects whose first diagnosis of depressive disorder was in adolescence (13-17 years: DEPRESSED-ADOLESCENT group) were compared in demographics, psychiatric comorbidity and rates of homotypic continuity in adulthood. Results: Five hundred twenty-eight patients with depressive disorders were selected. The DEPRESSED-CHILD and DEPRESSED-ADOLESCENT groups differ in gender distribution but did not differ on other demographic variables studied or rates of psychiatric comorbidity. Of those subjects who continued to be followed up in adult mental health facilities, 57.2% were diagnosed with a depressive disorder. The DEPRESSED-ADOLESCENT group was more likely to show homotypic continuity of the depressive disorder in adulthood than the DEPRESSED-CHILD group (?2 =6.19, df=1, p=0.013). Psychiatric comorbidity was associated with greater risk of follow up in adult mental health services (?2 =1.30, df=1, p<0.001), but was inversely related to homotypic continuity of depressive disorder in adulthood (?2 =2.55, df=1, p<0.001). High rates of anxiety disorders, bipolar disorder and personality disorders in adulthood were observed in subjects of the DEPRESSED-CHILD and DEPRESSED-ADOLESCENT groups. Conclusion: In this clinical sample it appears that subjects with onset of depressive disorder in adolescence may have a high level of homotypic continuity in adulthood. Both children and adolescents with depressive disorders are at risk for the development of other psychiatric disorders in adulthood.

NR5-29

PALIPERIDONE FOR IRRITABILITY IN ADOLESCENTS AND YOUNG ADULTS WITH AUTISTIC DISORDER

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SUMMARY:
Objective: To determine the effectiveness and tolerability of paliperidone for irritability (aggression, self-injury, tantrums) in adolescents and young adults with autistic disorder (autism). Methods: This is a prospective, 8-week open-label study of paliperidone in 30 subjects (12-21 yrs) with autism. Subjects with severe irritability [Clinical Global Impression-Severity (CGI-S) score > 4 and Aberrant Behavior Checklist-Irritability (ABC-I) score > 18] were eligible. Concomitant medications (except antipsychotics) were allowed if doses were stable for > 2 months. Subjects were antipsychotic-free for > 2 weeks prior to screen. Paliperidone initiated at 3 mg/d could be increased to a maximum of 9 mg/d over 4 weeks. Primary outcome measures were CGI-Improvement (I) and ABC-I. Results: To date, 18 subjects aged 12-20 yrs (mean 15.3 yrs) have enrolled. One subject never began medication (unable to swallow capsules). One subject exited at week 2 (moderate sedation) and one exited at week 4 (nonresponse). Mean IQ was 42.6 (range 36-73). Final mean paliperidone dose was 6.5 mg/d (range 3-9 mg/d). Fourteen of 17 (82%) subjects responded (CGI-I of 1 or 2 and > 25% improvement on ABC-I). Mean baseline ABC-I was 29.1 (range 22-45), while mean week 8 ABC-I was 14.5 (range 0-31). Mean endpoint CGI-I was 1.7. Paliperidone was well tolerated; moderate adverse effects included headache (n=2), drooling (n=1), and sedation (n=1). Mild adverse effects included increased appetite (n=6), rhinitis (n=6), cough (n=4), tiredness (n=4), drooling (n=2), and tremor (n=1). Mean age- and sex-normed BMI increased from 21.1 at baseline to 21.6 at endpoint. Conclusion: Preliminary data suggest that paliperidone may be effective and well tolerated for severe irritability in adolescents and adults with autism. Given these positive preliminary findings, large scale controlled studies are needed to elucidate the efficacy and tolerability of paliperidone for irritability in autism.

NR5-30

POLYPHARMACY REDUCTION LEADS TO POSITIVE EFFECTS ON BOTH TREATMENT OUTCOME AND HEALTHCARE COST: ANALYSES FROM A RESIDENTIAL TREATMENT CENTER

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SUMMARY:
Background: The use of polypharmacy is increasing in children, more so when severe behavior disturbance is present. The severely disturbed frequently end up in a trajectory of multiple placements and providers and consequently a lack of appropriate monitoring of efficacy and justification for these medications. In addition, unjustified prolonged prescribing caries a high financial burden. Objectives: Assess whether 1) treatment of severely disturbed youth in a residential setting leads to reduction in the number of prescribed pre-admission medications, 2) reduction of medication regimens provides positive immediate and long-term treatment outcome, and 3) polypharmacy reduction leads to cost savings. Method: Data were collected for 103 children (31 girls, 72 boys) aged 11-18 years old, admitted and discharged from a residential treatment center between July 2007 and December 2009. Six month post-discharge data were available for 36 children. Data include demographics, referral source, admission diagnoses, admission and discharge medications, and post discharge data including level of stability and types of ongoing treatment. Descriptive analyses of demographic data were performed and admission and discharge data including number and class of medications, number of admission diagnoses and interactions between findings were assessed. A cost reduction analysis at endpoint was based on reduction by medication class. Results: Mean age was 14.71 ± 1.6 year. Only 6% of children were admitted from home, 94% from prior placements. Mean number of prior placements was 5.81 ± 5.1. Mean number of admission medications was 2.2 ± 1.29 compared to 1.0 ± 0.94 discharge medications, without difference by age, sex, or race. Of the 103 children, 22 (21.3%) were not on medication upon admission. One patient was on 5, 9 patients on 4 medications. At endpoint 1 patient was on 4 medications, an 89% decline. The number of patients needing 3 or 2 medications declined by 75 and 36%; 37 patients were discharged without medication, a 68% increase. The largest reductions were seen in the number of antipsychotics (24.3%; N=25) and antidepressants (14.6%; N=15). Twenty-two patients received 2 mood stabilizers upon admission, at endpoint only 7, a 68% decrease. At 6 months post-discharge 66.6% of children were doing well and 13.9% were doing poorly. Seven children (19%) were re-hospitalized. Cost analysis based on discontinued medication class by patient showed potential total monthly savings of $13,000.

NR5-31

EXTENDED-RELEASE DEXMETHYLPHENIDATE 30 MG IMPROVES LATE-DAY ADHD SYMPTOM CONTROL IN CHILDREN WITH ADHD: A RANDOMIZED, DOUBLE-BLIND, CROSSOVER STUDY

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SUMMARY:
Objective: Evaluate the efficacy of dexmethylphenidate extended-release (d-MPH-ER) 30 mg compared to d-MPH-ER 20 mg as measured by pre- to postdose change of the average Swanson, Kotkin, Agler, M-Flynn, and Pelham (SKAMP) Combined (Attention and Deportment) score at 10-, 11-, and 12-hours post-dose. Methods: In a randomized, double-blind, 3 periods x 3 treatments, crossover study, children 6-12 years old with ADHD stabilized on MPH 40-60 mg/d or d-MPH 20-30 mg/d were randomized to receive d-MPH-ER 20 mg/d, 30 mg/d, and placebo for 7 days each. The final dose of each treatment was administered in a laboratory-classroom setting. Primary efficacy outcome measured changes in the average SKAMP-Combined score from predose to 10, 11, and 12 hours postdose (Avg 10-12). Adverse events (AEs) and vital signs were noted. Results: A total of 165 children (94 boys; mean age: 9.6±1.8 years) were randomized and 162 were included in the intent-to-treat analysis. Mean Average 10-12 change from predose in all efficacy outcome measures were significantly greater for d-MPH-ER 30 mg compared with d-MPH-ER 20 mg: SKAMP-Combined score, -4.47 vs -2.02, respectively, P=0.002; SKAMP-Deportment score, -1.49 vs -0.39, respectively, P=0.019; SKAMP-Attention score, -2.62 vs -1.33, respectively, P<0.001; Math Test-Attempted score, 28.03 vs 18.76, respectively, P=0.002; Math Test-Correct score, 28.02 vs 18.45, respectively, P=0.002. Most common AEs (=3%) were decreased appetite, headache, abdominal pain, and tachycardia. Conclusion: ADHD symptoms improved significantly with d-MPH-ER 30 mg versus d-MPH-ER 20 mg at hours 10-12. Thus, d-MPH-ER 30 mg may provide further benefit to patients who do not obtain optimal later-day symptom control with d-MPH-ER 20 mg.
This study was supported by Novartis Pharmaceuticals Corporation.

NR5-32

DEFICIENT EMOTIONAL SELF-REGULATION

IS A CORE DEFICIT THAT PREDICTS ADAPTIVE IMPAIRMENTS IN ADULTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

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SUMMARY:
Introduction: Recent reviews have argued that emotional impulsiveness and deficient emotional self-regulation (EI/DESR) are central components of attention-deficit/hyperactivity disorder (ADHD), not merely associated features or consequences of comorbidity. Methods: The frequency and severity of problems with EI/DESR were examined in 3 groups: adults with ADHD (n=146), clinical control adults not diagnosed with ADHD (n=97), and a community control group (n=109). Self- and other ratings of EI/DESR were utilized. The extent to which EI/DESR contributed to the prediction of global ratings of self- and other-rated impairments in 10 different domains beyond the contribution made by the traditional 2 dimensions of ADHD symptoms was also examined. Finally, the impact of EI/DESR was evaluated using more detailed measures of occupational impairment, educational history, criminal history, adverse driving outcomes, marital satisfaction, parenting stress, and severity of ADHD, oppositional defiant disorder, and conduct disorder in offspring. Results: Adults with ADHD exhibited significantly more EI/DESR (51-76%) than either clinical or community control adults, whether measured by self- or other reports and whether symptoms were studied individually or in total (p<.001) EI/DESR uniquely contributed to 6 of 10 domains and overall impairment. Severity of EI/DESR independently contributed to most measures of impairment (occupational functioning, educational history, driving risks, criminal history, marital dissatisfaction, parenting stress) as well as to the severity of offspring disruptive disorders beyond the 2 ADHD symptom dimensions and, in many cases, EI/DESR was the only predictor. Conclusions: EI/DESR is a central component of ADHD as are its 2 traditional symptom dimensions. EI/DESR severity is not merely redundant with the other ADHD symptom dimensions but adds explanatory and predictive power to understanding the numerous types of impairment that impact major life activities in adults with ADHD.

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NR5-33

LONG-TERM SAFETY AND EFFECTIVENESS OF OPEN-LABEL COADMINISTRATION OF GUANFACINE EXTENDED RELEASE AND STIMULANTS FOR ADHD IN CHILDREN AND ADOLESCENTS

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SUMMARY:
Introduction: Though use of combination stimulant and alpha-2a agonist therapy for attention-deficit/hyperactivity disorder (ADHD) is not approved by the US Food and Drug Administration, it is often used in clinical practice. The current analysis aims to characterize the long-term safety and effectiveness of combination therapy with the selective alpha-2a agonist guanfacine extended release (GXR) and stimulants (methylphenidate or amphetamine) in both children (aged 6-12 years) and adolescents (aged 13-17 years) with ADHD. Methods: This long-term (<=24 months) open-label extension study enrolled 262 subjects aged 6-17 years with ADHD, including 208 subjects who received GXR alone and are not included in the present analysis. The remaining 53 subjects had experienced suboptimal response to stimulants and had participated in an antecedent open-label safety study of GXR and stimulant coadministration. These subjects continued to receive combination therapy with GXR and a stimulant throughout the present study. Doses of the stimulant and GXR (<=4 mg/d) were adjusted for clinical effect and tolerability at the investigator's discretion. Effectiveness measures included change in ADHD Rating Scale Version IV (ADHD-RS-IV) total score from baseline (the pretreatment baseline score from the antecedent trial) to endpoint (the last postbaseline assessment while on treatment). Results: At baseline, mean (SD) ADHD-RS-IV total scores were 30.2 (10.79) for children aged 6-12 years and 26.7 (11.12) for adolescents aged 13-17 years. Significant mean (SD) reductions in ADHD-RS-IV total score from baseline to endpoint were observed for both children (-16.9 [10.76]; P<0.001) and adolescents (-13.7

[11.84]; P<0.001), yielding mean (SD) ADHD-RS-IV total scores at endpoint of 13.3 (9.0) for children and 13.0 (6.9) for adolescents. Treatment-emergent adverse events (TEAEs) were reported by 86.8% of subjects. TEAEs were generally mild or moderate with severe TEAEs reported by 3.8% of subjects. The most common TEAEs were upper respiratory tract infection (24.5%), headache (22.6%), upper abdominal pain (15.1%), nasopharyngitis (15.1%), and decreased appetite (13.2%). Conclusions: Although controlled trials are needed, the results from the present analysis support the long-term safety and effectiveness of coadministration of GXR and stimulants for the treatment of ADHD in both children and adolescents with suboptimal responses to stimulants.

NR5-34

THERAPEUTIC ALLIANCE BUILDING DURING THE CHILD PSYCHIATRIC INTAKE: DOES VTC MAKE A DIFFERENCE?

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SUMMARY:

Background: Video teleconferencing (VTC) has allowed mental health professionals to provide diagnostic and therapeutic services to underserved children. However, because the VTC interview sharply contrasts with an in-person session, one may question VTC's efficacy in establishing therapeutic alliance, an established predictive determinant of treatment success. Objectives: This study examines the development of therapeutic alliance during a child's initial diagnostic interview from the parent's perspective. It was designed to determine whether there is a difference in parental perceptions of "parental" alliance when comparing VTC to conventional, face to face (FTF) interviews both before and after the diagnostic session. It was predicted that parental alliance would be more favorable after a FTF encounter relative to a VTC intervention. Procedure: Two cohort groups participated in the study between August 2000 and October 2005. In the first cohort (2000-2003), children who needed a psychiatric intake were recruited from two semi-rural pediatric Army clinics (VTC) and from a major Army medical center (FTF). The second cohort (2005) consisted of children from the same Army medical center. The protocol procedure was to have parents complete questionnaires immediately before (pre-q) and after (post-q) their interview. Main Outcome Measures: The pre-q requested demographic information, opinions regarding the anticipated quality of the parents' relationship with the therapist, as well as their various perceptions of how the interview went. The post-q included similar questions but tapped opinions after the interview. All questionnaires were collected the same day as the intake. Results: There were no significant differences in pre-q parental alliance scores among FTF parents in both cohort I and cohort II as well as VTC parents in cohort I. In contrast, a significant difference was found between the VTC group and the FTF group on the post-q, with FTF parents indicating more positive parental alliance compared to VTC parents. Conclusions: The results suggest that parents, prior to both VTC and FTF intakes, had similar expectations of parental alliance. However, parents felt more of a parental alliance with the mental health professional when the therapist was physically present in the session. This would suggest that there is some intangible quality to interviewing someone FTF that helps foster therapeutic alliance.

NR5-35

FAMILY-FOCUSED TREATMENT AND HEALTH-PROMOTING INTERVENTION: STABILIZING BIPOLAR MOOD SYMPTOMS THROUGH PROMOTING SELF-CARE AMONG FAMILY MEMBERS

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SUMMARY:

Objective: Family members of patients with bipolar disorder experience high rates of burden which compromise their coping resiliency and place them at risk for adverse health and mental health outcomes. We present preliminary efficacy data from a novel variation of Family Focused Treatment that aims to reduce symptoms of bipolar disorder by working with family members alone. Method: The primary family caregivers of 46 patients with SCID-diagnosed bipolar I (40) or II (6) disorder were recruited through a medical school-affiliated mental health clinic or a local chapter of the Depression and Bipolar Support Alliance and randomized to receive either: a 12-15 intervention designed to enhance skills for managing the bipolar relative's illness, improving self-care and reducing caregiver strain and depression (Family-Focused Treatment-Health Promoting Intervention -FFT-HPI); or 8 sessions of health education delivered via videotapes

(HE). Patients were assessed pre- and post-treatment on the HAM-D and YMRS. Caregivers were assessed on measures of depression (QIDS) objective and subjective burden, health behavior and coping. The association of treatment group to patient and caregiver outcome variables was evaluated using hierarchical linear modeling. Results: Randomization to FFT-HPI was associated with significant decreases in caregiver depressive symptoms (ß = -.306, p<.05), health risk behavior (ß = -.400, p< .01) and patient depressive symptoms (ß = -.337, p< .05). Caregivers in FFT-HPI had 41% and 57% decreases in depression and health risk, respectively; patients had a 63% decrease in HAM-D. Reduction in patient depression was partially mediated by reductions in caregiver depression and burden, and decrease in caregiver depression was in turn mediated in part by reductions in avoidance coping. Conclusions: Patients with bipolar disorder may benefit from family interventions through changes in family mood and stress management, even when the patient is not available for treatment. Because these patients underutilize mental health services and have high rates of nonadherence and relapse, this treatment has the potential to help reduce the burden of illness.

NR5-36

ENHANCING RESIDENCY TRAINING OF INTERNATIONAL MEDICAL GRADUATES IN PSYCHIATRY

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SUMMARY:
IMGs represent 25.9% of the total practicing physicians nationwide, 25.8% of the total physicians involved in patient care and 28.5% of all physicians in residency/fellowship training, according to Physician Characteristics and Distribution in the US, a yearly publication of the AMA (2009 edition). Of this group, 73.6% were in office-based practice. Of all IMG physicians, only 19.6% were in research, 16.7% in medical teaching, and only 13.5% of IMG physicians were in administration. In 2007, a total of 13,146 out of 243,457 IMGs were in the practice of Psychiatry (5.4%). Twelve thousand five hundred twelve out of 13,146 were in direct patient care, either office-based, hospital-based or in training (95.2%), while the rest were involved in research (1.3%), administration (2.3%), or academics and education (0.8%). IMGs make up approximately 40% of the first-year residents in psychiatry. NRMP data (2009) match summary for Psychiatry – categorical shows the total number of programs at 182, positions offered at 1,063, numbers of US applicants at 732, of IMG applicants at 1,268, 62.3% were filled by US graduates and 37.7 % were filled by IMG's. We discuss the suggested value of a number of changes in training. These changes include, among others, individual supervision to allow a more detailed exploration of issues that may arise, language training focusing on pronunciation, accent reduction, and familiarity with slang usage, courses in American history and culture and providing mentoring relationships. What is striking here is the very low numbers of IMG psychiatrists involved in the administrative practice of psychiatry as well as the educational and training aspects of the profession. This becomes a significant piece of information when we address the training needs of IMG psychiatrists. Many IMGs face multiple challenges, such as language and acculturation, that impact clinical practice. The educational experience in psychiatric residency training for IMGs must be examined and improved to ensure that the competence level attained by all psychiatric residents is compatible. Addressing these issues early can lead to better personal adjustment and care of patients and also help dispel myths about IMGs.

NR5-37

THE USE OF MCGILL ILLNESS NARRATIVE INTERVIEW (MINI) IN FIBROMYALGIA PATIENTS

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SUMMARY:
Background: The McGill Illness Narrative Interview (MINI), is a qualitative interview useful to explore individuals' illness narratives in sociocultural context, but has not yet been used in fibromyalgia. Methods: A study was conducted using the MINI, with 15 female patients, who were recruited from a referral Rheumatology Service during 2009, and met criteria for fibromyalgia syndrome (FMS), trying to explore narrative of illness experience, salient prototypes related to current health problem, and explanatory models, including causal attributions and expectations for treatment. The interviews were audiorecorded, and then the narratives were transcripted and analyzed according to their structure and content. Results: The physical cause was the most common causal attribution. Fatigue and memory disturbances were also

frequent. Most of them had been treated for different specialists, for a long time, and reported problems in seeking diagnosis and help from health professionals. Some of the patients were also diagnosed by rheumatologists with celiac disease, lactose intolerance and undifferentiated spondylitis, what were termed "False Fibromyalgia." Like previous research, negative emotional states were frequently correlated with worsening pain, but also we found that in some patients there was an improvement when attention was withdrawn and they were able to control the symptoms themself. Many changes were related to their way of life, although few changes were related to their identity. Conclusion: The use of the MINI can be helpful to examine different meanings and modes of reasoning of fibromyalgia patients. The exploration of the explanatory models may complement quantitative research methods, and also may give access to a popular cultural construct related to somatic conditions, not yet documented in the literature. Adequate training of the interviewers is necessary, in order to avoid large variation in the ways that interviews are conducted.

NR5-38

LATINOS AND WOMEN ARE LESS LIKELY TO RECEIVE EMERGENCY ANTIPSYCHOTIC MEDICATIONS DURING ACUTE PSYCHIATRIC HOSPITALIZATION

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SUMMARY:
Objective: To study the relationship among ethnicity, gender, and the pattern of emergency antipsychotic medications given to patients admitted to a large urban psychiatric emergency room (ER). Methods: Following approval by the USC Institute Review Board, 1500 charts of patients admitted to the ER between January 2002 and December 2007 were randomly selected and reviewed. Charts of subjects with more than one ER admission, (n=661), younger than 18 or older than 65 (n=96) were excluded. Of the remaining 743 subjects (M=452, F=291), 39% were Latino, 26% were Caucasian, 23% were African American (AA), and 12% were of other ethnicities. Fifty-five percent (n=408) were diagnosed with psychotic disorders, 35% (n=262) with mood disorders, and 29% (n=216) had comorbid substance use diagnosis. About a third (31%, n=233) received emergency antipsychotics (18% typical, 17% atypical, and 4% both) during ER stay. Chi-square statistics were used to examine the relationship among gender, ethnicity, and administration of emergency antipsychotic medications. A linear regression model examined the administration of antipsychotic medications by ethnicity and gender after adjusting for age, diagnosis including comorbid substance use. Results: 1.) Latinos diagnosed with psychotic disorders were less likely to receive antipsychotic medications than African Americans ($P<0.001$) and Caucasians ($P<0.01$). No significant difference between African Americans and Caucasians. 2.) Latinos (regardless of diagnosis) received significantly fewer antipsychotic medications compared to African Americans ($p < 0.01$), but not at a significantly different rate from Caucasians. 3.) Women (regardless of ethnicity and diagnosis) were less likely to receive typical antipsychotics than men ($P<0.01$). 4.) Among women diagnosed with psychotic disorders, Latinas received significantly less antipsychotic medication than African Americans ($p < 0.03$). Discussion: Latinos and women were less likely to receive antipsychotic medications during psychiatric ER stays after adjusting for diagnosis, age and comorbid substance use. Among other potential explanations, this finding could be due to 1) selection bias: Latinos, for example, may lack access to care and are more likely to use the ER as a usual source of care rather than for emergency illness; 2) Differing presentation of illness: women may be less likely to present with aggressive or threatening behaviors.

NR5-39

WHAT DO PSYCHIATRIC PATIENTS MEAN BY BEING COERCED INTO HOSPITALIZATION?

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SUMMARY:
Introduction: Psychiatric inpatients sometimes feel that they are hospitalized involuntarily. But we are unclear as to what they mean by perceived coercion to hospitalizations. This study aimed to investigate the relationship among perceived coercion to hospitalization, perceived coercion to adhere to treatment, procedure justice in hospitalizations and general pressure to adhere to treatments. Methods: The study population was psychiatric patients who were admitted in acute wards, chronic wards and day hospitals in 11 psychiatric institutions throughout Taiwan between

June 2008 and September 2008 (N=1131). We used the Chinese version of modified Assisted Outpatient Treatment Evaluation Client Interview Instrument to perform interviews. We conducted a factor analysis with an orthogonal varimax rotation using principle factor estimation on perceived coercion to hospitalization and questionnaires inquiring the following items: perceived coercion to adhere treatments, procedure justice in hospitalizations and general pressure to adhere to treatments. Results: Twenty-eight percent of the patients reported that they were admitted involuntarily. Among the items investigated, the factor analysis identified 6 factors, within which the items of general pressure to adhere to treatments split into three factors, the items of procedure justice to hospitalizations split into two factors and items of perceived coercion to adhere to treatments maintained as one factor. Perceived coercion to hospitalizations was loaded in the same factor as the items of perceived coercion to adhere to treatment with a factor loading of 0.34 (Cronbach's alpha = 0.8990). Discussion: Perceived coercion to hospitalizations was more related to not feeling free to do what they wanted about treatments, their inability to choose treatments, and no control or influence over whether to get treatments rather than not being respected or treated fairly by family or therapists upon admissions, or being threatened if not being compliant to treatments. Among psychiatric patients, the sense of autonomy is more crucial than distress or pressure from family or therapists. To improve their compliance for treatments, caretakers have to empathize with patients' suffering and enhance their sense of autonomy in decisionmaking.

NR5-40

PREVENTING VIOLENCE: A FEMALE ADOLESCENT COMMITTING VIOLENT MURDER DUE TO PARANOID DELUSIONS

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SUMMARY:

Background: Paranoid delusions are exaggerated fears of others in an adolescent's mind which may cause impairment in functioning at school, work, personal relationships and various other social dimensions. In a clinical setting, adolescents with paranoid thinking can present with diverse presentations, ranging from social concerns like fear of rejection to severe threat including fear of people trying to cause significant physical harm. A feeling of low self esteem and anger may emerge and grip the mind of a patient having paranoid ideations. The possibility exists that when anger starts escalating in an adolescent's mind, it may erupt at one point into violent behavior. Purpose: The purpose of this case report is to describe a forensic homicide case that could have been prevented by providing earlier psychiatric care for a severely mentally ill teenager. We recommend an approach in the form of a flowchart (Figure 1) which highlights the importance of the early interventions and more aggressive treatment. This approach may prevent violent crimes. Many times, the first medical professional who comes to know about thoughts of suspiciousness is the Primary Care Provider (PCP) and hence, this treatment approach will prove helpful to a larger audience including pediatricians and family practitioners besides psychiatrists. Method: This case report describes aggressive impulsive behavior of B.V., a 16 year-old female with paranoid ideations which built up to the point of killing her younger sister. Also, relevant articles were cited in the case report after completing the literature search using PubMed and the Pratt medical library resources. Conclusion: The family should be educated about the child's paranoid ideation and associated aggressive behavior. Focus in such teaching sessions should be on improving the overall insight of the family and the patient about the psychosis to improve treatment adherence. In clinics, gaining more clinical history about the paranoia is important. After gathering sufficient evidence, the clinician can help patients improve their reality testing.

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NR5-41

IDENTIFYING CORRELATES OF COMPETENCY TO STAND TRIAL (CST) AMONG YOUTH ADMITTED TO A JUVENILE MENTAL HEALTH COURT

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SUMMARY:
Assessment of the competency of juvenile delinquents is a relatively new and understudied phenomenon in the judicial system. As more mentally ill youth have contact with the law and the numbers of juvenile delinquents increase in both the adult and juvenile court systems, evaluation of competency to stand trial (CST) has become more imperative and complex. Among youth admitted to the Los Angeles County Juvenile Mental Health Court (JMHC), the current study aimed to assess correlations between competency status and (1) demographic, social, psychological, and criminal factors, and (2) types of court-ordered treatment and rehabilitative services offered, and (3) treatment outcome. All data were obtained from archival admission interviews and court files for 390 youth referred for processing though the Los Angeles County JMHC between 2001 and 2009. Data analysis was performed using the software packages, SAS/STAT ® software, version 9.1. Missing data were examined by performing range and value checking for all key variables. Descriptive statistics were used to determine the prevalence of demographic, social, psychological, and criminal variables, competency designation, psychiatric and rehabilitative services among juveniles. For continuous and categorical response variables, ANOVA and logistic regressions were used to describe the relation between CST status and each predictor variable. The majority of the sample was aged between 12 and 16 and racially identified as African American or Hispanic. Forty eight percent of the sample was found incompetent to stand trail. In analyses of a subsample of 61 participants, incompetent juveniles were significantly younger (M =14.3, SE = .41) than their competent counterparts (M = 15.4, SE = .29), x2 (1, 61) = 4.14, p < .05. While not clinically significant, only 28% of incompetent juveniles had a history of receiving psychological treatment compared to 40% of those CST. Juveniles found incompetent were significantly more likely to have committed a violent offence than their competent counterparts, x2 (1, 61) = 3.76, p < .05. Determining factors associated with incompetence is imperative to identifying those who may benefit from competency training, necessary to proceed with their legal case. Further, assessing these factors is necessary to identify those who may benefit from mental health, educational and rehabilitative services, providing hope for those who have historically been lost in legal no man's land.

NR5-42

CLINICAL AND DEMOGRAPHIC DIFFERENCES BETWEEN INVOLUNTARY AND VOLUNTARY ADMISSIONS IN A NATIONAL REFERENCE HOSPITAL IN BRAZIL

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SUMMARY:
Background: Involuntary hospitalization (IH) is a medical procedure commonly surrounded by controversy. The literature about the clinical and socio-demographic characteristics of IH is scant. There is evidence that IH is directly related to psychosis but data regarding demographic aspects such as gender, marital status, employment etc. are conflicting. Since 2001, Brazilian law requires that IHs be informed to the judiciary and the medical governing body recommends that they be reviewed by an expert panel. The Institute of Psychiatry of the Medical School of University of São Paulo, Brazil (IPq-HCFMUSP) is a public national reference center that provides outpatient and inpatient care. Objective: To evaluate the trends in IHs from 2001 to 2008 and to determine the associated clinical and socio-demographic characteristics. Methods: This is a retrospective cohort study. Demographics and relevant clinical information from the case register system on all adult admissions from 2001 to 2008 were collected. Hospitalizations were classified as either voluntary (VH) or involuntary (IH) based on the admission records. Data from IH and VH were compared using chi-square test for categorical variables and Mann-Whitney test for continuous non-parametric variable. The relative risk of certain events was estimated by the "odds ratio" statistic. Results: From the total of 2,465 admissions in the eight-year period, 305 (12%) were involuntary. There was an increasing percentage of IH from 2001 to 2008 (X2=132.69, df=7, p<0.001). Age at admission was 39±15 and 41±18 years old for VH and IH, respectively. That difference was not significant (p=0.988). Among the IH there were slightly more women (56% vs. 50%) (X2=4.43, df=1, p=0.035), fewer actively working patients (56% vs 70%) (X2=18.69, df=1, p<0.001) and fewer married patients (22% vs 31%) (X2=8.85, df=1, p=0.003). Regarding diagnosis, psychosis was more common in IH than in VH (54% vs 37%) (X2=33.06, df=1, p<0.001, ODDs=2.06, CIodds95%=1.60 to 2.64). Conclusion: During the 8-year period analyzed, there was an increase in rates of IH in the Brazilian sample studied. IH was likely to be associated with female gender, psychotic states, not

being married and not being actively working.

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NR5-43

DIRECT TESTS OF THE ATTACHMENT HYPOTHESIS OF THE DEVELOPMENT OF CRIMINAL BEHAVIORS

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SUMMARY:
Objective: This study attempted to systematically test Bowlby's (1944) hypotheses and correlational research (Levitt 2005) that has hypothesized that mother-child attachments underlie much of criminal behavior. Method: The incarcerated participants were 61 male offenders between the ages of 18 and 20 who were serving time at a maximum-security juvenile correctional facility. The control group (n = 131) was selected to match in terms of parental education, income, etc. All filled out the 29 scale ACIQ as well as questions asking for information on types and frequencies of past criminal activity. The ACIQ is a 29 scale instrument measuring secure, avoidant, anxious/resistant, codependent/preoccupied, and disorganized attachments to mother, father, and partner, as well as measuring clinical issues such as anger, abusiveness, shame, anxiety, peer relations, two family scales, mistrust, two sex scales, etc. (Lindberg, 2008; Lindberg & Thomas 2007). Results: Significant correlations between crimes committed and measures of insecure attachments to both mothers and fathers were found. Furthermore, correlations to several clinical issues were found as well when looking within the group of criminals. The between data using the control group converged upon the same conclusions. For example, a significant Group X Parent interaction $F(1, 178) = 8.65$, $p < .01$ was found with attachment scores lower for the Father relative to the Mother for the Incarcerated group. Summary: As predicted, the Insecure Mother scales of all correlated significantly with the frequencies of the criminal behavior within this population. Furthermore, in the between subject analyses using the control group, the father scores entered differently than the mother scores, pointing to the importance of looking at these qualitatively different but important attachment contributions.

NR5-44

THE CURRENT STATUS OF FORENSIC PSYCHIATRY IN JAPAN

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SUMMARY:
In 2005, the Medical Treatment and Supervision Act was enacted in Japan to hospitalize the criminally insane and to promote self-supporting life after deinstitutionalization. As of November 3, 2009, 430 patients are hospitalized in 20 high-secured forensic hospitals. Most patients are diagnosed as schizophrenic in chronic stage with drug resistance symptoms. Battery is the most criminal acts they committed. The increase of combination with drug dependence is the common problem to other countries. It is a serious problem that diversity with the prison medical care or court liaison has not been prepared. The feature that is characteristic of Japan is that the patients should go back to the place where they lived and are restricted to live in the limited area close to the designated outpatient hospitals and the residential district where public health centers are located after deinstitutionalization. To achieve rehabilitation more effectively, we established a strategy that makes it possible for the patients to live in the community without treatment interruption through comprehensive and supportive activities by a multidisciplinary team that consists of staff members of the hospital, the public health center and other local municipalities. Once the place where the patients would live is determined before deinstitutionalization, staff members of the multidisciplinary team have a conference in the hospital to assess whether that place is suitable for rehabilitation and to prepare for self–supporting life. After discharge, the conference is held at the designated hospital at least once a month to share the information on the patients provided by home visiting nursing. We can easily know the whereabouts, psychiatric condition and aspect of daily life for each patient. As a result, the patients who were hospitalized at our hospital succeeded in deinstitutionalization and self-supporting life without treatment interruption or repeating similar criminal acts. We named these activities maintaining involvement. We strongly believe that maintaining involvement is an effective method for the patients to promote rehabilitation

in Japan.

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NR5-45

CHILD MURDER BY PARENTS AND MENTAL ILLNESS IN A NATIONAL LEVEL SAMPLE IN NEW ZEALAND

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SUMMARY:

Objectives: Filicide, or child murder by parents, is both a complex phenomenon and an important public health concern around the world. To date, research to help in its prevention has been limited. World literature review indicates that mothers who kill their children are often poor, full-time caregivers who are socially isolated victims of domestic violence. Many suffer from psychosis, depression, suicidality, substance abuse and a multitude of social stressors. Fathers who kill often also attempt suicide, and mental illness is not uncommon. Analysis of existent literature recommended that for this rare but serious event, national-level studies be completed. Methods: New Zealand is a first world country which has a population of 4 million and is ideal to study the problem of filicide on a national level. We utilized records from the police, the coroner, the justice system, and the mental health system. As of 2009, a database of all homicides in New Zealand over a 13-year period had been constructed. We plan to expand the number of years covered by the database, and anticipate that the sample size will be further increased by the time of the conference. This poster will examine more closely the specific group of cases in which children were murdered by their parents, in order to better understand the rare event of filicide, and to ultimately assist in avenues for prevention. Results: Over the 13 years studied, there were 63 child victims killed by 55 parents—a relatively large sample size for this rare offense. This included 8 filicide-suicides. We will compare and contrast the 25 maternal filicides and 30 paternal filicides. The majority (85%) of perpetrators resided with their child. The majority were married or in a de facto relationship (55%), while 15% were separated or divorced and 4% were single. The bulk (44%) were in their 20s, while 29% were in their 30s. Regarding victim age, over one-quarter (28%) were infants. More than half were under age 10. Mental illness and substance use history and treatment will be described. Conclusions: Filicides are multi-factorial. Through further investigation of national-level samples and understanding of commonly occurring factors, prevention may be advanced.

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NR5-46

QUANTITATIVE ASSESSMENT OF PSYCHOSOCIAL DISTRESS OF ELDERLY INDIVIDUALS WITH COPD AND WITH CHRONIC PAIN, ACCORDING TO THE AMA GUIDES SIXTH EDITION

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SUMMARY:

The study objective was to examine the psychosocial distress of COPD patients with chronic pain using responses from the Pain Disability Questionnaire (PDQ), a quantitative assessment for rating pain-related impairments (PRI) by the AMA Guides to the Evaluation of Permanent Impairment, Sixth Edition. Results from the Self-Administered Comorbidity Questionnaire (SCQ) were used to identify 30 out of 100 elderly outpatient COPD subjects who were afflicted with chronic pain. The PDQ and Physical Performance Tests (6-Minute Walk Test, Berg Balance Scale, & Dynamic Gait Index) scores were also recorded. Using the SCQ, one-third of the subjects identified significant chronic pain as being: 10% osteoarthritis, 20% low back pain, 47% both, and 23% unidentified. The PDQ consisted of 15 items scored on a 10-point scale (maximum score of 150, i.e. high pain and disability) and

was broken down into sub-categorization of PRI severity, resulting in: 64% mild, 27% moderate, 3% severe and 3% extreme PRI. The PDQ total was also further divided into Functional Status (FS) versus Psychosocial Distress (PD) Status component. The PD scores ranged from 7 to 59 out of 60 points with an average score of 19/60 points. Comparing the effect of the PD over the FS component revealed that 33% of the total PDQ score (range 12-50%) was due to PD of the COPD patients with chronic pain. The PDQ rating demonstrated a close trend relationship between the total PDQ scores and low scores achieved in the physical performance tests (PPT). The majority of COPD patients, who identified pain as a significant problem, scored in the mild pain-related impairment category. Although the observed trend was a significantly greater effect on the FS versus PD performance, the PD status of the patients still tended to have an effect on the overall disability of the COPD patients with chronic pain. The ratio of functional/psychosocial performance in relationship to total PDQ score remained consistent when subjects were separated based on PRI, and there was little variation in physical performance status. These findings suggest that the pain disability status of COPD patients, regardless of severity, results in significant loss in health-related quality of life that can be attributed to the PD status of the elderly individuals. Further research on the FS & PD sub-scores of the PDQ and their correlations to decreased PPT scores would be beneficial.

NR5-47

EFFECT OF EXTENDED RELEASE QUETIAPINE FUMARATE (QUETIAPINE XR) ON QUALITY OF LIFE AND SLEEP IN ELDERLY PATIENTS WITH GENERALIZED ANXIETY DISORDER

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SUMMARY:
Objective: Generalized anxiety disorder (GAD) is a chronic, disabling disorder, with patients experiencing impaired functioning and quality of life (QoL). This analysis evaluated the effects of quetiapine XR versus placebo on quality of life and quality of sleep in elderly patients with GAD. Methods: This was an 11-week (9-week randomized, 2-week post-treatment phase), double-blind, placebo-controlled Phase III study (D1448C00015). Eligible patients were >=66 years of age and had a DSM-IV diagnosis of GAD. At enrollment and randomization patients were required to have a HAM-A total score >=20, HAM-A Item 1 and 2 scores >=2, CGI-S score >=4, and MADRS total score <=16. Patients were randomized to quetiapine XR (flexible dosing 50-300mg/day) or placebo. Primary endpoint was least squares (LS) mean change from baseline to Week 9 in HAM-A total score. Secondary endpoints included change from randomization to Week 9 in Q-LES-Q-SF % maximum total score, Q-LES-Q Item 15 (satisfaction with medication) score, Q-LES-Q Item 16 (overall quality of life) score and PSQI global score. Results: In total, 450 patients were randomized (mean age 70.4 years; 12.9% patients were >75 years): 223 received quetiapine XR (mean dose 167.6mg/day), and 227 received placebo. At Week 9, quetiapine XR significantly improved HAM-A total score versus placebo (LS mean change -14.97 vs -7.21; p<0.001). Improvement in Q-LES-Q-SF % maximum total score was significantly greater with quetiapine XR versus placebo (LS mean change 14.82 vs 4.94; p<0.001), with improvements also seen with quetiapine XR compared with placebo in Q-LES-Q Item 15 and Item16 scores. Quetiapine XR significantly improved PSQI global score versus placebo (LSM change -6.25 vs -2.09; p<0.001). Conclusion: In elderly patients with GAD, quetiapine XR monotherapy (50-300 mg/day flexibly dosed) significantly improved patients' quality of life and quality of sleep.
Funded by AstraZeneca.

NR5-48

RELATIONSHIP BETWEEN SLEEP QUALITY AND ANXIETY SYMPTOMS IN THE ELDERLY

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SUMMARY:
Background: We aimed to investigate the relationship between sleep quality and anxiety symptoms in the elderly. Methods: Data from 2137 subjects (492 men and 1645 women) aged 60 years old and above was collected from the Suwon geriatric mental health community center. All subjects completed the study questionnaire including demographic characteristics, history of current and past illnesses, drug history, SGDSK (Korean version of Geriatric Depression Scale-Short Form), BAI (Beck Anxiety Inventory) and PSQ-I (Pittsburg Sleep Quality Index). Results: Mean age was 76.6±6.5 and mean educational level was 5.2±4.4. Of the total 2137 subject, 52.9% were poor sleepers. Multiple regression analysis

revealed that the sleep quality (PSQ-I score) was associated with anxiety (BAI score) in the elderly after adjusting for age, sex, educational level and SGDSK (ß=0.336, p<0.0001, adjusted R2=0.341). On analysis of covariance, the interaction of sex with sleep quality on anxiety was observed after adjusting for the age, sex, educational level and SGDSK (F=5.094, p=0.024). Conclusion: These results suggest that the sleep quality may be associated with anxiety in the elderly.

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NR5-49

WHITE MATTER CHANGE AND COGNITIVE DYSFUNCTION

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SUMMARY:

Objective: White matter hyperintensities(WMH) on cerebral MRI are generally viewed as evidence of small vessel disease (SVD). The clinical significance of SVD in terms of risk factors and cognitive domains has not been completely clarified. The aim of this study is to evaluate the relationship between the severity of WMH, risk factors and cognitive domains. Methods: Forty-nine subjects over 55 years old with subjective memory complaints were evaluated. SVD were assessed by MRI T2-FLAIR images and divided into 1) 3 groups of mild (24) versus moderate (18) versus severe (7) and 2) 2 groups mild-moderate (42) versus severe (7). The risk factors were examined in hypertension and heart disease history, blood pressure, total cholesterol (T-chol), high density lipoprotein (HDL), low density lipoprotein (LDL), homocysteine, folic acid and vitamin B12. They were assessed with Mini-Mental State Examination, Seoul Verbal Learning Test, Rey Complex Figure Test (delayed recall and copy), Boston Naming Test, Stroop test interference score (STIS), Controlled Word Association Test, Digit span Backward. The elderly with dementia, depression or medical and neurological conditions which affect cognitive dysfunction were excluded. Results: Comparing with 3 groups (mild versus moderate versus severe), hypertension was identified for risk factor of SVD. The degree of SVD was significantly associated with Digit span Backward (working memory) and STIS (inhibition). And comparing with 2 groups (mild-moderate versus severe), T-chol and LDL were identified for the risk factor of SVD. Digit span Backward and STIS were significantly different between 2 groups. Conclusion: We suggest that the risk factors of SVD were hypertension and hyperlipidemia and extent of SVD was associated with executive dysfunction in the elderly with subjective memory impairments. Compared with mild or moderate SVD, severe SVD was associated with executive dysfunction among the elderly.

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NR5-50

WITHDRAWN

NR5-51

FACTORS INFLUENCING THE SUICIDE-RELATED BEHAVIOR IN COMMUNITY-DWELLING KOREAN ELDERS

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SUMMARY:

Objectives: The aims of this study were to disclose frequency of suicide-related behavior in Korean elders, and to identify influencing factors. Methods : The demographic and suicide-related data for one hundred (37 males and 63 females) Korean elders with age over 60 living in Seoul were obtained by the structured interviews

with questionnaire. Results: Over one year, suicidal thoughts were experienced in 62% of Korean elders, and the most important motivations were family discord (24%), loneliness (19%), economic poverty (18%) and illnesses (8%). Only 4% of Korean elders attempted suicide. Sixty-three percent of Korean elders planned but did not attempt suicide. With regards to therapeutic intervention, the Korean elders having suicidal thoughts tried to overcome them by themselves (44%), none (23%), religion (20%), doctor (6%), talking to family or friends (6%), and using hot-line (1%). The most common Korean elders' attitudes/ values toward suicide were as follows: suicide shoud not be performed because it is an unforgivable sin (72%), suicide is not arguable because it is one's own right (14%), suicide seems to be better in the case of terminal cancer (8%), and suicide with companion seems to be better (6%). The suicidal thoughts had statistically significant correlation with sex (Rho=-0.339, p<0.01), age (Rho=0.317, p<0.01), monthly income (Rho=-0.198, p<0.05), illnesses (Rho=0.357, p<0.01), depression (Rho=-0.216, p<0.05), cancer (Rho=-0.215, p<0.05), arthritis (Rho=-0.204, p<0.05), suicide planning without attempt (Rho=0.680, p<0.01), motivation (Rho=-0.522, p<0.01) and therapeutic intervention (Rho=-0.412, p<0.01). The suicide planning without attempt had statistically significant correlation with sex (Rho=-0.271, p<0.01), monthly income (Rho=-0.272, p<0.01), illnesses (Rho=0.297, p<0.01), disc (Rho=-0.258, p<0.01), suicidal thoughts (Rho=0.680, p<0.01), motivation (Rho=-0.747, p<0.01) and therapeutic intervention (Rho=-0.493, p<0.01). The suicidal attempts had statistically significant correlation with educational levels (Rho=0.218, p<0.05), motivation (Rho=-0.204, p<0.05), osteoporosis (Rho=-0.336, p<0.01) and dementia (Rho=-0.562, p<0.01). Conclusions : Though the frequency of having suicidal thoughts in Korean elders was very high, actual attempt of suicide was rare. The most important factors influencing the suicide-related behavior seemed to be family discord, loneliness, poverty, and illness.

NR5-52

EFFECTS OF EXTENDED RELEASE QUETIAPINE FUMARATE (QUETIAPINE XR) ON QUALITY OF LIFE AND SLEEP IN ELDERLY PATIENTS WITH MAJOR DEPRESSIVE DISORDER (MDD)

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SUMMARY:
Objectives: MDD in later life is associated with decreased quality of life and frequently complicated by somatic symptoms including sleep disturbance. A key issue for MDD in later life is the misinterpretation of depressive symptoms as 'normal aging' entailing a missed opportunity for treating elderly patients with depression and improving quality of life in these patients. This analysis evaluated the quality of life and sleep quality with once-daily extended release quetiapine fumarate (quetiapine XR) monotherapy in elderly patients with MDD. Methods: This was an 11-week (9-week randomized; 2-week post-treatment phase) double-blind, placebo (PBO)-controlled study (D1448C00014). Elderly patients (aged >=66 years; DSM-IV diagnosis of MDD, HAM-D total score >=22, HAM-D Item 1 score >=2) were randomized to quetiapine XR (flexible dosing 50-300mg/day) or PBO. Primary efficacy endpoint was LS mean change from baseline to Week 9 in MADRS total score. Secondary efficacy endpoints included changes from baseline in Q-LES-Q-SF% maximum total score, Q-LES-Q Items 15 (satisfaction with medication) and 16 (overall quality of life) scores, and PSQI global score. Results: 338 patients were included in the study (mean age 71.3 years; 19.4% patients were >75 years): 166 received quetiapine XR and 172 received placebo. Median daily quetiapine XR dose (range) was 158.7 (50-253) mg/day. At Week 9, quetiapine XR significantly reduced MADRS total score from randomization versus placebo (-16.33 vs -8.79; p<0.001). At Week 9, Q-LES-Q-SF% total score was significantly improved with quetiapine XR (16.86; p<0.001) versus PBO (9.17), with improvement seen in both Q-LES-Q Items 15 and 16. Significant improvement in PSQI global score was shown with quetiapine XR (-6.42; p<0.001) versus PBO (-2.89) at Week 9. Conclusions: These data show that quetiapine XR monotherapy significantly improved quality of life and sleep quality in elderly patients with MDD.
Funded by AstraZeneca

NR5-53

MULTI-SITE, OPEN-LABEL, PROSPECTIVE TRIAL OF LAMOTRIGINE FOR GERIATRIC BIPOLAR DEPRESSION

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SUMMARY:
Background: Prospective trials to examine efficacy, dosing, and tolerability of pharmacotherapies in depressed bipolar elders are lacking. We conducted a multi-site, 12-week, open-label trial of add-on lamotrigine in aged adults with type I or type II bipolar depression. This is a preliminary analysis of outcomes. Methods: Fifty-one non-demented adults aged >60 years with bipolar I or II depression meeting inclusion criteria for depressive symptom severity (score of 18 or greater on the Hamilton Depression Rating/ HAMD-24) received lamotrigine. The primary study outcome was change from baseline on the Montgomery Asberg Depression Rating Scale (MADRS). Secondary outcomes included global psychopathology (Clinical Global Impression/CGI) and side effects using the Udvalg for Kliniske Undersogelser (UKU). Medical illness burden was assessed with the Cumulative Illness Rating Scale (CIRS-G). Results: Mean age of the sample was 66.9, range 60-90 years; 56.9% were male, 84.3% Caucasian, 13.7% African-American, 2% Asian, 3.9% Hispanic, 74.5% Bipolar I and 25.5% Bipolar II. Mean baseline MADRS was 25.8 (SD ± 8.4). Mean CIRS-G was 9.8 (SD ± 4.7), which is consistent with other reports of geriatric bipolar samples. Mean lamotrigine dose was 160 mg/day (range 25-400 mg/day). There was significant improvement from baseline in MADRS and HAM-D ($p < .0001$) and overall CGI ($p<.001$). There were 14/51 (27.5%) of individuals who dropped out of study prematurely, with primary reasons for study drop-out being clinician decision (71.4 % N=10) and patient non-adherence with either study medication or study procedures (21.4% N=3). There were a total of four rashes, two non-study related, and two possibly study related. Skin rash resolved with study drug discontinuation in the two individuals with possible lamotrigine-related rash. Mean change in weight over the 12-week trial was -0.83lb. One individual gained over 7% in baseline body weight. Discussion: Lamotrigine was associated with substantial improvement in depression and global psychopathology, and was relatively well tolerated. Prospective randomized, controlled trials are needed to further evaluate the utility of lamotrigine therapy in geriatric bipolar depression.
This study was supported by GlaxoSmithKline.

NR5-54

CORRELATION OF WHITE MATTER CHANGES WITH BEHAVIORAL AND PSYCHOLOGICAL SYMPTOMS AND COGNITION IN ALZHEIMER'S DISEASE PATIENTS

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SUMMARY:
Purpose: Some studies have reported that cerebral white matter changes on MRI are associated with several behavioral and psychological symptoms of dementia (BPSD) such as depression, apathy, suicidal ideation, aberrant motor behaviors, and psychotic symptoms in Alzheimer's disease patients. However, these findings are inconsistent and were not replicated by other studies, except for findings regarding psychotic symptoms. The aim of this study is to evaluate the relationship between white matter changes with BPSD and cognition in Alzheimer's disease patients. Method: This study was performed to explore the relationship between white matter changes on MRI and BPSD and cognitive function in Alzheimer's disease patients. Forty-one patients with probable Alzheimer's disease were assessed with MRI, Neuropsychiatric Inventory (NPI) and Seoul Neuropsychological Screening Batteries including Mini-Mental State Examination (MMSE), digit span, Boston Naming Test, Rey osterrieth Complex Figure test (RCFT), Seoul verbal learning test, Controlled Oral Word Association Test, Color word Stroop Test. Result: White matter changes in the right basal ganglia significantly corresponded with the score of the disinhibition item of NPI, although global and other regional white matter changes were not significantly correlated with BPSD items of NPI. There is no specific relationship between white matter changes and cognition, although white matter changes of the right parieto-occipital area are significantly correlated with the performance of the verbal and visual memory tests (recognition). Conclusion: This is the first report that demonstrates the relationship between white matter changes without infarcts or lacunae and disinhibition in Alzheimer's disease patients. Disinhibition is socially inappropriate and impulsive behavior. There is evidence that a complex brain network involving frontal and subcortical structures including basal ganglia mediates social behavior. The results of this study suggest that white matter changes in Alzheimer's disease patients probably contribute to the disinhibition of BPSD.

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NR5-55

THE EFFECT OF EXTENDED-RELEASE MEMANTINE ON BEHAVIORAL DOMAINS IN PATIENTS WITH MODERATE TO SEVERE ALZHEIMER'S DISEASE

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SUMMARY:
Objectives: Memantine, approved in the US for the treatment of moderate to severe Alzheimer's disease (AD), is currently available in an immediate-release formulation (10 mg BID; 20 mg/day). We recently reported results of a large Phase III trial of once-daily, extended-release (ER) memantine (28 mg/day), which showed significant cognitive, behavioral, and global benefits over placebo in outpatients with moderate to severe AD taking cholinesterase inhibitors. Here we present a post hoc evaluation of the behavioral data, based on a face-valid grouping of NPI domains, according to the results from a previously published factor analysis (Frisoni et al, 1999). Methods: All patients completed a 2-week, single-blind, placebo-only period, followed by a 24-week period of double-blind, once-daily treatment with memantine ER (28 mg) or placebo. The 12 Neuropsychiatric Inventory (NPI) items were grouped into 4 domains based on a previous factor analysis: Mood (anxiety, depression/dysphoria, apathy), Frontal (disinhibition, euphoria/elation), Psychosis (agitation/aggression, hallucinations, delusions, irritability/lability), and Other (aberrant motor behavior, nighttime behavior, appetite/eating change). For each domain, baseline-to-endpoint changes were calculated using the LOCF and OC approaches, and analyzed by means of an ANCOVA model with treatment group and study center as factors, and with baseline values as covariates. Results: A total of 677 patients (mean MMSE 10.8 [range 3-17]) were randomized to receive memantine ER (n=342) or placebo (n=335). At study endpoint, memantine ER was associated with significant benefits over placebo for the domains of Psychosis (LOCF, P=0.008; OC, P=0.002) and Other (LOCF, P=0.027; OC, P=0.035). Score changes for two other domains were not statistically different between the two groups. Conclusion: The significant behavioral benefits of once-daily memantine ER (28 mg) in patients with moderate to severe AD appear to be associated with the clinical domain of psychosis, as well as with a group of symptoms characterized by neurovegetative changes.

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NR5-56

SYNERGISTIC EFFECTS OF DEPRESSION AND APOLIPOPROTEIN E4 ON THE INCIDENCE OF DEMENTIA

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SUMMARY:
Objectives: A study with Japanese-American men suggested the interactive effects of depression and apolipoprotein E e4 allele (apo E4) on incident dementia. This study aimed to replicate the findings and to explore individual depressive symptoms where this interaction is evident. Methods: Of 625 elders without dementia at baseline, 518 (83%) were followed over a 2.4-year period and were clinically assessed for incident dementia. Depression was identified by Geriatric Mental State Schedule, and nine individual depressive symptoms relevant to DSM-IV major depressive episode criteria were extracted. Apo E polymorphism was ascertained. Covariates included age, gender, education, and disability. Results: There were synergistic interactions of depression and apo E4 on incident dementia independent of covariates. This interaction was particularly significant in four depressive symptoms: depressed mood, worthlessness, concentration difficulty, and suicidal idea. Conclusions: Depressive elders with particular symptomatology are at great risk for incident dementia in the presence of apo E4.

NR5-57

THYROID STIMULATING HORMONE,

COGNITIVE IMPAIRMENT, AND DEPRESSION IN AN OLDER KOREAN POPULATION

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SUMMARY:
Background: The associations of thyroid dysfunction with cognitive impairment and depression in late life have largely been controversial. This study aimed to investigate the associations of serum thyroid stimulating hormone (TSH) levels with cognitive impairment and depression after controlling for potential confounding factors. Methods: The sample consisted of 495 community residents aged 65 or over. Blood assays for TSH were conducted. Cognitive impairment was evaluated by the Community Screening Interview for Dementia, and depression was diagnosed by the Geriatric Mental State schedule. Age, gender, education, smoking history, physical activity, blood pressure, diabetes, and serum total cholesterol and albumin were included as covariates. Results: There was a significant association between lower serum TSH levels (<0.5 mIU/L) and cognitive impairment after controlling for confounding factors [OR (95% CI): 7.12 (1.35-37.46)]. However, no association was found between TSH levels and depression. Conclusions: These findings suggest that elders with cognitive impairment are recommended for evaluating thyroid function.

NR5-58
WITCHCRAFT OR MENTAL ILLNESS?

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SUMMARY:
Madness has been known in all ages, and its symptoms have always been recognized as something different, as an abnormal behavior. In ancient times, madness was considered a punishment of the gods but also as the distinctive characteristic of the chosen ones, the manifestation of the symptoms interpreted as the sign of a divine message. But although mental disorder was later considered by the Greeks as an organic problem (Porter), this naturalistic point of view changed in the Middle Ages after the epidemic of the Black Pest, which devastated half the population of Europe, about 30 million people. Under those circumstances, disease could not be seen any more as the product of natural causes but of supernatural forces, or malignant spirits that physicians were not able to deal with. At the end of the Middle Ages, but more properly, during the Renaissance, the blame fell on witches and diabolical possession. All the tragedies and calamities of Humanity were witches' fault, and so they should be severely punished, because no one could be able of doing such things if it wasn't because they were under the power of the devil. Women were blamed as witches more frequently than men. Witch crazes took place especially in northern Europe (López-Piñero, Porter). Even in the New World this mentality was extended and witches were burned in Salem in the eighteen century (Woolf). Hysteria and epilepsy were the two illnesses that were most frequently confused with witchcraft or demonic possession, especially if they were accompanied by tremors, convulsions or loss of consciousness. Different treatises were written in order to instruct the people, but especially doctors and priests on how they could recognize a witch or a possessed one. The "Malleus Maleficarum", written by Sprenger and Kramer, Dominican friars, was by far the most famous of all and its influence lasted for more than 200 years. Women were more prone to diabolical possession because they were weaker and more imperfect in nature than men: "woman is an imperfect animal, inferior to men" (Chodoff; Risse; Werner, Isaksen and Malterud), and her reproductive system was the proof of this, the uterus being considered the source of evil. Women were thought to be full of venom during menstruation, so that they were contaminated and capable of contaminating others (Porter, Laqueur, Schiebinger). The uterus was also an unstable organ which could move from one place to another in the body.

NR5-59
SOCIAL SUPPORT AND ACCULTURATION: PREDICTORS OF PSYCHOLOGICAL HEALTH OF INTERNATIONAL MEDICAL GRADUATES PURSUING PSYCHIATRIC RESIDENCIES

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SUMMARY:
Objective: The authors aimed to determine whether social support and acculturation could predict the mental health of international medical graduates pursuing ACGME accredited psychiatric residencies in the United States. Methods: A 55-item valid and reliable survey instrument

was assembled online and opened to respondents between December 2008 and February 2009. The survey was composed of demographic questions and items intended to measure the respondent's social support, acculturation and mental health. The survey link was sent via email to training directors of all psychiatry residency and fellowship programs and they were requested to forward it to their international medical graduate (IMG) residents. Screening questions helped weed out residents who did not meet the inclusion criteria. One hundred eight psychiatry residents and fellows (who were also international medical graduates) from across 70 different psychiatry residency programs completed the entire survey. Results: Mental health scores of the respondents were found to be normally distributed. Acculturation (dominant society immersion), social support (appraisal), and the year of post graduate training were significant predictors of mental health in this population. The above mentioned constructs can together explain 24.1% of the variance in mental health of the respondents. Conclusion: Residency training programs should attempt to incorporate measures that would help boost the social support & acculturation of international medical graduates (especially junior-level trainees). Acculturation could be improved with the aid of language training and courses in American history, culture and customs while the social support could be developed with the help of mentoring relationships.

NR5-60

CHANGES IN EMPATHY DURING KOREAN MEDICAL COLLEGE AND MEDICAL SCHOOL EDUCATION: 1-YEAR-FOLLOW UP

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SUMMARY:

Purpose: This study investigated changes in empathy among medical college (MC) students and medical school (MS) students after one year. Methods: One hundred thirteen medical college students and 120 medical school students participated in this study, completing questionnaires on sociodemographic data, Jefferson Scale of Empathy, S-version, Korean edition (JSE-S-K), and Temperament and Character Inventory (TCI). Results: Reward Dependence (RD), Cooperativeness (C), and Self-directedness+ Cooperativeness (SC), which are subscales of the TCI, correlated significantly with JSE-S-K score. The seniors of medical college and medical school had higher scores on the JSE-S-K than students in the lower grades. The scores on JSE-S-K showed upward trend after 1 year. However, there were no significant differences in empathy with regard to age, sex, motivation toward medical science, club activity, and applied specialty. Conclusion: These results suggest that empathy increased one year after Korean medical education, and that the medical education curriculum contributes incrementally to students' empathy.

NR5-61

EMPATHY IN KOREAN PSYCHIATRIC RESIDENTS

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SUMMARY:

Objectives: This study investigated the relationship between empathy and grades, marital status and personality in psychiatric residents. Methods: We sent questionnaire packages to a total of five hundred ninety-two psychiatric residents in eighty-two psychiatric residency training hospitals, which include sociodemographic data, Jefferson Scale of Empathy, HP-version, Korean edition (JSE-HP-K), and Temperament and Character Inventory (TCI). Results: The 4th–year residents had significantly higher scores on the JSE-HP-K than 1st-year residents. The marital status and empathy had significant correlation. The married showed significantly higher scores on the JSE-HP-K. There were no significant differences in empathy with regard to age, sex, motivation toward medical science and club activity. The authors found no significant correlation between the subscales of the TCI and JSE-HP-K score. Conclusion: These results suggest that empathy is associated with marital status and psychiatry residency program contributes incrementally to empathy for residents.

NR5-62

VOLUME OF ORBITOFRONTAL CORTEX AND CLINICAL SYMPTOMS IN PATIENTS WITH POSTTRAUMATIC STRESS DISORDER AFTER A TRAFFIC ACCIDENT

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SUMMARY:
Introduction: Using voxel-based morphometry (VBM), previous structural neuroimaging studies on post traumatic stress disorder (PTSD) have reported smaller brain volume in anterior cingulate cortex (ACC), orbitofrontal cortex (OFC), and hippocampus. Recent functional imaging studies suggested that patients with PTSD showed dysfunctional activation of orbitofrontal cortex (OFC) in response to symptom provocation. OFC is thought to be involved in the extinction of learned responses in reinforcement learning, such as fear conditioning. In addition, OFC lesions impaired rapid reward-based updating of representations of rule value. We hypothesized that the volume of the OFC in patients with PTSD would be smaller than healthy subjects. Furthermore, the volume of the OFC in patients with PTSD would be negatively correlated with clinical symptoms and cognitive function. Methods: To increase the homogeneity of our study subjects, we restricted study enrollment to patients with 'trauma' which was associated with traffic accidents. Magnetic resonance images of 35 patients with PTSD and 20 healthy control subjects were used to measure regional orbitofrontal gray matter volumes. Lateral and medial regions within each hemisphere were manually traced. Clinical symptoms and cognitive functions were assessed with Post-traumatic Stress Diagnostic Scale (PDS), Stroop color test, and Wisconsin Card Sorting Test (WCST). Results: The volumes of right lateral (8.13±0.97) and medial OFC (3.67±0.42) in patients with PTSD were smaller that those (lateral: 9.01±1.01. medial: 4.00±0.39) of healthy control subjects (lateral: t=2.53p=0.003; medial , t= 2.04, p=0.02). In the PTSD group, PDS scores were negatively correlated with volumes of right lateral (r=-0.47, p=0.04) and medial OFC (r=-0.51, p=0.02). The score of inhibitory ability in WCST was positively associated with left medial OFC (r=0.46, p=0.04). Discussion: Current results suggested that the volume of orbitofrontal cortex would be associated with post traumatic stress disorder. In addition, the imbalance between left and right OFC would be correlated with clinical symptoms in patients with PTSD.

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NR5-63

ANTIDEPRESSANT MEDICATIONS IN PREGNANCY AND POSTPARTUM: ADHERENCE VERSUS DECLINE

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SUMMARY:
Objective: To examine patient-centered choice of pharmacotherapy throughout pregnancy/postpartum. Background: Although antidepressants remain the treatment of choice for moderate/severe antenatal depression despite FDA warnings, it remains unclear why some women engage in pharmacotherapy while others refuse. This study examines factors that govern this decision, monitors illness trajectory, and tracks dose titration. Methods: Sixty pregnant participants recruited through Reproductive Psychiatry Program, Vancouver, Canada, comprised of three groups: adhering to medications, declining medications, declining antenatally but starting postpartum. Mood was evaluated with MINI, Hamilton Depression Scale and Hamilton Anxiety Scale, through second/third trimester and one month postpartum. Results: Qualitative analysis revealed that of 33% of the participants who declined medication due to denial of diagnosis/fear of exposure antenatally, 35% went on medications in postpartum. Seventy-seven percent adhered throughout. Statistical analysis revealed a significant difference in Hamilton Anxiety scores between adherence and decline groups, $t(34) = 2.51$, $p<.05$. Further examination revealed higher mean Hamilton Anxiety scores at 26 weeks, 34 weeks and postpartum in declined group. Examination of the mean Hamilton Depression score demonstrated that declined group had higher scores at 26, 34 weeks gestation and postpartum, although no statistically significant difference was noted>.05. Despite adherence, women relapsed at 30 weeks gestation and with dose increase responded at 34 weeks. Conclusions: Preconceived notions about the illness regardless of severity govern the choice of pharmacotherapy in pregnancy. Alarmingly, women chose to remain symptomatic rather than take medication, thus exposing the unborn baby to the illness. Treatment to remission remains a challenge. Funding: This study was funded by the Vancouver Foundation, Study No. BCM06-0001, UBC reference 20R42483.

NR5-64

AN OPEN-LABEL TRIAL OF ESCITALOPRAM IN POSTPARTUM WOMEN WITH MOOD AND ANXIETY DISORDERS

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SUMMARY:

Objective: To examine the efficacy of Escitalopram in non-breast feeding postpartum women with anxiety/mood disorders. Background: Moderate/severe postpartum mood and anxiety disorders have short- and long-term consequences with negative implications for the mother and her newborn. Choice of an appropriate antidepressant is critical in minimizing suffering, promoting wellness and enhancing bonding. Methods: Twenty postpartum subjects were enrolled in the study, of which fifteen completed the required six study visits. A structured clinical interview and the Mini-International Neuropsychiatric Interview (M.I.N.I.) were used to diagnose Major Depressive Disorder (MDD) with comorbid anxiety disorders. Symptoms were monitored two weeks apart with the Montgomery and Åsberg Depression Rating Scale (MADRS), Hamilton Rating Scale- Anxiety (HAM-A), Yale-Brown Obsessive-Compulsive Scale (YBOCS), Penn State Worry Questionnaire (PSWQ), and Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q). Subjects started on a dose of 10mg of Escitalopram which was titrated up to 20mg when needed. Side effects were documented and weight was recorded at each visit. Results: At visit 6, remission rates were: 93.4% for depression (MADRS), 73.4% for anxiety (HAM-A), 66.7% for Obsessive Compulsive Disorder (YBOCS); for Generalized Anxiety Disorder (PSWQ) scores decreased by 26.15% from Visit 1 to Visit 6, but they did not go into complete remission. The Q-LES-Q showed significant reduction on their scores in all eight domains. Ninety-three point thiry-three percent of participants reached remission at 20mg dose. Common transient side effects included change in appetite/sleep, headache, nausea, diarrhea, shakiness, jitteriness, and decrease in sexual desire. Only one participant reported decreased sexual desire as a persistent side effect at Visit 6. The average weight loss was 0.46 lbs. Conclusions: The majority of the patients with MDD reached remission at 20mg of Escitalopram with minimal side effects. However, patients with comorbid GAD and OCD improved but did not show high remission rates. The quality of life for all of these patients changed significantly for the better. It is noteworthy that 93.33% did not have any sexual side effects at the end of the study, and Escitalopram appears to be a fairly weight-neutral compound.

Funding: This study was funded by Lundbeck Canada, Study No. 12185A, UBC reference 20R06226.

NR5-65

WITHDRAWN

NR6-01

DOSE-ASSOCIATED CHANGES IN SAFETY AND EFFICACY PARAMETERS OBSERVED IN A 24-WEEK MAINTENANCE TRIAL OF OLANZAPINE LONG-ACTING INJECTION IN PATIENTS WITH SCHIZOPHRENIA

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SUMMARY:

Objective: To investigate possible associations between dose and safety or efficacy parameters in a maintenance trial of olanzapine long-acting injection in patients with schizophrenia [1,2]. Methods: Outpatients with schizophrenia who had maintained stability on open-label oral olanzapine for 4-8 weeks were randomly assigned to "low" (150mg/2-weeks; N=140), "medium" (405mg/4-weeks; N=318), or "high" (300mg/2-weeks; N=141) doses of olanzapine long-acting injection for 24 weeks. Potential relationships between dose and several safety or efficacy measures were examined via regression analysis, the Jonckheere-Terpstra test (continuous data), or the Cochran-Armitage test (categorical data). Results: Safety parameters significantly related to dose were mean weight change (low: +0.67 [SD=4.38], med: +0.89 [SD=3.87], hi: +1.70 [SD=4.14] kg, p=.024), mean change in prolactin (low: -5.61 [SD=12.49], med: -2.76 [SD=19.02]), hi: +3.58 [SD=33.78] µg/mL, p=.001), fasting triglycerides change from normal to high (low: 6.5%, med: 9.8%, hi: 24.5%, p=.002) and fasting HDL cholesterol change from normal to low (low: 20.7%, med: 21.8%, hi: 35.5%, p=.036). Efficacy measures significantly related to dose were PANSS total score mean change (low: +2.66 [SD=14.95], med: -0.09 [SD=13.47], hi: -2.19 [SD=13.11], p=.005), relapse rate (low: 16%, med: 10%, hi: 5%, p=.003), all-cause discontinuation rate (low: 36%, med: 30%, hi: 24%, p=.037), and rate of discontinuation due to efficacy-

related reasons (low: 20%, med: 14%, hi: 6%, p<.001). Time to all-cause discontinuation and time to relapse were also significantly related to dose. Conclusions: Analyses of several safety and efficacy parameters revealed significant correlations with dose of olanzapine long-acting injection, with the highest dose generally showing greater efficacy as well as greater changes in certain safety measures. With olanzapine long-acting injection, as with all antipsychotics, it is important to carefully weigh the potential benefits and risks when choosing medications for individual patients. Research supported by Lilly.

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NR6-02

EFFICACY OF LURASIDONE IN SCHIZOPHRENIA: SUMMARY OF RESULTS FROM THE CLINICAL DEVELOPMENT PROGRAM

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SUMMARY:

Objective: Lurasidone is a novel compound currently under development for the treatment of schizophrenia. The aim of this analysis is to provide an overview of the 4 available Phase 2/3 placebo-controlled trials demonstrating efficacy in patients with schizophrenia. Methods: In all 4 studies (D1050006; D1050196; D1050229 [Pearl 1]; D1050231 [Pearl 2]), subjects meeting DSM-IV criteria for schizophrenia with an acute exacerbation were randomized to fixed doses (40 mg, 80 mg or 120 mg) of double-blind lurasidone (LUR) for 6 weeks. The primary efficacy outcome was change in BPRSd (006; 196) and change in PANSS total score (Pearl 1; Pearl 2). Secondary measures included CGI-Severity and PANSS positive and negative symptom subscales. Results: In study 006, treatment with LUR-40 and LUR-120, respectively, was significantly superior to placebo on the BPRSd (p=0.018; p=0.004), and on the CGI-S (p=0.002; p=0.001). In study 196, treatment with LUR-80 was significantly superior to placebo on the BPRSd (p=0.012) and on secondary measures--PANSS total (p=0.004), and positive (p=0.006) and negative (p=0.025) subscale scores; and on the CGI-S (p=0.007). In Pearl 1, treatment with LUR-80 was significantly superior to placebo on the PANSS total and CGI-S, respectively (p=0.011; p=0.005), but these assessments were not significant for LUR-40 or LUR-120. In Pearl 2, treatment with LUR-40 and LUR-120, respectively, were significantly superior to placebo on the PANSS total score (p<0.001; p=0.011) and on secondary measures--PANSS positive (p=0.018; p=0.035) and negative (0.002; p=0.045) subscale scores; and on the CGI-S (p=0.006; p=0.040). Conclusion: Lurasidone has demonstrated efficacy in four placebo-controlled trials in patients with acute schizophrenia, for both primary and secondary outcome measures. Lurasidone fixed doses of 40, 80 and 120 mg have each shown efficacy at the primary study endpoint in two studies, providing replicated evidence of efficacy for each dose.

Funded by Dainippon Sumitomo Pharma

NR6-03

GLUTAMATE QUANTIFICATION IN THE ASSOCIATIVE STRIATUM OF PATIENTS WITH SCHIZOPHRENIA BEFORE AND AFTER ANTIPSYCHOTIC TREATMENT

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SUMMARY:

Objective: Glutamate (Glu) has been implicated in the pathophysiology of schizophrenia. Its receptor blockers can induce schizophrenia-like symptoms. There is evidence of a complex interaction between dopamine (DA) and Glu neurotransmission in schizophrenia, but little is known about the role of Glu in a dense DA-innervated region like the associative striatum. The aim of this study was to compare the Glu levels using proton magnetic resonance spectroscopy (1H-MRS) in patients with schizophrenia, before and after antipsychotic treatment (risperidone), with appropriate controls in the associative striatum

(anterodorsal caudate) and the cerebellar cortex as a negligible DA region.
Methods: Nineteen patients with schizophrenia (age: 24.4?4.7, 12-males) and 19 healthy controls (age: 26.6?5.9, 12-males) were included. Patients were included during an acute psychotic episode (PANSS= 87.6?17.96), drug-free for at least 1-month, and able to consent to the procedures involved. They were treated with risperidone for 6-weeks with doses (3.45?1.27 mg/day) adjusted based on clinical judgment (PANSS-post treatment= 54.7?11.27). Concomitant medications were not allowed during the study. Patients underwent two 1H-MRS studies, one before treatment and another after 6 weeks of daily risperidone treatment. Controls underwent one 1H-MRS study. 1H-MRS were performed on a 3.0-T GE scanner using a PRESS pulse sequence with TR=1500 ms, TE=35 ms, 128 repetitions in 4ml voxels (2x2x1 cm) localized on the anterodorsal caudate and cerebellar cortex. Glu concentrations were estimated with the LCmodel software and corrected for the proportion of cerebrospinal fluid in the voxel. Results: The associative striatum in patients showed higher levels of Glu during the drug-free condition (df=36, p=0.03) and after antipsychotic treatment (df=36, p=0.05) than controls. No differences were shown between the drug-free and post-treatment states. On the contrary, there were no differences in Glu cerebellar levels between the 3 groups. Discussion: Our results indicate that the increase of Glu in the associative striatum in schizophrenia is related to the illness and does not change after 6-weeks of antipsychotic treatment. Moreover, the lack of change in the cerebellum suggests that the increase of Glu in schizophrenia is not ubiquitous within the brain and may be associated with DA target regions. The results might tie with the glutamatergic hypothesis of schizophrenia.

NR6-04

EVALUATION OF THE RELATIONSHIPS AMONG CHANGE IN FUNCTION, SYMPTOMS AND DURATION OF SCHIZOPHRENIA

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SUMMARY:
Objective: To explore the relationships between change in function, change in symptoms and duration of schizophrenia. Methods: This was a post hoc analysis of completed clinical trial data from the paliperidone palmitate treatment arms of three 13-week double blind and one 52-week open label trial. Patient function was measured using the Personal and Social Performance (PSP) scale, symptoms using the Positive and Negative Syndrome Scale (PANSS) and overall clinical status using the Clinical Global Impression of Severity (CGI-S). PSP scores from baseline to last observation were categorized as improved (>5 point), no change (-5 to +5 points), or declined (<-5 points). The relationship between function category, change in PANSS, change in CGI-S and categorical duration of schizophrenia (<5 vs =5 years) was evaluated descriptively and by using proportional odds models. Results: Of the 1443 patients included in the analysis, 44.2% had improved PSP scores, 38.5% had no change and 17.3% declined. Average age was 39.1 (SD 10.9) and 65.1% were male. Mean change in PANSS score was -21.5 (SD 15.7) points in the group with improved function, -5.1 (SD 13.2) for the no change group and +8.5 (19.2) in the group that declined (all pairwise P<0.0001). Across all patients 22.8% had a duration of schizophrenia of less than 5 years. The odds of a shift in PSP category increased by a multiple of 4.4 for each unit improvement in CGI-S score (P<0.0001). Similarly, the odds of a shift in PSP category increased by a multiple of 2.4 for every 10-point increase in PANSS (P<0.0001). When duration of schizophrenia was less than 5 years the odds of a shift in PSP category increased by a multiple of 1.5 times compared with when duration was 5 or more years (P<0.05).
Conclusion: Change in PANSS, change in CGI-S scores and shorter duration of schizophrenia (<5 years) were associated with change in functional category as measured by the PSP. Sponsored by Ortho-McNeil Janssen Scientific Affairs, LLC

NR6-05

ONSET OF EFFICACY WITH PALIPERIDONE PALMITATE IN PATIENTS WITH ACUTELY EXACERBATED SCHIZOPHRENIA

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SUMMARY:
Introduction: Paliperidone palmitate (PP) is a long-acting atypical antipsychotic administered by once monthly injection. The recommended initiation dose (234mg Day 1 and 156mg Day 8, both deltoid) was designed to rapidly attain steady-state levels. Objective: To evaluate the onset of efficacy of PP (234mg on Day 1, followed

by 39, 156 or 234mg on Day 8 and thereafter), without oral antipsychotic supplementation in subjects with acutely exacerbated schizophrenia. Methods: Subjects with exacerbated schizophrenia enrolled in a 13-week, double-blind, placebo-controlled trial (NCT00590577). PP dosing was 234mg on Day 1, followed by the randomization dose (39, 156, or 234mg) on Day 8 and monthly thereafter. PANSS scores were assessed at baseline, Days 4, 8, 22, 36, 64, 92 and endpoint. Onset of efficacy was defined as the first time point at which PP showed a significant PANSS improvement compared to placebo, using ANCOVA models and LOCF methodology without adjusting for multiplicity. Results: Six hundred thirty-six subjects were in the intent-to-treat population (n=476 PP; n=160 placebo). PP treatment (234mg Day 1) was first associated with significantly greater improvement than placebo on mean PANSS total score at Day 8 (LS mean[SE] change from baseline -8.2[0.87] versus -5.8[1.20]; p=0.037). All PP dose groups continued to show greater PANSS improvement than placebo at all subsequent time points (all p<0.022). Most common AEs (5% or more any group) reported more frequently in any PP group than placebo: headache (7.3% placebo, 10.6% 39mg, 6.7% 156mg, 6.1% 234mg), agitation (6.7%, 7.5%, 4.8%, 3.7%, respectively), akathisia (4.9%, 1.3%, 4.8%, 5.5%, respectively), and injection site pain (3.7%, 8.8%, 6.1%, 8.0%, respectively). Discussion: This dataset showed significant symptom improvement with PP versus placebo at Day 8 in subjects who received 234mg on Day 1, without oral antipsychotic supplementation. This significant improvement continued at each assessment with once-monthly doses of 39, 156, and 234mg.

Supported by Ortho-McNeil Janssen Scientific Affairs, LLC

NR6-06

THE CARDIOVASCULAR SAFETY OF INHALED LOXAPINE (AZ-004)

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SUMMARY:

Background: AZ-004 (inhaled loxapine) is being developed for the treatment of agitation in patients with schizophrenia or bipolar disorder. Loxapine was administered via inhalation using the Staccato® system, which delivers thermally-generated drug aerosol to the deep lungs for rapid systemic absorption with IV-like kinetics. Objective: To describe the cardiovascular safety of inhaled loxapine from 2 separate clinical protocols: a Phase 1 study in 32 subjects on chronic antipsychotic medication, and a thorough QT (TQT) study in 48 healthy volunteers. Methods: Consenting male and female adults, 18 to 65 years of age, were enrolled in the studies and randomly assigned to treatment. The Phase 1 study was a double blind, placebo controlled, parallel group investigation of the safety of repeat doses (at time 0, 4 or 8 hours) in subjects on chronic antipsychotic medication. Each cohort received either 5 mg x 3 doses, 10 mg x 3 doses, placebo x 3 doses, or 10 mg followed by two doses of 5 mg. The TQT study was a double-blind, double-dummy, active- and placebo-controlled, 3 period crossover study investigating the effect on QT interval of single doses of 10 mg AZ-004, 400 mg oral moxifloxacin, and placebo. Results: In the Phase 1 study, there were no important changes in vital signs with repeat dosing in subjects on chronic antipsychotic medication. In the highest dose group (10 mg x 3), mean changes from baseline in systolic BP were -1.75, -3.13, and -4.38 mmHg at 10 minutes after the first, second, and third doses, respectively. In the TQT study, AZ-004 did not increase QT intervals, as demonstrated by the upper bound of the one-sided 95% CIs placed on the point estimate of the placebo-subtracted change of QTcI being less than 10 ms at all 11 post-dose timepoints. Moxifloxacin significantly prolonged QTcI demonstrating assay sensitivity. Conclusions: AZ-004 had no significant hemodynamic effect in subjects on chronic antipsychotic regimens, and did not significantly prolong the QT interval at therapeutic doses.

This research was funded by Alexza Pharmaceuticals

NR6-07

LONG-TERM SAFETY, TOLERABILITY AND PHARMACOKINETICS OF PALIPERIDONE PALMITATE: A ONE-YEAR OPEN-LABEL STUDY IN PATIENTS WITH SCHIZOPHRENIA

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SUMMARY:

Objective: To evaluate the pharmacokinetics (PK), long-term safety and tolerability of the highest marketed dose of paliperidone palmitate (PP; 234 mg [150 mg eq.])

in stable patients with schizophrenia. Methods: In this 1-year open-label study, eligible patients (aged 19-65 yrs; PANSS total score =70) received an initial deltoid injection of 234 mg PP. The second injection of PP a week later and subsequent once-monthly injections were deltoid or gluteal. All injections were planned to be 234 mg PP. Patients willing to participate in intensive PK sampling were classified as Group A. Patients unwilling to undergo intensive PK sampling or unable to tolerate the 234 mg dose (consequently receiving flexible doses of 78, 156 or 234 mg) were classified as Group B. Results: Of the 212 patients (safety analysis set), 73% were men; 45% White; 20% Black; 34% Asians; mean (SD) age 41 (10.2) years, and mean (SD) baseline PANSS total score 54.9 (9.03). One hundred thirteen patients completed the study; 104 received 234 mg PP throughout. Fifty-five percent of patients received deltoid injections only. Mean (SD; range) dose of PP was 228 (20; 117 – 234) mg. As a result of the dosing initiation regimen used, therapeutic paliperidone levels were rapidly achieved and maintained (average concentrations during the dosing interval were 34.7, 40.0, and 47.7 ng/mL after the 2nd, 8th, and 14th injection respectively). Frequent TEAEs (=5% of all patients) were nasopharyngitis (n=37), insomnia (n=32) and injection-site pain (n=32). Akathisia (n=19) and tremor (n=11) were the most common EPS-related TEAEs. Thirty-three patients had an SAE and 27 patients discontinued due to TEAEs. No deaths were reported. The mean (SD) weight change from baseline was 2.5 (5.41) kg at endpoint. Patients' psychosis remained stable. Conclusion: Safety results after long-term therapy with the highest available dose of once-monthly PP were consistent with results from previous studies, with no new signals noted. Plasma concentrations were within the expected range.

NR6-08

EDUCATIONAL LEVEL OF THE RATER PREDICTS QUALITY OF SYMPTOM ASSESSMENT INTERVIEWS IN SCHIZOPHRENIA CLINICAL TRIALS

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SUMMARY:

Introduction: In clinical trials, agreement among raters and ultimately signal detection may be complicated by variations in raters' credentials and interview skills. The Positive and Negative Syndrome Scale (PANSS) is the most widely recognized and utilized measure in schizophrenia clinical trials. There is no universal agreement regarding the level of professional credentials required to rate the PANSS. We have previously reported a relatively lower use of doctorate-level PANSS raters in the United States compared to the rest of the world (1). The impact of educational level on the quality of the ratings interview in clinical trial settings is not well defined. Methods: We examined the relationship between the educational level of PANSS raters (doctorate vs. non-doctorate) and competency to conduct an interview as measured by the total score on the Research Interview Assessment Scale (RISA). All raters were from the United States and were undergoing training to rate in an antipsychotic clinical trial. Results: The mean total RISA score of doctorate-level raters (mean=27.8, n=45) was higher than non-doctorate raters (mean=26.2, n=55) ($t=2.21$, $df=98$, $p<.03$), Wilcoxon $p < 0.02$). Discussion: The current findings are consistent with the notion that in clinical trials PANSS raters with doctorate degrees on the whole exhibit modestly higher quality interview skills than raters without doctorate degrees. Interview quality is an important factor in the validity and consistency of clinical trials ratings. The current findings must be viewed in light of the relatively small sample size and the possibility of sampling bias. The findings may have relevance for selection of raters in clinical trials. This analysis was paid for by United BioSource Corporation.

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NR6-09

INCREASED MATERNAL AGE AT BIRTH HAMPERS REVERSAL LEARNING IN SCHIZOPHRENIA

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SUMMARY:

Objective: Impairments in reinforcement learning appear to be prominent aspects of schizophrenia which

may relate to symptoms of the disorder. Advanced parental age at birth has been associated with the risk of schizophrenia and has been linked to cognitive deficits in children. We examine the effects of parental age at birth on reinforcement learning in adults with schizophrenia. Method: Forty-two consecutively admitted patients with schizophrenia in an acute psychiatric ward and 22 healthy controls were tested on the intra-dimensional/extra-dimensional set-shifting task (IEDS) of the Cambridge Neuropsychological Test Automated Battery (CANTAB). The paternal and maternal age at birth were also registered. Statistical correlation analyses and the Mann-Whitney test were performed using SPSS. Results: Maternal age at birth positively correlated with intra-dimensional reversal errors (rho=0.507, p=0.004) in schizophrenia. This association was not found in the control group. When we divided our patients into two groups according to their maternal age at birth (= and <30 years), patients whose mothers were = 30 years at their birth demonstrated more intra-dimensional reversal errors than those born by mothers < 30 years old (p=0.013). We failed to detect any significant effects of the parental age at birth on IEDS performance in patients or controls. Conclusions: Our results raise the possibility that increased maternal age at birth is associated with deficits in reinforcement (reversal) learning in offspring with schizophrenia.

NR6-10

PALIPERIDONE EXTENDED RELEASE AS MONOTHERAPY OR ADJUNCTIVE THERAPY TO MOOD STABILIZERS/ANTIDEPRESSANTS IN SUBJECTS WITH SCHIZOAFFECTIVE DISORDER

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SUMMARY:
Background: Antipsychotics are often used with mood stabilizers and/or antidepressants (MS/ADs) for patients with schizoaffective disorder. Clinical studies showed that paliperidone ER (pali ER) is effective for schizoaffective disorder, as monotherapy or adjunctive to MS/ADs. This analysis explores the effects of pali ER by type of adjunctive therapy. Methods: Data was pooled from double-blind, placebo-controlled 6-week studies (CR010498, CR013099). Subjects (n=414 pali ER, n=200 placebo) met SCID-confirmed criteria for schizoaffective disorder; PANSS total score =60, score =4 on =2 PANSS items (hostility, excitement, tension, uncooperativeness, poor impulse control); YMRS and/or HAM-D-21 =16. Subjects receiving stable doses of MS/ADs could continue ongoing treatment. Randomization stratified by MS/AD use. Data analyzed by type of adjunctive therapy (none n=339; MS only n=140; AD only n=84; both MS and AD n=50). Endpoints: PANSS and AE reports. ANCOVA models and LOCF methods were used. Results: Mean (SD) modal dose of pali ER: 8.4 (2.9) mg/d in the pali ER monotherapy group, 8.8 (2.7) mg/d in the adjunctive therapy group. Improvement was greater with pali ER than placebo in PANSS total score at end point in subjects with or without MS/ADs. Differences versus placebo in LS mean change (95%CI): -6.0 (-10.8,-1.3) and -9.2 (-13.6,-4.8), respectively. For subjects who received pali ER + MS only or AD only, differences versus placebo: -9.6 (-17.1,-2.1) and -8.4 (-16.6,-0.2), respectively. Results for subjects who received both MS and AD: 2.9 (-7.1,12.9). Most common AEs (pali ER vs placebo) were headache (13.2% vs 18.9%) and insomnia (6.8% vs 10.0%) in the adjunctive group; headache (15.2% vs 11.6%) in the monotherapy group. Conclusion: Pali ER as monotherapy or adjunctive to MS or AD only was effective in the acute treatment of schizoaffective disorder. The tolerability of pali ER appeared similar across these subpopulations.
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NR6-11

EMOTIONAL MUSICAL RECOGNITION DEFICITS IN PARANOID SCHIZOPHRENIC PATIENTS

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SUMMARY:
Introduction: In schizophrenia, many studies reported problems in recognizing visual facial emotions (Russell et al., 2007), visual non-facial emotions (Seok et al., 2006) and also vocal emotions (Bozikas et al., 2004), particularly for negative emotions. Up to now, however, there are no available data about the recognition of emotions expressed by musical excerpts in this psychiatric condition. Methods: Thirty paranoid schizophrenic patients in remission with low level of negative symptoms and 30

control subjects matched for gender, age and sociocultural level were exposed to 56 musical excerpts (14 stimuli per emotion category) that conveyed four intended emotions (happiness, sadness, threat and peacefulness) (Vieillard et al., 2008). They had to judge to what extent they recognized each of the four emotions in each excerpts on a 10-point scale, where 0 indicated "absent" and 9, "present." When the maximal rating corresponded to the label that matched the intended emotion, a score of 1 was given. Skin conductance measurements where obtained and the amplitude of variation from baseline was measured for each emotion. Results: An ANOVA with Group (Schizophrenia, Controls) and Emotion (happiness, sadness, threat and peacefulness) as between- and within-subjects factors, respectively, was conducted on the number of correct responses. The analysis revealed a significant Group effect ($F(1,58)=8.16, p=.006$) indicating lower scores in schizophrenic patients, a significant effect of Emotion ($F(3,58)=15.93, p<.05$) reflecting sad = peacefulness < threat < happiness but no Group x Emotion interaction ($F(3,174)=1.38$, $p=.25$). In patients, the global performance in emotional recognition was negatively correlated with positive symptoms on the PANSS scale ($r = -0.64$, $p<.001$). A subgroup analysis showed that only female patients (n=11) had impaired emotional recognition and that patients on atypical antipsychotics (n=22) did not show any deficit in emotional recognition (as compared with patients on a mixture of typical and atypical antipsychotics). A similar analysis of the skin conductance responses revealed a significant Group effect ($F(1,58)=4.58$, $p=.037$) with larger amplitudes in patients, no effect for Emotion ($F(3,58)=1.64$, $p=.19$) and no Group x Emotion interaction ($F(3,115)=1.44$, $p=.24$). In patients, skin conductance responses were positively correlated with positive symptoms ($r = 0.409$, $p=.025$).

NR6-12

A RANDOMIZED, DOUBLE-BLIND, COMPARATIVE STUDY OF PALIPERIDONE PALMITATE AND RISPERIDONE LONG-ACTING THERAPY IN PATIENTS WITH SCHIZOPHRENIA

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SUMMARY:

Objective: To show that paliperidone palmitate (PP), a once-monthly injectable atypical antipsychotic (recently approved in the US) was noninferior to risperidone long-acting injectable (RIS-LAI) in the treatment of schizophrenia in adults. Methods: In this 13-week double-blind (DB) trial, consenting adults (N=1220) with schizophrenia were randomized (1:1) to either a) PP: deltoid injections on day 1 (150 mg eq.), day 8 (100 mg eq.), and once-monthly flexible dosing (50-150 mg eq., deltoid or gluteal), and placebo-injections (matched to RIS-LAI) or b) RIS-LAI: gluteal injections on days 8, 22 (25 mg), days 36, 50 (25 or 37.5 mg) and days 64, 78 (25, 37.5 or 50 mg), and placebo injections (matched to PP). Patients in RIS-LAI group received oral supplementation (RIS 1–6 mg/day; days 1-28) and in PP group received oral placebo. Results: For the per-protocol analysis set (n=765), mean [SD] change from baseline in PANSS total score improved similarly in the 2 groups from day 4 onwards, and at DB endpoint (primary measure) was -18.6 [15.45] in the PP, and -17.9 [14.24] in RIS-LAI group. PP treatment was declared noninferior to RIS-LAI (point estimate [95% CI]: 0.4 [-1.62;2.38]) as the lower limit of the 95% CI on change in PANSS total score exceeded the predetermined noninferiority margin of -5. Mean [SD] change from baseline to endpoint in CGI-S (PP: -0.9 [0.97], RIS-LAI: -0.9 [0.93]) and PSP scores (PP: 8.5 [11.82], RIS-LAI: 8.8 [11.65]), improved similarly in both groups. The incidence of individual TEAEs (=2% of patients, either group) was generally similar in both groups. Conclusion: PP, with no oral supplementation, was statistically noninferior to RIS-LAI plus oral RIS treatment in patients with schizophrenia. Similar results on the primary efficacy measure between the 2 treatment groups were seen from day 4 onward with the approved initiation regimen of PP used in this study. PP was generally tolerable at the doses tested.

NR6-13

PREDICTORS OF FAVORABLE LONG-TERM OUTCOME IN THE TREATMENT OF SCHIZOPHRENIA

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SUMMARY:

Objective: This study aimed to identify patients with schizophrenia who experience favorable outcomes over a 3-year period and determine baseline predictors of

favorable long-term outcomes. Methods: We used data of a 3-year prospective, observational study of individuals treated for schizophrenia in the United States (US-SCAP; N=2327). A hierarchical cluster analysis was performed to group patients using baseline clinical, functional, and resource utilization measures. Clinical status was based on symptom severity. Functional level reflected patient-reported productivity and occupational role functioning. Resource utilization of psychiatric hospitalization and emergency services was systematically abstracted from medical records. A patient was classified as having a favorable long-term outcome if their outcome values had the closest distance to the defined "best baseline cluster" at each point over the 3-year follow-up; stepwise logistic regression was used to determine baseline predictors. Results: Of 1604 patients with sufficient data to assess 3-year outcomes, only 191 (12%) experienced favorable outcomes. Overall, 5 distinct outcome clusters were identified, ranging from best to worst. The baseline predictors of the most favorable outcomes sustained over the 3-year period included better quality of life, more daily activities, patient-reported clearer thinking, less severe positive symptoms, lower AIMS score, higher level of global functioning, being employed, not having health insurance, being female, and not having help with shopping, leisure, or social activities. Conclusions: This study identified 5 distinct clusters of patients with schizophrenia based on their baseline clinical, functional, and resource utilization factors. Current findings suggest that clinicians could make early projections of long-term outcome, thus enabling early tailored therapeutic interventions that could enhance patients' likelihood of achieving more favorable long-term outcomes.

This research was supported and conducted by Eli Lilly and Company.

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NR6-14

PATIENTS' EARLY PERCEPTIONS OF MEDICATIONS' BENEFITS PREDICT SUBSEQUENT RESPONSE IN THE TREATMENT OF SCHIZOPHRENIA

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SUMMARY:
Objective: To assess whether a brief and simple assessment of patients' early perceptions of medications' benefits can predict subsequent response or non-response to continued treatment with the same antipsychotic medication. Methods: This post-hoc analysis used data from a cost-effectiveness study of antipsychotics in the treatment of schizophrenia (HGGD) in which the Rating of Medication Influences scale (ROMI) was assessed following 2 weeks of treatment. Patients rated ROMI items on a scale from 1 (no agreement) to 3 (strong agreement). Patients' scores on the ROMI's "Perceived Medication Benefits," a 4-item subscale identified in prior research, were used to predict subsequent response to continued treatment with the medication at Week 8. Response was defined as at least 20% reduction on the Positive and Negative Syndrome Scale (PANSS) total score from baseline to Week 8. Logistic regression was used to assess whether the ROMI "Perceived Medication Benefits" score was a strong predictor of subsequent response and identify the best cut-off score for the prediction model. Analysis was conducted on 439 patients who had PANSS and ROMI data at the 2-week and 8-week time points. Results: A score of 2.75 or higher on the Perceived Medication Benefits subscale at Week 2 predicted subsequent response (per PANSS) at Week 8 with high specificity (72%) and negative predictive value (70%), moderate sensitivity (44%) and positive predictive value (47%) and with a 38% misclassification rate. Conclusions: A brief assessment of patients' early perceptions of medications' benefits (at Week 2) appears to be a good predictor of subsequent response/non-response to continued treatment with the same medication. Predictive values appear comparable to those reported in prior studies in which early response was assessed with a clinician-rated symptom scale, which requires special training and repeated assessments. Further research is needed to replicate the current findings.
Funded by Eli Lilly and Company.

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NR6-15

LURASIDONE IN THE TREATMENT OF ACUTE SCHIZOPHRENIA: RESULTS OF THE DOUBLE-BLIND, PLACEBO-CONTROLLED PEARL 2 TRIAL

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SUMMARY:
Objective: The aim of this study was to evaluate the short-term efficacy and safety of lurasidone in patients with an acute exacerbation of schizophrenia. Methods: Patients who met DSM-IV criteria for schizophrenia were randomized to 6 weeks of double-blind treatment with lurasidone 40 mg, lurasidone 120 mg, olanzapine 15 mg or placebo. An MMRM analysis was performed for the main efficacy measures: PANSS total and subscale scores and CGI-S. Results: Baseline characteristics were similar among patients randomized to lurasidone 40 mg (n=119; mean PANSS total, 96.6); lurasidone 120 mg (n=118; mean PANSS total, 97.9); olanzapine 15 mg (n=122; mean PANSS total, 96.3); and placebo (n=114; mean PANSS total, 95.8). Treatment with lurasidone was associated with significantly greater LS mean improvement on the PANSS total score vs. placebo (-16.0) among patients in the 40 mg (-25.7; P<0.001) and 120 mg (-23.6; P=0.011) dose groups at Week 6. Treatment with both doses of lurasidone were also associated with significantly greater improvement on the PANSS positive and negative subscales, and on the CGI-S on both the 40 mg (-1.5; P=0.006) and 120 mg (-1.4; P=0.040) doses of lurasidone. Olanzapine 15 mg/day also produced significantly greater improvement than placebo on the PANSS total score, PANSS positive and negative subscales, and the CGI-S. The proportion of patients experiencing =7% weight gain was 5.9% for combined lurasidone doses, 34.4% for olanzapine and 6.9% for placebo. Median endpoint change in triglycerides was also similar for lurasidone and placebo (+1.0 vs. -1.0 mg/dL0), but increased by +24.0 mg/dL on olanzapine. Conclusion: The results of this study indicate that lurasidone is an effective treatment for patients with an acute exacerbation of schizophrenia. Changes in lipids, glucose, and weight among patients treated with lurasidone were comparable to placebo, while treatment with olanzapine was associated with marked effects on weight and metabolic parameters.
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NR6-16

EFFICACY, SAFETY AND TOLERABILITY OF PALIPERIDONE EXTENDED RELEASE IN ADOLESCENT PATIENTS WITH SCHIZOPHRENIA

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SUMMARY:
Background: Optimal management of childhood-onset schizophrenia is difficult due to a limited number of controlled clinical trials in adolescents and few approved therapies. Paliperidone ER is currently under investigation for use in the pediatric population. This study assessed the efficacy and safety of paliperidone ER in adolescents with schizophrenia. Methods: In this study, adolescent patients (n=201; ages 12-17) with schizophrenia were randomized in a 6-week, double-blind (DB) study to receive either placebo or a fixed weight-based dose of paliperidone ER daily. Patients weighing 29 to <51 kg at baseline received paliperidone ER 1.5 mg (low), 3 mg (medium) or 6 mg (high), and patients = 51 kg received paliperidone ER 1.5 mg (low), 6 mg (medium) or 12 mg (high). The primary efficacy variable was the change in the PANSS total score from baseline to the DB endpoint. Results: One hundred thirty-eight (69%) of 201 patients completed the study. The mean (SD) baseline PANSS total score was 91.1 (13.03). The mean (SD) change from baseline to DB endpoint in PANSS total score was -7.9 (20.15) in the placebo group, -9.8 (16.31) in the paliperidone ER low dose group (1.5 mg, regardless of weight; p=0.51 vs. placebo), -17.3 (14.33) in the medium dose group (3 mg or 6 mg, based on body weight; p=0.006) and -13.8 (15.74) in the high dose group (6 mg or 12 mg, based on body weight; p=0.09). By actual dose, paliperidone ER 3, 6 and 12 mg each significantly (p<0.05 versus placebo)

improved PANSS total score, and the secondary measures Clinical Global Impression-Severity score and Children's Global Assessment Score from baseline to endpoint. Three patients discontinued the study due to a TEAE. There were dose-related increases in TEAEs, EPS-related adverse events, and measurements related to weight. Conclusions: Paliperidone ER doses of 3, 6, and 12 mg/day, but not 1.5 mg, were efficacious versus placebo in this study in adolescents with schizophrenia. All doses evaluated (1.5 to 12 mg/day) were tolerable.

NR6-17

EFFECTS OF PALIPERIDONE PALMITATE TREATMENT IN SCHIZOPHRENIA PATIENTS PREVIOUSLY TREATED WITH ORAL RISPERIDONE

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SUMMARY:
Introduction: Paliperidone palmitate (PP), a once-monthly injectable atypical antipsychotic, is hydrolyzed to 9-hydroxyrisperidone, the active metabolite of risperidone. This analysis examined the effects of PP in subjects with schizophrenia recently treated with oral risperidone but still experiencing an acute exacerbation. Methods: Post hoc analysis of a 13-week, double-blind, placebo-controlled study of 636 subjects with an acute exacerbation of schizophrenia randomly assigned to PP (39, 156, or 234 mg) or placebo (CRO12550). PP subjects received an initiation dose of 234 mg on day 1, followed by their assigned dose on day 8 and monthly thereafter, with no oral supplementation. This analysis focused on the subgroup of subjects who received oral risperidone within 2 weeks prior to randomization. Assessments: PANSS, CGI-S and PSP scores and AE reports. ANCOVA models and LOCF methodology evaluated change scores at week 13 end point. Results: Two hundred sixteen subjects received risperidone within 2 weeks of randomization (PP n=159; placebo n=57) and were included in this analysis. Mean (SD) duration of previous risperidone use: 242 (704) days. Mean (SD) PANSS total score at baseline: 88.4 (11.8). 52.8% of PP and 38.6% of placebo subjects completed the study. Significant improvement with PP versus placebo was observed in mean (SE) PANSS total (-14.0 [2.1] versus -1.4 [2.9], P<0.001); CGI-S (-0.8 [0.1] versus -0.3 [0.2], P=0.003); and PSP (9.7 [1.6] versus 2.8 [2.3], P=0.004) scores at end point. Most common AEs (=10%, PP vs placebo): insomnia (19.5% versus 14.0%), schizophrenia (9.4% versus 19.3%) and agitation (8.8% vs 12.3%). Conclusion: In subjects with schizophrenia who had recently received oral risperidone but remained sufficiently symptomatic for study enrollment, once-monthly dosing with PP significantly improved clinical symptoms, global ratings of illness and functioning vs placebo. No unexpected safety or tolerability findings were observed.
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NR6-18

HEMATOLOGICAL CLOZAPINE MONITORING WITH A POINT-OF-CARE DEVICE

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SUMMARY:
Background: Clozapine remains the drug of choice for treatment-resistant schizophrenia, but its use has been restricted due to the propensity to cause agranulocytosis and consequently the need for regular blood monitoring (1, 2). CHEMPAQ XBC is a portable device for analyzing neutrophil count using capillary blood, which makes it possible to measure WBC and neutrophil count from a single blood drop drawn in the home of the patient by a primary care person or in an outpatient clinic. Case report: Mr X was a 41 year-old man diagnosed with paranoid schizophrenia, and considered a revolving-door patient. Paranoid delusions about being chased by the police and commenting external auditory hallucinations had constantly been present for the last five years. He had been treated with several antipsychotic drugs with only partial response, which made him eligible for treatment with clozapine. However, he continued to refuse clozapine due to the mandatory blood monitoring and especially the fear of loosing too much blood during the blood sampling. He was offered capillary blood monitoring with CHEMAPAQ XBC and subsequently accepted treatment with clozapine. The reason for accepting the treatment was that only a single blood drop was needed for doing the analyses and the fact that he could see the result within two minutes. After two weeks of treatment with clozapine, the patient's paranoid delusions disappeared and he was discharged to an outpatient clinic. He continued to

comply with the blood monitoring, which was done in the outpatient clinic. After two months of treatment, he began to paint, which he had not been doing since the onset of schizophrenia. Conclusion: This case illustrates the importance of initiating treatment with clozapine for patients not responding to other antipsychotic drugs and the usefulness of a point-of-care device for the mandatory haematological monitoring during treatment with clozapine. The capillary blood count point-of-care device has the potential to enhance clozapine acceptability and its appropriate use.

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NR6-19

DIFFERENTIAL METABOLIC PROFILES OF LURASIDONE AND OLANZAPINE: DATA FROM A 6-WEEK, DOUBLE-BLIND, PLACEBO-CONTROLLED SCHIZOPHRENIA TRIAL

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SUMMARY:

Objective: Lurasidone is a novel antipsychotic under development for schizophrenia. The aim of this study was to compare the effect of short-term lurasidone and olanzapine treatment of schizophrenia on weight and metabolic parameters. Methods: Data are presented from an international, multi-center, double-blind, 6-week schizophrenia trial of two doses of a novel antipsychotic, lurasidone (40 mg, n=120; 120 mg, n=119), versus placebo (n=116), with olanzapine 15 mg (n=123) as the active comparator. Results: Mean LOCF endpoint weight gain was +0.7 kg for the combined lurasidone dosage groups, +4.2 kg for olanzapine, and +0.6 kg for placebo. The proportion experiencing =7% weight gain was 5.9% for combined lurasidone, 34.4% for olanzapine and 6.9% for placebo. The mean change in BMI was 0.35 kg/m2 for lurasidone, +1.39 kg/m2 for olanzapine and 0.21 kg/m2 for placebo. Median endpoint change in lipids were as follows: triglycerides, +1.0 mg/dL for combined lurasidone, +24.0 mg/dL for olanzapine, and -1.0 mg/dL for placebo; total cholesterol -7.0 mg/dL for lurasidone, +9.0 mg/dL for olanzapine, and -5.0 mg/dL for placebo; similar trends existed for LDL and HDL changes. There were no differences for the combined lurasidone group versus placebo for mean endpoint change in glucose (-1.0 mg/dL vs. +1.0 mg/dL), while glucose increased by +4.0 mg/dL on olanzapine. There were also no differences for the combined lurasidone group versus placebo in mean endpoint change in insulin (-0.55 mU/L vs. -0.1 mU/L), while insulin increased by +1.5 mU/L on olanzapine. Conclusions: Lurasidone treatment was associated with changes in metabolic parameters that were comparable to placebo, while olanzapine therapy resulted in deleterious changes across these parameters compared to baseline values. Lurasidone may emerge as another metabolically benign option for patients with schizophrenia, thus minimizing the drug-related cardiovascular risks seen with other atypical antipsychotic agents.

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NR6-20

SAFETY OF LURASIDONE: POOLED ANALYSIS OF FIVE PLACEBO-CONTROLLED TRIALS IN PATIENTS WITH SCHIZOPHRENIA

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SUMMARY:

Objective: Lurasidone, a novel antipsychotic, has demonstrated efficacy in the treatment of schizophrenia across multiple placebo-controlled studies. The aim of this analysis is to provide a comprehensive summary of the effect of lurasidone, in the dosing range of 20-120 mg/day, on key safety parameters. Methods: Data were pooled from five double-blind, placebo-controlled, acute treatment studies of subjects who met DSM-IV criteria for schizophrenia with an acute exacerbation. The safety analysis sample consisted of patients treated with lurasidone (total N=1004), haloperidol (N=72), olanzapine (N=122) and placebo (N=455). Results: In the pooled lurasidone group, 4 adverse events were reported with an incidence >/=10% and >/=2-times placebo, akathisia (15.0% versus 3.3%), nausea (12.0% versus 3.9%), sedation (11.9%

versus 5.5%) and somnolence (10.7% versus 4.6%). Discontinuations due to adverse events were 8% in the pooled lurasidone group versus 4% on placebo, with no consistent between-dose differences in the 40-120 mg dosing range. Measures of EPS were similar to placebo for lurasidone and olanzapine. On metabolic parameters, the median endpoint change (mg/dL) in the lurasidone, olanzapine, haloperidol and placebo groups for total cholesterol was -8.0, +9.0, -8.0 and -10.0, respectively; for triglycerides was -5.0, +25.0, -3.0 and -7.0; and for glucose was 0.0, +4.0, +2.0 and +1.0. Clinically significant weight gain (>/=7%) was observed more frequently on olanzapine (34.4%) compared to lurasidone (5.6%), haloperidol (4.2%) or placebo (4.0%). The mean QTcF change was minimal for lurasidone and placebo (+1.5 vs. +1.9 msec). Mean endpoint change in prolactin (µg/L) was +1.1 on lurasidone, +3.7 on olanzapine, +8.5 on haloperidol, and -0.5 on placebo. Conclusion: Across five placebo-controlled trials in patients with schizophrenia, lurasidone was found to be safe and generally well-tolerated, and was not associated with clinically significant changes in weight or metabolic parameters.

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NR6-21

TOLERABILITY OF PALIPERIDONE PALMITATE INITIATION DOSES IN SUBJECTS WITH RECENTLY DIAGNOSED SCHIZOPHRENIA

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SUMMARY:

Introduction: Early in their illness, patients with schizophrenia are generally responsive to treatment but they may be more likely to experience adverse events (AEs). Objective: To examine the tolerability of the recommended initiation dosing regimen of paliperidone palmitate (PP), a once-monthly injectable atypical antipsychotic, in subjects recently diagnosed with schizophrenia. Methods: Subjects with acutely exacerbated schizophrenia enrolled in a 13-week, double-blind trial (PSY-3007; NCT00590577) and were randomized to placebo or PP at 39, 156, or 234 mg. This post-hoc analysis focused on recently diagnosed subjects (diagnosed ≤5 year, n=146 ITT analysis) who received placebo or the recommended initiation dosing regimen of PP: 234 mg on Day 1 (all subjects randomized to PP) and 156 mg on Day 8 (subjects randomized to the 156 mg arm). To assess the tolerability of the initiation dosing, AE reports were summarized during post-injection intervals: days 1-7 and 8-36. Efficacy endpoints included PANSS, CGI-S, and PSP; change scores were assessed at the week 13 endpoint by ANCOVA models and LOCF methodology. Results: Among the 146 recently diagnosed subjects, 109 received a Day 1 dose of PP 234 mg and 37 received placebo. In the week following the Day 1 dose, AE rates were 37.6% with PP and 29.7% with placebo. The most common AEs reported in more PP than placebo subjects were: injection site pain (5.5% versus 2.7%), agitation (4.6% versus 2.7%) and headache (3.7% versus 0.0%). Thirty-nine recently diagnosed subjects received a Day 1 dose of PP 234 mg and a Day 8 dose of 156 mg. In the month following the Day 8 dose, AE rates were 41.0% with PP and 37.8% with placebo. The most common AE reported in more PP than placebo subjects was anxiety (5.1% versus 0.0%). In these recently diagnosed subjects, PP (Day 1 dose of 234 mg, Day 8 dose of 156 mg and monthly thereafter) was associated with a significantly greater improvement than placebo in mean PANSS total score at study endpoint (-17.19 vs. -5.53, p=0.0102). Conclusion: Recently diagnosed subjects with schizophrenia may report more adverse events during the first 7 days with paliperidone palmitate relative to placebo, with the most common being injection site pain, agitation, and headache. Paliperidone palmitate was efficacious in these patients, with no new or unexpected tolerability findings.

Supported by Ortho-McNeil Janssen Scientific Affairs, Titusville, NJ.

NR6-22

GAMMA OSCILLATION AND SERUM NITRIC OXIDE METABOLITES IN CHRONIC SCHIZOPHRENIC PATIENTS

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SUMMARY:

Background: Several lines of evidence have implicated nitric oxide (NO) in the pathophysiology of schizophrenia. While subchronic application of the NMDA receptor antagonist such as phencyclidine and ketamine induce schizophrenia-like features in animals and humans, these agents reduce parvalbumin (PV) interneurons partially through NO activation. PV neurons play an important

role in the generation of gamma oscillation associated with cognitive functions. In the schizophrenics, reduction of PV neurons and the gamma oscillation generation are reported. Here we hypothesized that hyperactivity of nitric oxide may produce the cortical dysfunction and show the reduction of gamma oscillation in the antipsychotics therapy resistant schizophrenic patients. Methods: The diagnosis of schizophrenia was made by the two independent psychiatrists according to the DSM-IV. All subjects who had any type of physical disorders were excluded. Informed consent was obtained from all subjects. Using the ELISA method, we selected the schizophrenic patients with higher serum NO metabolites (high NO group) and lower serum NO metabolites (low NO group), and age matched control subjects (control group). Each group consisted of 13 subjects. There were no differences in the duration of illness or the amount of antipsychotics administration between the two patient groups. We investigated the EEG spectral power and coherence analysis in gamma band (30-40 Hz) at the frontal area (Fp1, Fp2, F3, and F4), and the PANSS evaluation for each group. Results: Compared with Low NO and control groups, the high NO group showed higher positive and negative symptoms, lower gamma power and higher interhemispheric gamma coherence in the frontal area. Conclusions: The present results suggest that the higher serum NO metabolites, hypogamma EEG power and higher interhemispheric gamma coherence in the frontal area after chronic antipsychotics treatment may be an unfavorable biomarker for schizophrenia.

NR6-23

CHANGE IN APPETITE AS A PREDICTOR OF WEIGHT CHANGES DURING TREATMENT WITH OLANZAPINE

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SUMMARY:
Objective: To examine if weight changes in olanzapine-treated patients are associated with increased appetite. Methods: Used were data from patients for whom both appetite and weight data were available from 4 prospective, 12- to 24-week clinical trials examining the safety and efficacy of olanzapine (5-20 mg/day) in patients with schizophrenia, schizoaffective disorder, related psychosis, or bipolar disorder. Studies 1 (N=59) and 2 (N=84) were double blind, Study 3 (N=188) was open label, and Study 4 (N=611) was observational. Patients' appetites were assessed with 5 scales: Eating Behavior Assessment (EBA, Study 1); Platypus Appetite Rating Scale (PARS, Study 2); Eating Inventory (EI, Study 3); Food Craving Inventory (FCI, Study 3); and Eating Attitude Scale (EAS, Study 4). Assessed were correlations of overall weight changes with score changes on appetite scales from baseline to 2-4 weeks and baseline to endpoint, and of overall weight changes with 2-week weight changes. Results: In Studies 1 (EBA) and 4 (EAS), patients who reported overall score increases on appetite scales, indicating an increase in appetite, experienced greater overall weight gain than patients reporting no score increases. However, in Studies 2 (PARS) and 3 (EI, FCI), patients who reported overall score increases on appetite scales, indicating increased appetite, did not experience greater weight changes than patients who reported no changes or decreased scores on those scales. Weight changes from baseline to the end of Week 2 of treatment were more positively correlated with overall weight changes than score changes on any appetite assessment scale from baseline to the end of Weeks 2-4. No additional information was gained by adding baseline to 2- to 4-week appetite change to baseline to 2-week weight change in correlation to overall weight change. Conclusions: Our analyses failed to demonstrate a consistent correlation between changes in appetite and weight change during treatment with olanzapine; results varied depending on study and appetite assessment scale. Overall, results suggest that early weight changes may be a better predictor for long-term weight changes than early score changes on appetite assessment scales.

NR6-24

STRATEGY FOR SELECTION OF VARIOUS SWITCHING DOSES FOR OLANZAPINE LONG-ACTING INJECTION

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SUMMARY:
Background: When switching patients to a depot antipsychotic, it is important to minimize risk of destabilization. Relapse data from an olanzapine long-acting injection (LAI) study was assessed to determine the optimal method of switching from oral olanzapine. Methods: Patients with schizophrenia stable on 10 (n=475),

15 (n=236), or 20 mg/day (n=353) oral were randomized to switch directly to 1 of 4 fixed olanzapine LAI doses, or to remain on the stabilized oral dose. Six-month relapse rates and Cox proportional hazard ratios (HR) were used to identify oral-to-LAI switching combinations which allowed patients on LAI to maintain a similar level of clinical stability as those remaining on a stabilized oral dose. Pharmacokinetic simulations were used to evaluate the resulting clinical recommendations. Results: Patients stable on 10 mg/day had relapse rates (6.3%) similar to those switched from 10 mg/day to 405 mg/4-weeks olanzapine LAI (5.7%, HR=1.03). Patients stable on 15 mg/day had relapse rates (5.0%) similar to those switched from 15 mg/day to 300 mg/2-weeks (3.3%, HR=0.68). Patients stable on 20 mg/day had relapse rates (8.2%) similar to those switched from 20 mg/day to 300 mg/2-wks (8.7%, HR=1.13). Pharmacokinetic simulations confirmed the appropriateness of the above oral-to-depot switch regimens for the first 8 weeks of treatment. After 8 weeks, patients switched from 10 mg/day oral to 405 mg/4-weeks should be decreased to a maintenance dose of 150 mg/2-weeks (or 300 mg/4-wks), and patients switched from 15 mg/day oral to 300 mg/2-weeks should be decreased to a maintenance dose of 405 mg/4-weeks (or 210 mg/2-wks) to maintain target olanzapine concentrations. Patients switched from 20 mg/day oral to 300 mg/2-weeks did not need to decrease their dose subsequently. Conclusions: Patients can be switched directly to olanzapine LAI from oral olanzapine without the need for oral antipsychotic supplementation if appropriate starting and maintenance doses are selected.

NR6-25

COST-EFFECTIVENESS OF PALIPERIDONE PALMITATE VERSUS ORAL ATYPICALS AND A CONVENTIONAL DEPOT FORMULATION IN THE U.S.

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SUMMARY:
Objective: To evaluate from a US payer perspective the cost-effectiveness of paliperidone palmitate (PP), a new long-acting therapy, compared with oral atypical antipsychotics (OAPs; olanzapine, quetiapine, aripiprazole and ziprasidone) and haloperidol decanoate (HAL-D) in patients with schizophrenia. Methods: A decision-tree model was constructed to compare the clinical and economic outcomes of PP and each treatment comparator over a 1-year time-horizon. Model input data were sourced from published and unpublished clinical trial data, published medical literature, administrative claims data and clinical expert opinion. Model inputs included rates of compliance, response and relapse, frequency and duration of relapse, AEs, resource use and unit costs. The HCUP database was used to determine mean length of stay for patients with schizophrenia. Unit costs of healthcare resource data were from the PharMetrics Patient-Centric Database. Outcomes were calculated per 100 patients per year (PY) and included number and duration of relapses and total direct medical costs (including medication, hospitalization and related costs). Costs were adjusted to 2009 $US. Results: Mean annual number of relapses per 100 patients was lowest with PP (50 PY) and highest with HAL-D (230 PY) and ranged from 130-150 PY with OAPs. Mean days of hospitalization per 100 patients were 330 PY with PP, 1140-1230 PY with OAPs and 1890 PY with HAL-D. Total annual costs of the different treatment arms were $15,689 PP, $16,562-$18,145 OAPs and $20,445 HAL-D. Possible mean cost-savings from reductions in hospitalizations with PP were $873-$4756 PPPY. Sensitivity analysis of clinical and economic inputs showed that relapse and adherence rates were key drivers of economic consequences. Conclusions: PP in the treatment of schizophrenia may lead to fewer relapses and hospitalization days resulting in potential medical cost-savings versus HAL-D and OAPs.
Supported by Ortho-McNeil Janssen Scientific Affairs, LLC

NR6-26

EFFECTS OF PALIPERIDONE PALMITATE IN ACUTELY ILL SUBJECTS WITH A MARKED TO SEVERE EXACERBATION OF SCHIZOPHRENIA

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SUMMARY:
Background: Effective symptom control is an immediate treatment goal for acutely ill schizophrenia patients, particularly those with marked-severe exacerbation. Paliperidone palmitate (PP) is an atypical antipsychotic given by once-monthly injection. The recommended

initiation dose (234 mg day 1 and 156 mg day 8, both deltoid) was designed to rapidly attain symptom control without oral antipsychotic supplementation. Objective: To assess PP use without oral antipsychotic supplementation in subjects with a marked-severe schizophrenia exacerbation. Methods: Subjects with exacerbated schizophrenia enrolled in a 13-week, double-blind trial (CRO12550) and randomized to placebo or PP (39, 156 or 234 mg). Post hoc analysis assessed subjects with baseline CGI-S scores =5 (markedly ill). PP dose: 234 mg on day 1 (deltoid) and assigned dose on day 8 (deltoid or gluteal) and monthly thereafter. Assessments: PANSS and CGI (baseline, days 4, 8, 22, 36, 64, 92 or end point) and AEs. ANCOVA models compared change scores for the pooled PP arm vs placebo with LOCF methods, without adjusting for multiplicity. Results: 312/636 subjects (49.1%) had marked-severe baseline illness (n=229 PP, n=83 placebo); completion rates 49.8% and 38.6%, respectively. PP associated with significantly greater improvement than placebo by day 4 on mean PANSS total and CGI-S score (both P<0.001); difference continued at all subsequent time points and end point. Most common AEs (=5%; PP vs placebo): insomnia (10.0% vs 15.7%), schizophrenia (8.7% vs 9.6%), agitation (5.2% vs 9.6%), anxiety (6.6% vs 7.2%), headache (11.4% vs 8.4%) and injection site pain (8.3% vs 6.0%). Conclusions: Results suggest that PP improved symptoms without oral antipsychotic supplementation by day 4 in schizophrenia subjects with a marked-severe exacerbation. Significant improvement continued through study end point with once-monthly dosing and no unexpected tolerability findings.

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NR6-27

WITHDRAWN

NR6-28

A THREE ARM DOSE FINDING STUDY OF LURASIDONE: EFFICACY AND TOLERABILITY DATA

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SUMMARY:

Background: Lurasidone is a new atypical antipsychotic agent that has shown superiority to placebo in several registration trials. This compound has also shown a side effect profile notable for minimal metabolic effects and weight gain. Previous short-term, fixed dose studies have not examined daily doses below 40 mg and have been limited to inpatient samples. We report here an 8-week dose-response study of lurasidone that compared 20, 40, and 80 mg/d in a sample of inpatients and outpatients in Japan. Methods: A total of 200 patients with schizophrenia were randomized in double-blind fashion to fixed, single-daily doses of lurasidone for 8 weeks, followed by a 44-week extension period. Assessments included the PANSS, BPRS and CGI. Subjects were switched directly from previous medications without a washout period. If the daily dose of the previous antipsychotic medication exceeded 12 mg/day of haloperidol or its equivalent, the medication was tapered to the 12 mg/day equivalence level prior to switching. Safety assessments included a comprehensive movement disorder measure (DIEPSS), laboratory measures, weight, ECG and vital signs. Results: ANCOVA LOCF analyses demonstrated that single-daily doses of 40 and 80 mg of lurasidone were associated with significant improvements from baseline on the PANSS and the BPRS. The 40 mg/d dose was significantly superior to 20 mg/d on the BPRS. Drop out rates were equivalent across the dose arms, with more dropouts due to lack of efficacy for 20 mg and more for adverse events for the 80 mg dose. Serious adverse events were rare and 5/7 occurred at the 20 mg dose. All three dose arms were associated with decreases in weight that were less than 1.35 kg. In all three arms of the study, 2% or fewer of the patients gained 7% or more in their body weight. In an exploratory analysis for the total sample, patients treated 28 or more days had equivalent improvements across the three medication dosages. In addition, there was a linear apparent dose-response relationship for inpatients, with 80 mg superior, but for outpatients 40 mg appeared to be the optimal dose for clinical response. Discussion: This dose response study indicated that a 40 mg dose of lurasidone had optimal efficacy, but that all three doses had minimal side effects, particularly weight gain.

NR6-29

LONG-TERM EFFICACY OF ASENAPINE IN PEOPLE WITH PERSISTENT NEGATIVE SYMPTOMS OF SCHIZOPHRENIA

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SUMMARY:

Objective: Asenapine is indicated in adults for acute treatment of schizophrenia and manic or mixed episodes associated with bipolar I disorder with or without psychotic features. The efficacy and safety of asenapine for persistent negative symptoms of schizophrenia have been reported in a double-blind olanzapine-controlled 26-week study and a 26-week extension conducted in the Eastern hemisphere. We report the results of a 26-week extension of an identically-designed 26-week trial conducted in the Western hemisphere. Methods: Subjects in the core study were randomized to flexible-dose asenapine (5 or 10 mg BID) or olanzapine (5–20 mg QD) under double-blind and double-dummy conditions. Those completing the core study who would benefit from extended treatment, as blindly judged by investigators, could participate in the 26-week extension on their existing treatment under blinded conditions. The primary endpoint, change from core study baseline to 1 year on the 16-item Negative Symptom Assessment (NSA-16) scale total score, was analyzed using a mixed model for repeated measures. Results: Of 264 subjects completing the core study, 196 (asenapine, 86; olanzapine, 110) entered the extension; 193 (asenapine, 83; olanzapine, 110) comprised the intent-to-treat population; 146 (asenapine, 57; olanzapine, 89) completed 1 year of treatment. Least squares (LS) mean ± SE changes in NSA-16 total score were –15.8±1.48 (mean ± SD at baseline, 62.3±9.81) for asenapine vs –11.0±1.27 (mean ± SD at baseline, 61.0±11.19) for olanzapine (P=0.0148). Quality of Life Scale changes were 12.4±2.05 (mean ± SD at baseline, 45.2±18.72) for asenapine and 11.7±1.73 (mean ± SD at baseline, 42.7±17.42) for olanzapine (P=0.8100). During 1 year of treatment, the incidence of treatment-emergent adverse events (AEs) was 82% with asenapine and 91% with olanzapine (treatment-related AEs: 72% and 74%, respectively). Incidence of extrapyramidal symptoms (EPS) reported as AEs was 24% with asenapine and 10% with olanzapine. The LS mean ± SE weight increase from core study baseline to week 52 was 1.2±0.78 kg with asenapine and 2.2±0.67 kg with olanzapine (P=0.3460). Conclusion: Asenapine was superior to olanzapine in reducing persistent negative symptoms of schizophrenia after 1 year in subjects with >6 months of exposure. Asenapine was well tolerated and associated with moderate EPS incidence and a small weight increase.

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NR6-30

PRELIMINARY RESULTS ABOUT CAREGIVERS' QUALITY OF LIFE OF FIRST-EPISODE PSYCHOSIS PATIENTS IN BRAZIL

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SUMMARY:

Introduction: First Episode Psychosis (FEP) can cause disruption in the family environment and is potentially harmful for caregivers' Quality of life (QoL). Methods: Twenty-eight patients' caregivers of patients consecutively admitted to the FEP program at the Federal University of São Paulo between January 8, 2009 and October 31, 2009 were interviewed by the Short-Form 36 (SF-36), a generic instrument to evaluate QoL, which consists of 8 domains (Functional Capacity, Physical Aspects, Pain, General Health Status, Vitality, Social Aspects, Emotional Aspects, and Mental Health). Patients' psychopathology were assessed at admission with SCID-I and Positive and Negative Syndrome Scale (PANSS). Results: Of the 28 caregivers, 21 were women (75%), and 19 were patients' mothers (67.9%). The mean age was 45.21 (SD: 11.9), 12 unemployed (43.9%) and 23 lived with the patient (82.1%). Regarding QoL the following averages were found for the eight domains: Functional Capacity: 81.60; Physical Aspects: 78.57; Pain: 68.96; General Health Status: 65.46; Vitality: 62.32; Social Aspects: 67.86; Emotional Aspects: 45.24 and Mental Health: 66.71. Of the in FEP patients, 17 were male (60.70%), the mean age was 24.93 (SD: 7.61), 11 with Bipolar Disorder (39.3%), 10 with Schizophreniform Disorder (35.70%) and 7 with other disorders (25%). The means for patients' PANSS were: Positive: 17.32 and Negative: 20.68. Discussion: Family members became the principal caregivers of patients with serious mental disorders in Brazil. FEP is a serious event and it directly affects the family. In this study, we found that FEP patients' caregivers already showed low scores in the beginning of the treatment, mainly in Emotional Aspects. Conclusions: The study of the FEP impact on the caregivers' QoL can identify early the individuals most strongly affected and it can facilitate early preventive measures, besides suggesting that they need support since the beginning of patient treatment. A service for FEP patients should provide assistance for the caregivers and must be aware of their difficulties.

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NR6-31

CAREGIVERS' EGO DEFENSE MECHANISMS IN FIRST-EPISODE PSYCHOSIS

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SUMMARY:

Introduction: Family members have become the main caregivers of individuals suffering from FEP in Brazil. A study of the defense mechanisms and how caregivers cope with the FEP event may be useful for the development of more effective family interventions. Methods: Twenty-eight caregivers of FEP patients consecutively admitted to a FEP Program at the Federal University of São Paulo between January 8, 2009 and October 31, 2009 answered the Self Defense Questionnaire (DSQ-40), an instrument that evaluates 20 ego defenses. The scores of each defense range from 2 to 18: the higher the score, the more ego defenses are employed. Results: Of the 28 caregivers of patients in FEP, 21 were women (75%), and 19 were patients' mothers (67.9%). The mean age was 45.21 (SD: 11.9), 12 unemployed (43.9%) and 23 lived with the patient (82.1%). The following scores were found: Maturity Factor - Anticipation: 12.46; Mood: 9.79; Suppression: 11.04; Sublimation: 11.04; and Rationalization: 12.04. For the Neurotic Factor, we obtained Pseudo-altruism: 10.39; Idealization: 7.39; Reactive formation: 9.5; and Annulation: 10.43. For the Immaturity Factor, we obtained: Projection: 5.68; Passive aggression: 6.61; Acting-out: 7.82; Isolation: 8.43; Devaluation: 7.82; Autistic fantasy: 5.43; Negation: 6.57; Displacement: 6.82; Dissociation: 6.32; Scission: 7.82; and Somatization: 7.43. An analysis of the scores by factors indicates: Mature: 11.27; Neurotic: 9.42 and Immature: 6.92. Discussion: In this study, the mature mechanisms were the most widely employed, nearly followed by the neurotic. With these data, we can assume that family interventions must deal with such neurotic defenses in their structure. Conclusions: Since the caregiver is the key player in the treatment and recovery of FEP patients, understanding the defense mechanisms most commonly employed by these caregivers enables us to develop more adequate psychotherapeutic and psychoeducational strategies for the development of desirable and effective defenses, reducing relapses of FEP patients.
This work was supported by FAPESP. Process number: 2008/10635-5.

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NR6-32

THE SELECTIVE NK3 ANTAGONIST AZD2624 DOES NOT IMPROVE SYMPTOMS OR COGNITION IN SCHIZOPHRENIA

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SUMMARY:

Objective: Increases in midbrain dopamine release in response to neurokinin (NK) receptor activation has led to the hypothesis that NK3 receptor antagonists may have antipsychotic effects, for which there is initial clinical evidence. To test this hypothesis, we examined antipsychotic efficacy and pro-cognitive effects of the NK3 receptor antagonist AZD2624 in symptomatic inpatients with schizophrenia. Methods: One hundred six adult patients with symptomatic DSM-IV schizophrenia were given informed consent, hospitalized in a clinical research unit, and after up to 7 days of washout from previous antipsychotic therapy, randomized to 28 days of treatment (2:2:1 ratio) with either 40 mg/D of AZD2624, placebo, or 15 mg/D of olanzapine under double-blinded conditions. Afterwards, inpatients were stabilized on standard neuroleptic therapy. Endpoints were the change at 28 days in the Positive and Negative Syndrome Scale (PANSS) total score and subscales and the Clinical Global Severity (CGI-S) and Improvement (CGI-I) scales on AZD2624 versus placebo (last observation carried forward). Effects on cognition, including psychomotor

ability, attention and memory were measured using the CogState battery. Safety was assessed utilizing laboratory and ECG measures and reports of adverse events. Data was analyzed using an ANCOVA model with olanzapine used for sample validation only. Results: There were no significant differences between AZD2624 and placebo on changes in symptom ratings or on cognitive measures. Olanzapine-treated patients improved (?PANSS total: -8.24 + 14.84). Conclusions: Despite previous evidence, results for AZD2624 do not support the hypothesis that NK3 receptor antagonists have antipsychotic or pro-cognitive effects in schizophrenia.

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NR6-33

TREATING AGITATION WITH INHALED LOXAPINE (AZ-004): EFFICACY ANALYSES IN PATIENTS WITH SCHIZOPHRENIA OR BIPOLAR DISORDER

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SUMMARY:

Objective: To analyze the components of efficacy from two Phase 3 clinical trials of inhaled loxapine for the treatment of agitation in patients with schizophrenia or bipolar disorder. Methods: Each of the trials was randomized, double-blind, and placebo-controlled. Loxapine was administered via inhalation using the Staccato® system, which delivers thermally-generated drug aerosol to the lungs for rapid systemic absorption with IV-like kinetics. Consenting male and female adults, 18 to 65 years of age, who met DSM-IV criteria for schizophrenia (Study 301) or bipolar I disorder (Study 302), and presented with a relevant degree of agitation at baseline, were enrolled in the studies. A total of 344 patients with schizophrenia (SC) and 314 patients with Bipolar I disorder (BD) received a single inhalation of either 0 mg, 5 mg, or 10 mg of loxapine in an in-patient treatment facility. The primary efficacy assessment was the change from baseline at 2 hours post-dose using the PANSS- Excited Component (PEC) total score. For each study, change from baseline for each of the 5 items comprising the total PEC score (hostility, uncooperativeness, excitement, poor impulse control, tension, each scored 1-7) was determined starting at 10 minutes post-dose. In addition, patients were grouped by baseline severity of agitation (median split) using the total PEC scores for each study, and response rates for the higher and lower agitation populations were compared. Results: Each of the 5 items comprising the PEC scale improved with treatment, starting at 10 – 20 minutes after dosing. On average, each item improved 1-2 units from baseline over the first 2 hours post-dose for both patient groups. The median PEC score at baseline was 17 across the 2 studies. For the 10 mg dose groups, there was on average an 8.3 (SC) and 8.5 (BD) unit improvement for patients < 17 at baseline while there was on average an 8.9 (SC) and 9.7(BD) unit improvement for patients > 17 at baseline. Conclusions: The change in total PEC score observed with inhaled loxapine treatment derives from similar changes in each of the 5 items assessed. AZ-004 reduces agitation equally well in patients with higher or lower levels of agitation at baseline.

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NR6-34

EFFICACY OF LONG-ACTING RISPERIDONE IN PATIENTS WITH SCHIZOPHRENIA: A 6-MONTH FOLLOW-UP FROM THE E-STAR DATABASE IN LATIN AMERICA

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SUMMARY:

Background: Treatment adherence is considered to have a major influence on achieving clinical remission. Risperidone long-acting injection (RLAI) has been shown to be efficacious, improve compliance, and increase long-term retention rate on therapy. Objective: To determine clinical outcomes and hospitalizations before and after the initiation of RLAI in patients with schizophrenia or schizoaffective disorder enrolled in the electronic Schizophrenia Treatment Adherence Registry (e-STAR) in Latin America. Methods: e-STAR is an international, long-term, ongoing, observational study of patients with schizophrenia who start treatment with RLAI. Data were

collected at baseline, retrospectively for the 12 months prior to baseline, and prospectively every 3 months for 24 months. Demographic data, relapses and treatment were registered. Hospitalization prior to therapy was assessed by a retrospective chart review. Efficacy and functioning were evaluated with Clinical Global Impression of Illness Severity (CGI-S), Personal and Social Performance scale (PSP) and Global Assessment of Functioning (GAF) scores. Results: Seventy-nine patients were recruited with the following distribution: Mexico (n=53), Brazil (n=11), Colombia (n=15). Sixty-five percent (n=52) of the patients were male. The mean age was 32.9 years (SD=8.8). Patients were classified as having Schizophrenia (n=73) or Schizoaffective disorder (n=6). The mean dose of RLAI at six months was 34.1 mg (SD=10.2). The CGI-S score improved significantly from 4.19 (SD=1.01) at the beginning of treatment to 3.02 (SD=1.31) at the end of the study ($p<0.001$). The GAF scores increased significantly after treatment with RLAI from 55.7 (SD=1.31) at baseline to 69.9 (SD=16.0) at six months ($p<0.001$). Improvement in PSP scores from baseline to endpoint was greater (49.4, SD=18.5 versus 65.8, SD=18.4, $p<0.001$). The percentage of hospitalized patients before treatment was 28.2% and 5.1% at 6 months after initiating RLAI ($p< 0.001$). Conclusions: RLAI was associated with treatment retention, improvement in clinical symptoms and functioning and greater reduction in hospitalization. The preliminary data indicate that RLAI offer the opportunity of substantial therapeutic improvement in schizophrenia and improve the adherence to medication, a key factor in relapse prevention.

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NR6-35

PERSONALITY DIFFERENCES IN FIRST EPISODE SCHIZOPHRENIA AND BIPOLAR DISORDER

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SUMMARY:

Objectives: To compare "big five" personality trait dimensions in psychiatrically healthy individuals and first episode psychosis (schizophrenia and bipolar disorder). Methods: Clinically stable patients with first episode schizophrenia (22M, 4F) and bipolar disorder (24M, 8F) and psychiatrically healthy subjects (101M, 36F) completed the NEO-FFI personality inventory. The NEO-FFI is a 60-item self-assessment questionnaire that measures the major personality trait dimensions of neuroticism (N), extraversion (E), openness (O), agreeableness (A) and conscientiousness (C); it has good reliability and cross-cultural validity (McCrae RR, Costa PT Jr, Martin TA, Oryol VE, Rukavishnikov AA, Senin IG, Hrebícková M, Urbánek T: Consensual validation of personality traits across cultures. J Res Person 2004; 38:179-201). Gender-specific T-scores were analyzed using standard multivariate statistical techniques. Results: As expected, age correlated with most personality dimensions in the entire sample (N= -.144, p= .045; O= -.169, p= .018; A= .228, p= .001; C = .150, p= .037). MANOVA with dimension scores as dependent variables, diagnosis as a fixed factor independent variable, and age as a covariate demonstrated statistically significant effects for age ($F[5,187]=4.26$, $p=.001$) and diagnostic group ($F[10,376]=10.27$, $p=.000$), and group differences for N, E, A, and C ($F[3,191]>9.40$, $p=.000$). Post hoc contrasts showed that schizophrenia and bipolar groups were statistically similar on N (mean (SE)=59.2(2.02) and 61.7(1.82), respectively), A (45.6(2.37) and 43.3(2.14)), and C (40.0(2.43) and 40.0(2.19)). Compared to both patient groups, comparison subjects were significantly lower on N (43.6(.88), $p=.000$) and higher on A (52.2(1.03), $p<.012$) and C (49.5(1.06), $p=.000$). All three groups differed significantly on E, with schizophrenia subjects scoring lowest (43.9(2.14)), comparison subjects scoring highest (57.0(.93)), and bipolar subjects scoring intermediately (51.7(1.93)) (all $p <$ or $=.014$). No groups differed on O. Conclusions: Personality deviations are present in first episode schizophrenia and bipolar disorder, and are similar to abnormalities previously described in patients with more chronic illness (Bagby RM, Bindseil KD, Schuller DR, Rector NA, Young LT, Cooke RG, Seeman MV, McCay EA, Joffe RT: Relationship between the five-factor model of personality and unipolar, bipolar and schizophrenic patients. Psychiatry Res 1997; 70:83-94).

NR6-36

NEW DIAGNOSTIC CRITERIA FOR NEUROLEPTIC MALIGNANT SYNDROME USING THE DELPHI CONSENSUS TECHNIQUE AND AN INTERNATIONAL EXPERT PANEL

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SUMMARY:
Objectives: To develop consensus-based clinical diagnostic criteria for neuroleptic malignant syndrome (NMS). Methods: A 17-member international expert panel of psychiatrists, neurologists, anesthesiologists and emergency medicine specialists was asked to identify clinical features that are most important or valuable in diagnosing NMS; when the feature was quantitative in nature, they were also asked to provide the corresponding critical value. The Delphi technique is a formal consensus procedure that employs a postal survey method to solicit opinions from each panel member, and to feed this information back to the entire panel in the form of anonymous, statistically aggregated data. This iterative process of information exchanges (opinions collected, group responses analyzed, feedback given to panel), or "rounds," continues until consensus has been reached (Milholland et al, 1973; Graham et al, 2003). In the present study, the predetermined consensus criterion was a round-round mean change of 10% or less for any survey item, and 5% or less across all items. Results: The expert panel reached consensus on the following diagnostic criteria in five iterations: (1) exposure to a dopamine antagonist, or dopamine agonist withdrawal, within past 72 hours; (2) hyperthermia; (3) rigidity; (4) mental status alteration; (5) creatine phosphokinase elevation; (6) sympathetic nervous system lability (two or more of blood pressure elevation, blood pressure fluctuation, diaphoresis, urinary incontinence); (7) tachycardia and tachypnea; and (8) negative work-up for infectious, toxic, metabolic and neurological causes. Conclusions: These are the first consensus-based diagnostic criteria for NMS, and may be preferred to existing ad hoc approaches to diagnosing this disorder.

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NR6-37

LONG-TERM SAFETY AND EFFICACY OF ASENAPINE VERSUS OLANZAPINE IN PATIENTS WITH SCHIZOPHRENIA OR SCHIZOAFFECTIVE DISORDER

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SUMMARY:
Objectives: Asenapine is indicated in adults for the acute treatment of schizophrenia and manic or mixed episodes associated with bipolar I disorder with or without psychotic features. Here, we describe the long-term safety and efficacy of asenapine versus olanzapine in patients with schizophrenia or schizoaffective disorder treated for up to 3 years. Methods: A 1-year, double-blind, randomized core study tested the safety and efficacy of asenapine (5 or 10 mg BID) versus olanzapine (10–20 mg QD). Patients completing the core study, and willing to continue treatment, received up to an additional 2 years of double-blind treatment. Safety evaluations included adverse events (AEs), vital signs, body weight, and extrapyramidal symptoms (EPS). Efficacy in observed cases from the intent-to-treat population was assessed as the change in Positive and Negative Syndrome Scale (PANSS) total score. Results: In 440 enrolled patients (asenapine, 290; olanzapine, 150), the mean ± SD daily dose was 13.4±4.1 mg for both asenapine and olanzapine; total exposure duration (including core study exposure) was 676.3±148.1 and 692.5±140.7 days for asenapine and olanzapine, respectively. Of the 114 patients (asenapine 87; olanzapine 27) who discontinued treatment during the extension, the most common reasons were withdrawn consent (asenapine, 11.0%; olanzapine, 12.7%) and AEs (10.3%; 2.0%). Mean weight gain from core study baseline was 1.6 kg with asenapine and 5.0 kg with olanzapine; incidence of clinically significant weight gain (>=7% increase from core study baseline) was 28% and 40%, respectively. The incidence of EPS-related AEs during the entire treatment period was 20% with asenapine and 11% with olanzapine (during extension alone: asenapine, 4.5%; olanzapine, 3.3%). AEs occurring in >=10% of patients treated for up to 3 years will be listed. Mean ± SD changes in PANSS total score over the course of the extension study were 1.7±11.0 with asenapine and –0.8±9.5 with olanzapine. Conclusions: Asenapine and olanzapine were well tolerated and maintained efficacy in patients receiving up to 3 years of treatment.
Supported by Schering Corp., a Division of Merck & Co., and by Pfizer Inc.

NR6-38

TIME TO NEGATIVE SYMPTOMS REMISSION AND PSYCHOSOCIAL FUNCTIONING IN SCHIZOPHRENIA: A 196-WEEK DOUBLE-BLIND STUDY OF ZIPRASIDONE VERSUS HALOPERIDOL

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SUMMARY:
Objective: Schizophrenia is a persistent, lifelong illness such that enduring functional improvements may only occur over the course of years. Our study objective was to conduct a post-hoc analysis of negative symptom remission and sustained functional recovery using a double-blind, randomized 40-week study of ziprasidone (80-160 mg/d - ZIPSTD; or 80-120 mg/d - ZIPLOW) versus haloperidol (5-20 mg/d - HAL), followed by a double-blind extension trial for 156 weeks. Method: Negative symptom remission criteria were met when subjects attained a rating of <3 for mild or less on all PANSS N1 to N7 items for at least 6 months. Sustained adequate functioning status was met when subjects attained a score >4 on all components of each of the 4 QLS subscales for 6 months: instrumental role, everyday objects and activities, interpersonal relations, and intrapsychic foundations. Cox survival models were applied to estimate relative benefits of ziprasidone versus haloperidol treatment for attaining negative symptom remission and adequate functioning status. Results: Both the ZIPSTD and ZIPLOW dose groups showed significantly greater likelihood of attaining negative symptom remission than the HAL group (NNT for attaining negative symptom remission=4, p=0.005; NNT=8, p=0.024, respectively). The ZIPSTD group had significantly greater likelihood of attaining sustained adequate functioning in instrumental role (occupation role, work functioning, work level, and work satisfaction) (p=0.04, NNT=6), and participation in the community (everyday activities) for 6 months (p=0.02, NNT=8) (vs. HAL). The ZIPLOW group showed significantly greater likelihood (versus the HAL group) of attaining adequate instrumental role functioning (but not other QLS subscales) (p=0.03, NNT=6). Conclusions: These findings support the potential for enhanced symptom remission and improved social and functional outcomes during long-term treatment with an atypical antipsychotic.
Supported by funding from Pfizer Inc.

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NR6-39

SHORT-TERM TOLERABILITY, SAFETY, AND PHARMACOKINETIC PROFILE OF ASENAPINE IN OLDER PATIENTS WITH PSYCHOSIS

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SUMMARY:
Objective: Asenapine is indicated in adults for acute treatment of schizophrenia and manic or mixed episodes associated with bipolar I disorder. We report short-term tolerability, safety, and pharmacokinetic (PK) profiles of asenapine in elderly patients with psychosis. Methods: This 6-week randomized trial enrolled patients aged =65 years with psychotic symptoms (not related to dementia), defined as a Positive and Negative Syndrome Scale (PANSS) score =4 on =1 of 5 predefined items (delusions, hallucinatory behavior, excitement, hostility, poor impulse control), PANSS total score >50, and Clinical Global Impression-Severity of Illness score =3. After a washout of =3 days, sublingual asenapine was given in 2 treatment schedules: 2 days at 2 mg BID, 2 days at 5 mg BID, and 10 mg BID thereafter; or 4 days at 5 mg BID and 10 mg BID thereafter. Tolerability and safety assessments included adverse events (AEs), anthropometric indices, and extrapyramidal symptoms (EPS). Asenapine PK profiles were assessed using samples taken on treatment days 3, 4, 7, 8, 21, and 42 (before the morning dose) and 0.5–12 hr after the morning dose on days 4 and 8. Results: Of 122 randomized patients (mean age, 71.2 y), 76 (62%) completed the trial. Tolerability was comparable with either treatment schedule. The overall incidence of treatment-emergent AEs was 72%. AEs reported by =5% of patients included hypertension (8.2%), headache (6.6%), and somnolence (6.6%); incidence of EPS-related

AEs was 5.7%. Mean weight change at endpoint was 0.4 kg; clinically significant weight gain was reported in 2 patients (1.6%). Median times to maximum asenapine concentration at 5 and 10 mg BID were 1.00 and 1.06 hours, respectively. Maximum asenapine concentrations (Cmax) at 5 and 10 mg BID, as measured by the geometric mean, were 4.73 and 7.93 ng/mL. Area under the curve from 0–12 hours at 5 and 10 mg BID was 32.1 and 56.3 ng?h/mL. Conclusions: Compared with previous findings in patients aged <65 years (asenapine Cmax: 4.23 ng/mL at 5 mg BID, 6.56 ng/mL at 10 mg BID), exposure was 12%–30% higher in elderly patients, indicating lower drug clearance in these patients. Despite the increased exposure, short-term asenapine treatment was generally well tolerated in elderly patients with psychosis during rapid dosage escalation. Supported by Schering Corp., a division of Merck & Co.

NR6-40

COMPARATIVE RECEPTOR BINDING PROFILE OF LURASIDONE AND OTHER FIRST AND SECOND GENERATION ANTIPSYCHOTICS

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SUMMARY:
Objective: To characterize the receptor binding profile of lurasidone compared to currently available first and second generation antipsychotics. Methods: Under comparable assay conditions using a membrane preparation from animal brain tissues or cells expressing cloned human receptors, binding affinities were evaluated for lurasidone and other antipsychotics. Results: Lurasidone was a full antagonist at dopamine D2 (Ki, 0.99 nM) and 5-HT7 (Ki, 0.49) receptors with affinities that were among the most potent of all tested antipsychotics. Lurasidone also had a higher affinity (antagonist) for 5-HT2A (Ki, 0.47) receptors than several other antipsychotic agents. Lurasidone is a weak partial agonist of 5-HT1A (Ki=6.4 nM). Among receptors with the potential for causing adverse events, lurasidone had one of the more favorable profiles among tested antipsychotics, with moderate affinity for a2C adrenoceptors (Ki, 10.8), and minimal affinity for a1 adrenoceptors (Ki, 48)--only olanzapine had lower a1 adrenoceptor affinity. Lurasidone had minimal affinity for 5-HT2C receptors (Ki, 415)--only haloperidol and quetiapine had lower 5-HT2C receptor affinity. Lurasidone had no affinity for histamine H1 (>1000) and cholinergic M1 (Ki>1000) receptors. In contrast, clozapine (Ki, 14), olanzapine (24) and asenapine (24) had more potent affinity for M1 receptors. Lurasidone also exhibits a high selectivity for the D2 receptor subtype compared to the D1 (264-fold higher), D3 (16-fold higher) and D4 (30-fold higher) receptors. Conclusion: The receptor binding profile of lurasidone is distinguished by its potent and selective antagonist activity at the D2 receptor, coupled with equally potent antagonist activity at both 5-HT7 and 5-HT2A receptors. This profile would be expected to be associated with antipsychotic efficacy, a low likelihood of EPS effects, a reduced potential for weight gain and related metabolic consequences, and the potential for mood enhancing and procognitive effects.
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NR6-41

REDUCTION OF HOSPITALIZATION IN PATIENTS INITIATED ON RISPERIDONE LONG-ACTING INJECTION IN THE U.S., SPAIN, AUSTRALIA AND BELGIUM

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SUMMARY:
Background: The purpose of this analysis was to describe the change in psychiatric hospitalization rates in patients with schizophrenia who were newly initiated on risperidone long-acting therapy (RLAT) in the US, Spain, Australia and Belgium. US data were from the Schizophrenia Outcomes Utilization Relapse and Clinical Evaluation (SOURCE) study. Spain, Australia and Belgium data were from the multinational electronic Schizophrenia Treatment Adherence Registry (eSTAR). Methods: The studies in each country were 2-year prospective, observational studies that collected resource use data on newly initiated RLAT patients. This analysis was a side-by-side description of the rates of psychiatric hospitalization. The number of psychiatric hospitalizations per person-year (PPPY) among patients with at least 1 postbaseline visit was evaluated. Differences within countries before and after initiation of RLAT were tested using bootstrap resampling to obtain P

values and confidence intervals. No statistical comparison between countries was done because of intrinsic differences in hospitalization rates among regional healthcare systems. Results: Ages ranged from mean (SD) 37.1 (12.5) to 41.9 (12.6) years, and from 62.8% to 69.9% of patients were male. The preperiod incidence density analysis showed 0.63 psychiatric hospitalizations PPPY in the US, 0.32 in Spain, 1.34 in Australia and 0.71 in Belgium. The rate of psychiatric hospitalizations PPPY decreased significantly in all 4 countries (P<0.001) after RLAT was initiated. In the US (n=435), Spain (n=1339) and Australia (n=734), the decline was approximately 50%, whereas in Belgium (n=393), the decline was 29.6%. Conclusion: Despite differences in healthcare systems across nations, in these samples of patients with schizophrenia there was a significant decline in psychiatric hospitalization after initiation of RLAT in all 4 countries.

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NR6-42

EFFICACY AND SAFETY OF QUETIAPINE FOR DEPRESSIVE SYMPTOMS IN PATIENTS WITH SCHIZOPHRENIA

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SUMMARY:

Methods: Thirty-nine patients fulfilling DSM-IV-TR diagnostic criteria for schizophrenia and having depressive symptoms were studied in a prospective 6-week open-label design using quetiapine monotherapy. Quetiapine was initiated at 100–800 mg/day (baseline) and titrated upwards in response to the clinical status of the patient by the treating psychiatrist. The brief psychiatric rating scale (BPRS), 17-item Hamilton depression rating scale (HAMD-17), Simpson-Angus rating scale, and the Barnes Akathisia rating scale (BARS) were used to assess patients at baseline, week 1, 2, 4, and 6. Results: Thirty patients (76.9%) completed this study. The dose of quetiapine at endpoint was 583 (±235 SD) mg/day. Treatment with Quetiapine was associated with significantly reduced depressive symptoms (HAMD-17 total score and BPRS depression/anxiety subscale) from the first week of treatment. Changes of mean score from baseline to endpoint were 7.8 ± 6.2 for HAMD-17 total score and 3.4 ± 3.6 for BPRS depression/anxiety subscale (LOCF, $n = 39$, $p < 0.001$). Quetiapine was well tolerated, with minimal extrapyramidal symptoms and non-significant increase in body weight (mean increase of 0.8 kg).

Conclusion: While the interpretation of findings from the open-label design of this study warrants appropriate caution, the results suggest that quetiapine may be an effective and tolerable treatment for depression in patients with schizophrenia.

NR6-43

RATES OF LEUKOPENIA AND AGRANULOCYTOSIS ASSOCIATED WITH CLOZARIL TREATMENT DURING 19 YEARS OF BLOOD MONITORING BY THE CLOZARIL NATIONAL REGISTRY

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SUMMARY:

Introduction: In 1990, the Clozaril National Registry (CNR) was established to record and track patient WBC values as a condition of dispensing Clozaril. The objective of the current analysis was to examine the rates of leukopenia and agranulocytosis associated with Clozaril at various time points during 19 years of monitoring. Methods: CNR data were analyzed for rates of moderate and severe leukopenia during 3 time periods when the mandatory WBC monitoring frequency was: a) weekly b) weekly for the first 26 weeks of Clozaril treatment, then every 2 weeks and c) monthly after at least 12 months of treatment and after monitoring every 2 weeks for at least 6 months. The incidence rates of agranulocytosis for the same 3 analysis periods were calculated using data from the Novartis Global Safety database. Results: For the first 8 years of the CNR, during which time WBC monitoring was performed on a weekly basis, the incidence rates of agranulocytosis, severe leukopenia, and moderate leukopenia were 1.06%, 2.34% and 12.44% respectively. From 1998 to 2005, during which time the frequency of WBC monitoring had been reduced, the incidence of agranulocytosis was markedly lower (0.15%), as were the rates of severe leukopenia (0.56%) and moderate leukopenia (4.79%). From 2005 to 2009, during which time the frequency of WBC monitoring had been further reduced, the incidence of agranulocytosis was again markedly lower (0.05%) as were the rates of severe leukopenia (0.65%) and moderate leukopenia (1.79%). Over the 19 years of WBC monitoring by the CNR, the incidence rate of agranulocytosis was 0.45%. Conclusion: The results demonstrate the effectiveness of the CNR, despite reductions in the frequency of WBC monitoring,

in markedly reducing the incidence rates of moderate leukopenia, severe leukopenia and agranulocytosis associated with Clozaril treatment, through early detection of clinically meaningful decreases in WBC values.
Funded by Novartis Pharmaceuticals Corporation.

NR7-01

GENDER-SPECIFIC EFFECTS OF PREMATURE BIRTH ON THE RISK FOR ALCOHOLISM GREATER IN MALES THAN FEMALES: A 45-YR DANISH BIRTH COHORT STUDY

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SUMMARY:
Objective: A large Danish birth cohort was used to test the independent and joint effects of perinatal measures associated with premature birth on the development of alcoholism in male and female subjects. Method: Subjects were born at the State University Hospital in Copenhagen, Denmark between 1959 and 1961 (N=9,125). A comprehensive series of measures were obtained for each of the 8,109 surviving infants before, during, and shortly after birth as well as at 1 year of age. The adult alcoholism outcome was defined as any ICD 10 F10 (Mental and Behavioral Disorders Due to Alcohol Use) or equivalent ICD 8 diagnosis extracted from the Danish Central Psychiatric Register or the Municipal Alcohol Clinics of Copenhagen by 2007. Results: Multiple perinatal markers of premature birth independently predicted the development of alcoholism in male but not female subjects. Low birth weight (p=0.0001), small body length (p=0.0004), small head circumference (0.0339), premature gestational age (p=0.0079) and a higher derived summary or global prematurity score (p=0.0005) were all associated with a significant increase in the likelihood of finding an alcoholism diagnosis among male subjects. Because the measures of prematurity were highly correlated, stepwise logistic regression modeling of the effects of the global prematurity score on alcoholism was performed, controlling for social status, maternal smoking and gender. The final model was significant (Wald=102.7, p< 0.0001) which included a significant prematurity score by gender interaction (p<0.0196). Modeled in male and female subjects separately after controlling for maternal smoking and social status, increases in the global prematurity score significantly increased the odds ratio for alcoholism in male subjects (OR=1.162, 95% CI 1.031-1.310) but not for female subjects (OR=1.041, 95% CI 0.862-1.257). Conclusions: The results suggest that the neurodevelopmental sequella of premature birth has gender-specific effects on the risk for alcoholism in the male baby: small, premature or growth- delayed male babies appear to be selectively vulnerable to alcoholic drinking years later. The findings implicate neurodevelopmental influences in the pathophysiology of alcoholism in males, suggesting that distinct, gender-specific pathways are implicated in the development of alcoholism.

NR7-02

DIAGNOSTIC ASPECTS OF PATHOLOGICAL INTERNET USE: A PROSPECTIVE STUDY ON PSYCHIATRIC PHENOMENOLOGY AND COMORBIDITY OF INTERNET DEPENDENCY

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SUMMARY:
Background and Objectives: With the rapid growth of Cyberspace, questions arise about its mental impacts. The presented study examines the question of whether the dependent use of the Internet can be understood as an impulse control disorder, an addiction or as a symptom of other psychiatric conditions. Methods: Patients seeking psychiatric assistance and fulfilling the criteria for pathological Internet use (1) were examined with the Structured Clinical Interview according to DSM-IV (SCID), and a variety of questionnaires including the Barrat Impulsiveness Scale (BIS), the Beck Depression Inventory (BDI) and the Dissociative Experience Scale (DES). The patient group was compared to a group of healthy controls matched in terms of sex, age and educational level. Results: The adult patient-group consisted of 25 subjects, 76 % male, with an average age of 29.36 years (SD=9.56). The average time spent in Cyberspace was 6.47 h/d (SD=4.07), mostly in massively multiplayer online role-playing games (MMORPG) and online first person shooters. According to SCID and BDI, 19 patients (76%) suffered from a depressive syndrome, with 10 cases of major depressive disorder (40%) and 8 cases of adjustment disorder with depression (32%). Compared to healthy control subjects, the patient group

presented significantly higher levels of depression (BDI), impulsivity (BIS) and dissociation (DES). Nine patients (36%) met the criteria for a personality disorder, eleven patients (44%) for an accentuated personality structure, with personality types from cluster B (dramatic-eccentric) dominating in 14 cases (56%). Six patients (24%) suffered from a comorbid anxiety disorder. Only two patients (8%) reported former substance abuse. Conclusions: Despite high rates of comorbidity (2), Internet and computer game dependency in adults do not only appear to be a symptom of other known psychiatric conditions, but can be viewed as a diagnostic entity in itself. Especially the combination of Computergames played in the Internet seems to contain an addictive potential comparable to substance abuse disorders.

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NR7-03

CHARACTERISTICS, PERSISTENCE AND OUTCOMES OF INSURED PATIENTS TREATED WITH EXTENDED-RELEASE NALTREXONE (XR-NTX) OR ORAL MEDICATIONS

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SUMMARY:

Objective: To examine utilization and cost outcomes of insured patients treated with psychosocial treatment alone or prescribed one of four different FDA-approved alcoholism medications. Methods: This naturalistic, retrospective analysis examined MarketScan® insurance claims data across many states and insurance plans. Patients had a claim for either psychosocial treatment alone, XR-NTX or an oral medication between July 2006 and Dec 2008. Patients were =18 yrs, continuously enrolled for =6 months pre- and post-index and had claims for =1 oral agent in the 3 months before index. Patient differences on demographic, clinical and service utilization variables were controlled for with propensity-score matching. Results: During the six month pre-period, XR-NTX patients (N=295) were more likely to have a diagnosis of an alcohol or drug use disorder, a diagnosis of bipolar disorder or depression, a psychiatrist visit, a detoxification admission or an alcoholism-related admission than patients treated with oral naltrexone (N=2,064), disulfiram (N=2,076) or acamprosate (N=5,068). Mean refill persistence on XR-NTX was approximately 81 days vs. approximately 73 days for oral agents. A greater pre-post reduction in detoxification days and alcoholism-related inpatient admission days was observed among patients treated with medication. Among these, XR-NTX was associated with significantly lower costs (per 1000 patients) versus oral naltrexone, disulfiram and acamprosate (Detox: $0.60-million vs. $1.48-million, $1.08-million, $1.40-million; respectively; P<0.01 for XR-NTX vs. naltrexone and acamprosate). Conclusion: In the largest real-world sample to date, patients prescribed medication had significantly and substantially less intensive medical service utilization. Of the approved medications, XR-NTX was associated with more persistence and larger reductions in alcoholism-related health care utilization.

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NR7-04

MISIDENTIFIED CONTENT AND CONTAMINANTS: FURTHER RISKS OF UNDERGROUND ANABOLIC STEROID USE

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SUMMARY:

Background: Current estimates place the number of anabolic steroid users in the United States at over 1 million. Demand for anabolic steroids to improve appearance and enhance athletic abilities remains high despite strong efforts to restrict use. Most users obtain anabolic steroids illicitly, and, as steroid manufacture is controlled in nearly all countries, through so-called "underground labs." These labs are unregulated and not subject to any established

form of pharmaceutical quality control or testing. High profits have also spurred on an increasing amount of anabolic steroid counterfeiting. Methods: A literature search was conducted using PubMed for studies involving the chemical analysis of illegally obtained anabolic steroids. In addition, further internet searches for independent, verifiable assays of black market anabolic steroids were conducted. For inclusion, laboratory methods had to be clearly identified and in accord with accepted standards. Results: There were 217 lab tests which were eligible for inclusion in this analysis. Assays revealed that 29.6% of black market anabolic steroids did not contain any of their purported drug, and there were frequent substitutions of other steroids. Of the steroids which were correctly labeled, nearly half (44.4%) contained dosages which were at least 20% in error, with a range of 0.75% to 460% of labeled content. Heavy metal contaminants (tin, lead, arsenic) were found in 20% of samples tested; on rare occasions, other potentially harmful chemicals, including some carcinogens, were found. Additional analysis raised concerns over sterility of product, as a number of samples were revealed to have infectious bacteria. Conclusions: Misrepresentation of anabolic steroid content is widespread in the black market, and as the vast majority (more than 90%) of steroid users obtain their drugs illicitly, they are at risk of previously unrecognized dangers associated with use. Use of substituted steroids or steroids at dosages other than intended may have significant consequences. Steroids with heavy metal or bacterial contaminants have clear public health implications. Physicians should be aware of and counsel their patients of the potential complications of the use of steroids obtained on the black market. Health risks of use of incorrectly labeled and contaminated steroids merits further recognition and treatment.

NR7-05

AN UPDATE ON TESTING FOR DRUGS OF ABUSE: SCIENTIFIC BACKGROUND AND PRACTICAL CLINICAL CONCERNS

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SUMMARY:

Introduction: Testing for drugs of abuse is a common and accepted practice in psychiatry. It is a recommended component of treatment for those with substance use disorders, and, given the high co-morbidity between several psychiatric conditions and substance abuse, routine screening tests for drugs of abuse are suggested in several published guidelines. Despite the ubiquity of testing for drugs of abuse there is often little discussion regarding either the basic laboratory science which makes testing possible or the statistical methods behind test interpretation. The central concepts involved in testing for drugs of abuse provide a rich opportunity for instruction in multiple areas of interest to psychiatrists which extend far beyond substance use disorders and include pharmacodynamics and pharmacokinetics, immunochemistry, sensitivity and specificity, and Baye's theorem, among others. In addition, there are several issues which frequently arise in clinical practice involving testing for drugs of abuse, such as the possibilities of false positive or false negative results, as well as the use of adulterants or other ways of defeating drug testing. Given the significance drug testing results often have in making clinical decisions, these issues also merit an informed and comprehensive discussion. Methods: A PubMed search was performed from January 1, 1980 to September 1, 2009 for literature regarding drug screening and testing. Further reports were identified through references cited in the PubMed search described above. Articles were then reviewed for relevancy and utility. Common substances identified with false positive results were noted, as well as conditions which would lead to a false negative test. Frequent methods of thwarting drug testing were also identified. Conclusions: The topic of testing for drugs of abuse offers a wealth of opportunities for instruction in both basic and clinical sciences which is all too frequently overlooked. In addition, practical clinical considerations involving drug of abuse testing are common. Clinicians should be aware of common substances which are associated with false positives on drug testing, as well as frequently employed methods and substances to defeat drug testing. They should also know the limitations of drug testing and recognize the importance of these limitations in clinical practice.

NR7-06

EFFICACY AND SAFETY OF EXTENDED-RELEASE INJECTABLE NALTREXONE (XR-NTX) FOR THE TREATMENT OF OPIOID DEPENDENCE

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SUMMARY:
Objective: To evaluate the efficacy and safety of once-monthly XR-NTX injections in maintaining an opioid-free state in opioid-dependent patients after detoxification. Methods: Patients who had completed a detox within the previous week, and were off all opioids for >7 days were randomized to 24 weeks of double-blind treatment with monthly IM XR-NTX 380 mg or placebo (PBO). The primary efficacy outcome was the response profile based on the rate of urine test results negative for opioids during the last 20 weeks of the 24-week DB treatment period. Secondary outcomes included retention, physiologic evidence of opioid dependence per naloxone challenge and a visual analog scale (VAS) of craving. Results: Patients were randomized to XR-NTX (N=126; mean age, 30 years; male, 90%) or PBO (N=124; mean age, 30 years; male, 86%). Mean (±SD) duration of opioid dependence was 10 (±4) years. A significantly higher proportion of XR-NTX patients versus PBO had opioid negative urines during the final 20 weeks of double-blind treatment (median: 90% vs. 35%; P=0.0002, van der Waerden test). Significantly more patients completed treatment with XR-NTX (N=67; 53%) versus PBO (N=47; 38%; CMH chi square, 5.69; P=0.017). Incidence of positive naloxone challenge was also significantly lower on XR-NTX (P<0.0001, Fisher's exact). XR-NTX (versus PBO) was also associated with significantly greater reduction in the VAS-craving score from Week 8 (-9.7 vs. -0.5; P=0.0048) through Week 24 (-9.4 vs. +0.8; P=0.0029). There were no significant between-group differences in the incidence of clinical adverse events, and no severe adverse events or premature discontinuations due to adverse events during treatment with XR-NTX. Conclusions: Once-monthly treatment with extended-release injectable naltrexone was generally well-tolerated and demonstrated clinically important efficacy in terms of reduced opioid use, decreased opioid craving and improved treatment retention in opioid-dependent patients.
Study sponsored by Alkermes, Inc.

NR7-07

LONGITUDINAL ASSOCIATIONS BETWEEN EARLY EMOTIONAL PROBLEMS, BEHAVIOURAL PROBLEMS AND SUBSTANCE USE: 20-YEAR FOLLOW-UP OF A FINNISH BIRTH COHORT

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SUMMARY:
Objective: Adolescence is the time for onset of substance use and mental health problems. We studied longitudinal associations between early emotional and behavioural problems and the initiation of substance use among adolescents. Methods: The sample was a population-based Northern Finland 1986 Birth Cohort (n= 6,349; 3,103 males). Subjects' emotional (internalising) and behavioural (externalising) problems were assessed with Rutter B2 Scale (teachers' ratings at age 8) and Youth Self-Report at age 15 to 16. Information related to substance use was collected by self-reports at the age of 15 to 16 years. In the follow-up, we recorded adolescents' hospital diagnoses for emotional disorders and their violent and property offences until the age of 20 years. Results: Behavioural problems at age 8 were associated (P<0.05) with later smoking and "other substance use" (mainly medicines for intoxication and solvents, adjusted Odds Ratios, OR, between 1.7 and 2.3). Early emotional problems were not a risk for later substance use, while current self-reported behavioural problems highly correlated with substance use at adolescence. Cannabis use among girls predicted emotional disorders in the follow-up, when adjusted for several covariates this association remained significant (OR = 5.9; 95% Confidence Interval: 1.9 to 18.8). Among boys, regular smoking (OR=2.9; 1.5-5.7) and cannabis experimentation (OR=2.5; 1.1-5.9) predicted later criminality. Conclusions: Mental health problems and substance use are strongly associated in adolescence and early adulthood. Behavioural problems often both precede and follow substance abuse, whereas emotional problems do not precede adolescent substance abuse, but may follow it, especially among girls.

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NR7-08

CHARACTERISTICS, PERSISTENCE AND OUTCOMES OF INSURED PATIENTS TREATED WITH EXTENDED-RELEASE NALTREXONE (XR-NTX) OR ORAL MEDICATIONS

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SUMMARY:

Objective: To examine utilization and cost outcomes of insured patients treated with psychosocial treatment alone or prescribed one of four different FDA-approved alcoholism medications. Methods: This naturalistic, retrospective analysis examined MarketScan® insurance claims data across many states and insurance plans. Patients had a claim for either psychosocial treatment alone, XR-NTX or an oral medication between July 2006 and December 2008. Patients were =18 years, continuously enrolled for =6 months pre- and post-index and had claims for =1 oral agent in the 3 months before index. Patient differences on demographic, clinical and service utilization variables were controlled for with propensity-score matching. Results: During the six month pre-period, XR-NTX patients (N=295) were more likely to have a diagnosis of an alcohol or drug use disorder, a diagnosis of bipolar disorder or depression, a psychiatrist visit, a detoxification admission or an alcoholism-related admission than patients treated with oral naltrexone (N=2,064), disulfiram (N=2,076) or acamprosate (N=5,068). Mean refill persistence on XR-NTX was approximately 81 days versus approximately 73 days for oral agents. A greater pre-post reduction in detoxification days and alcoholism-related inpatient admission days was observed among patients treated with medication. Among these, XR-NTX was associated with significantly lower costs (per 1000 patients) versus oral naltrexone, disulfiram and acamprosate (Detox: $0.60-million versus $1.48-million, $1.08-million, $1.40-million; respectively; P<0.01 for XR-NTX versus naltrexone and acamprosate). Conclusion:. In the largest real-world sample to date, patients prescribed medication had significantly and substantially less intensive medical service utilization. Of the approved medications, XR-NTX was associated with more persistence and larger reductions in alcoholism-related health care utilization.

Sponsored by Alkermes, Inc; and by NIAAA grant K24 AA13736 (Dr. Kranzler)

NR7-09

WITHDRAWN

NR7-10

WITHDRAWN

NR7-11

THE DIAGNOSTIC AND ABSTENTION SUPERVISION WITH MARKERS OF ALCOHOL DEPENDENCY

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SUMMARY:

In our study we wanted to confirm the alcohol dependency by means of questionnaires and laboratory markers according to time and the mean of monitoring changes in the activity of laboratory markers of alcoholism as an effective yet overlooked aid. Investigated were 68 (92.6% males, 7.4% females) general-practice healthy patients and blood donors and 186 (89.2% males, 10.8% females) inpatient alcoholics. A blood sample was taken once from every healthy subject and three times to every alcoholic: on admission to hospital, after 12 days and again after 42 days. In alcoholics we found statistically significantly elevated CDT, glutamate dehidrogenase (GLDH), aspartate-aminotransferaze (AST), alanine-aminotransferaze (ALT), gama-glutamyl transferaze (GGT) and mean corpuscular volume (MCV) and decreased urea values. CDT was the most reliable marker with high specificity (91.2%) and sensitivity (81.4%). The area under ROC-curve was exceptional with 99.9%. The kinetics of CDT, AST, ALT, GGT, MCV and creatinine normalisation after 14 days were also statistically significant as well as kinetics of CDT, AST, GGT, MCV and creatinine normalization after 42 days. We estimated the course of CDT value normalisation as the most applicable. The most important diagnostic marker's combination was composed of CDT, MCV and AST. GGT had lower importance as expected. Pathological values return to reference values if the alcohol-dependent person abstains. Direct biochemical supervision over the maintenance of abstinence from last drink could be performed by the normalization of the activity of particular markers.

NR7-12

PRELIMINARY EVALUATION OF EXTENDED-RELEASE NALTREXONE (XR-NTX) IN MICHIGAN AND MISSOURI DRUG COURTS

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SUMMARY:
Objectives: Drug courts are designed for offenders who commit crimes while under the influence of drugs or alcohol. XR-NTX was designed to be a once-monthly injection, which theoretically might facilitate treatment for alcohol dependence in criminal justice. This pilot study examined the feasibility and effectiveness of treatment with XR-NTX in the drug court setting. Methods: Data were collected on clients treated with XR-NTX and a similar number of matched controls (i.e., no XR-NTX) from 4 courts in Michigan (2 drug courts; 2 DUI-specific courts; combined annual clients, 3,789) and 3 courts in Missouri (1 drug court; 2 DUI-specific courts); combined annual clients, 382. Treatment with XR-NTX was open-label, voluntary and was combined with psychosocial treatment. Referral was primarily for treatment of alcohol dependence, with some cases of concurrent alcohol dependence and other drug use disorders. Referrals came from judges, probation officers, court coordinators and treatment providers. All of the clients were considered by the courts to be the most difficult cases, and typically had been charged with previous DUI offenses. Results: An initial sample of 51 clients was identified. Compared to the control group, treatment with XR-NTX was associated with a reduction in new arrests while under drug court supervision (OR=0.224) and in the number of new arrests per month (OR=0.327). Treatment with XR-NTX was also associated with a reduction in the average proportion of positive alcohol screening tests per month (OR=0.242) and a reduction in the number of missed drug court sessions (OR=0.388). Conclusions: The current pilot sample was difficult to obtain, suggesting why effectiveness research in this setting is so rare. Nonetheless, treatment with XR-NTX appeared to be feasible and was associated with a consistently large treatment effect across multiple outcomes relevant to the drug court setting.
Treatment of the Missouri clients was funded by a grant from the State of Missouri. Drug court evaluation sponsored by Alkermes, Inc. under a contract with NPC.

NR7-13

ALCOHOL USE AND ADDITION OF LOW DOSE NALTREXONE IN OPIOID DETOXIFICATION

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SUMMARY:
Objective: Alcohol use is associated with worse outcomes in long-term methadone treatment, but its influence on the course of methadone detoxification remains to be determined. Our previous studies have shown that the addition of very low-dose naltrexone (VLNTX) to methadone taper is associated with reduced withdrawal intensity during detoxification. We now present the results of an evaluation of withdrawal characteristics and detoxification outcomes in opioid dependent patients with alcohol use at admission to treatment. Method: 174 opioid addicts received naltrexone 0.125/0.250 mg per day or placebo in a double-blind, randomized design, during methadone-based, 6-day inpatient detoxification in a community setting. Results: There were no statistically significant differences in demographic and clinical measures between those individuals who were abusing alcohol (n= 79) and the remaining opioid dependent patients. Alcohol users who did not receive VLNTX-enhanced detoxification showed increased subjective opioid withdrawal intensity (p=0.001), craving (p=0.01) and rate of treatment discontinuation (p=0.02), compared to non-users of alcohol. Alcohol-abusing, opioid-dependent individuals treated with VLNTX showed reduced anxiety (p=0.01, nausea (p=0.002), perspiration (p= 0.01) and craving (p=0.02), compared to those receiving placebo. Conclusions: The abuse of alcohol contributes to worsened opioid detoxification outcomes. The addition of VLNTX was associated with improved outcomes among alcohol-abusing opioid-dependent patients. Further studies should test the utility of this method in helping with alcohol detoxification and with the induction to full-dose naltrexone alcohol craving treatment. This research was supported by grant DA15469 from the National Institute on Drug Abuse.

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NR7-14

WITHDRAWN

NR7-15

AN ANALYSIS OF CO-OCCURRING TOBACCO SMOKERS, DEPRESSION, AND SUBSTANCE USE

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SUMMARY:

Objectives: The aim of this study was to elucidate gender and tobacco smoking associated with depression, substance use, and severity of dependence. Methods: Tobacco Smokers (n=167) were recruited from a cigarette-smoking cessation service and non-smokers (n=269) were recruited from a blood donation center. The instruments used were: a questionnaire, the Alcohol, Smoking and Substance Involvement Screening Test (ASSIST), the ICD-10 for depression, and the Fagerström Test for Nicotine Dependence (FTND). Results: Differences were reported to substance use, men smokers reported more cannabis use, and women smokers reported more sedative use than non-smokers. Women reported smoking fewer cigarettes per day and were less nicotine-dependent than men smokers. Similarities were observed between men and women smokers in depression, more mental disorder in family, when compared to those men and women who never smoke. Conclusion: This study suggests that the professional to assist smoking cessation should recognize co-occurring psychiatric disorders in smokers and similarities and differences in substance use correlates that may be potentially useful for treatment programs.

NR7-16

EXTENDED-RELEASE INJECTABLE NALTREXONE (XR-NTX) REDUCES BRAIN RESPONSE TO ALCOHOL CUES IN ALCOHOL-DEPENDENT VOLUNTEERS: A BOLD FMRI STUDY

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SUMMARY:

Aims: Oral naltrexone reduces heavy drinking via diminished reward and craving, but is less consistent as an abstinence promoter, whereas once-monthly XR-NTX appears to help maintain abstinence as well. Because enhanced reactivity to conditioned cues is thought to play an important role in relapse, the present study was conducted to determine if cue reactivity is attenuated by XR-NTX. Method: Twenty-eight detoxified alcohol-dependent adult (48.36 ± 7.43 yrs) male (N=21) and female healthy volunteers participated in a structured cue reactivity paradigm during BOLD fMRI. They were randomized to receive a single i.m. injection of either XR-NTX (N=15) or placebo under double-blind conditions; the fMRI/cue reactivity procedure was repeated two weeks later. Both visual (neutral and alcohol) and odor (rose water or preferred alcoholic beverage) cues were presented in an interleaved manner for 28 minutes during the fMRI procedure. Participants responded to queries "want to drink alcohol" and "want to avoid drinking alcohol" every 2 minutes while in the scanner via a 9-point Likert scale. Results: Alcohol-related visual and olfactory cues elicited significant increases in multiple brain regions including orbital and cingulate gyri, inferior frontal gyrus and middle frontal gyrus. Compared to baseline, BOLD signal activation in these regions during the second scan was significantly attenuated in XR-NTX-treated individuals compared with the placebo-treated group. Mean craving scores decreased 1.1 ± 0.52 with XR-NTX vs. 0.47 ± 0.54 with placebo (p=NS). Conclusions: As the affected brain regions in this study are associated with the integration of emotion, cognition, reward, punishment and learning/memory, these findings suggest that XR-NTX may attenuate the salience of cues that have been associated with alcohol. Such an effect on brain function may interrupt the processes associated with "slips" and relapse and thus may contribute to XR-NTX's ability to maintain abstinence.

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NR7-17

TREATMENT OF CHRONIC PAIN WITH BUPRENORPHINE IN A VETERAN WITH TRAUMATIC BRAIN INJURY

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SUMMARY:
Case Presentation: We report a case of a 27 year-old Iraq War veteran with no previous psychiatric history who sustained severe traumatic brain injury (TBI) following a blast injury from an improvised explosive device. The patient subsequently suffered severe anxiety symptoms controlled only by combination therapy with benzodiazepines and venlafaxine. Even more disabling, the patient also experienced intractable headache and shoulder pain unresponsive to non-steroidal anti-inflammatory agents, tramadol, gabapentin, or NMDA-receptor antagonists. Given the risk of respiratory depression with his current medications, opioid analgesics were not favored for the management of his pain. The patient was started on sublingual buprenorphine at a dose of 8mg three times daily with significant improvement. This dose was maintained and the patient was able to function relatively pain-free. Discussion: Chronic pain is a significant complication in patients with TBI and is reported by a majority of patients with TBI, regardless of the severity of the injury. The treatment of chronic pain among individuals can be challenging. Patients with TBI may be on other medications for impulse control, such as anticonvulsants and benzodiazepines. Further treatment with narcotic analgesics may therefore increase the risk of respiratory depression. Buprenorphine is a partial mu agonist whose effects plateau at higher doses, at which time it begins to act like an antagonist. It is this property at higher doses that limits its dose-dependent respiratory depression. Buprenorphine thus has the advantage of effective analgesia with minimal sedation and may be useful for treating chronic pain among TBI patients already taking benzodiazepines. While clinicians should be aware of these possible benefits, more studies are necessary to evaluate the efficacy of buprenorphine among TBI patients with chronic pain.

NR7-18

MORTALITY FOLLOWING TREATMENT FOR CANNABIS, COCAINE, AMPHETAMINE, ECSTASY, AND OPIOID USE DISORDERS: A NATIONWIDE FOLLOW-UP STUDY FROM DENMARK

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SUMMARY:
Objective: To estimate mortality rates following substance abuse treatment among primary users of cannabis, cocaine, amphetamine, ecstasy, and opioids. Methods: This was a register-based cohort study of 20581 individuals in treatment for illicit substance use disorders in Denmark between 1996 and 2006. The register of individuals in treatment for illicit substance disorders was linked with registers on psychiatric treatment and mortality. The mortality rates were calculated by dividing the observed number of deaths following the first day of the first registered treatment episode for substance use disorders with the expected number of deaths based on data from the background population. All mortality rates were standardized with respect to age and gender distribution. Data on mortality in the general population were available for one-year age strata. All in all, there were 1441 deaths recorded during 111445 person-years of follow-up. Results: At the time of first treatment contact for illicit substance use disorders the mean age among the 20581 individuals was 29 years (median: 28 years, 25th percentile: 22 years, 75th percentile: 35 years), the mean follow-up time was 5.4 years (median: 5.0, 25th percentile: 2.5, 75th percentile: 8.4), 76% were males, 73% were single, 78% had no children, 8% did not have a permanent address, and 71% had no education beyond elementary school. Only 14% were currently employed whereas the remainder lived off of subsidies from the state. The study showed a high degree of excess mortality in general. Standardized Mortality Ratios (SMRs) for primary users of specific substances were: 4.9 for cannabis, 6.4 for cocaine, 6.0 for amphetamine, 9.1 for heroin, and 7.7 for other opioids, which includes illegally acquired opioids such as morphine, methadone, and buprenorphine. The study, however, showed no evidence of excess mortality among primary users of ecstasy as the SMR was not significantly elevated. Overall, and specifically among heroin and cocaine users, females had slightly higher SMRs, indicating that substance abuse has a higher impact on the mortality rates of females. Conclusions: Significantly elevated SMRs were found among individuals who had received treatment for cannabis, cocaine, amphetamine, and opioid use disorders. Although the SMR of primary users of cannabis is slightly smaller than what was found for cocaine, amphetamine, and opioids, it is still noteworthy.

NR7-19

TRANSLATIONAL DEVELOPMENT OF NOVEL PHARMACOTHERAPEUTIC STRATEGIES FOR PSYCHOSTIMULANT DEPENDENCE

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SUMMARY:
Background: Psychostimulant abuse generates profound socioeconomic, legal and medical problems worldwide, and is a significant comorbid factor that can adversely affect the clinical courses of other psychiatric disorders. Several agents, all employed as monotherapies, have failed to show consistent clinical efficacy against psychostimulant dependence. These failures highlight a critical, unmet medical need for the development of more robust treatment strategies. Based on recent advances in the learning and memory field, we have hypothesized that combinations of a psychostimulant or a non-abused "substitute" agonist with a 5-HT3, 5-HT2A/2C, or NK-1 antagonist may show enhanced efficacy in both animal models and human abusers. Methods: Combinations of a "substitute" agonist (e.g., pergolide) and a selected receptor antagonist (e.g., ondansetron) have been tested in animal models. In a Phase II Clinical study, a combination of delayed-release ondansetron and immediate-release methylphenidate formulations is being tested utilizing multiple psychological assessment tools and neuroimaging. Results: Preclinical data have demonstrated that the combined agonist/antagonist treatments can: (1) reverse consolidated behavioral sensitization; (2) attenuate cocaine self-administration under a progressive ratio paradigm; (3) attenuate cocaine- or methamphetamine-induced psychostimulant self-administration reinstatement; and (4) normalize associated neurobiological marker changes in selected brain regions. It is critical that the 5-HT3 antagonist ondansetron is given 3.5 hours after pergolide; furthermore, monotherapies using either agonists or antagonists alone are ineffective. Conclusions: Combinations of a "psychostimulant substitute" and an antagonist at selected neurotransmitter receptors may hold therapeutic promise against psychostimulant dependence. Results from the current phase II study will help to translate preclinical findings into the clinical field and improve our understanding of the role of learning and memory mechanisms in stimulant dependence.
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NR7-20

SUBSTANCE INTOXICATION SIGNIFICANTLY REDUCES SERUM THYROTROPIN (TSH) LEVELS IN ACUTE PSYCHIATRIC PATIENTS: PRELIMINARY RESULTS

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SUMMARY:
Objective: To study the effect of substance intoxication on TSH in patients admitted to a large urban Psychiatric Emergency Room (PER). Method: Charts of all patients admitted to PER (2002-2007) at Los Angeles County Hospital were reviewed (n=18,836). TSH and urine toxicology screening are performed on every patient admitted as part of routine clinical care. Subjects without TSH values (n=9,571) and those with more than one PER admission (n=1,565) were excluded. From the remaining 8,743, we report the findings of the first 3000 charts. Those younger than 18 or older than 65 (n=301) were excluded, yielding a final sample of 2,699 (M/F=1743/956), 34% of whom were Caucasians, 26% African Americans, 25% Latinos, and 16% were of other races. Geometric means and SD were calculated based on log-transformed TSH. Unadjusted p-values for gender, METH, cocaine, cocaine or METH, and other substance positive were calculated using independent sample t-tests of ln(TSH). The p-value for race was calculated using ANOVA of ln(TSH) with Bonferroni multiple comparison adjustment. The p-values were adjusted for age, gender and African-American race using separate general linear regression models. Results: One thousand three hundred sixty-four subjects had urine tox, 35% Latinos (n=479), 26% African Americans (n=351), and 23% Caucasians (n=310). Thirty-nine point seven percent (n=524) tested positive [Cocaine: 20.7% (n=283), METH: 12% (n=163), and other substances including opiates, barbiturates, and benzodiazepines: 14.4% (n=196)]. Cocaine was most prevalent in African Americans: 44.7% (n=157) vs. 15.2% (n=47) for Caucasians and 12.3% (n=59) for Latinos. Fifteen percent of Caucasians (n=46) and 16% of Latinos (n=75) tested positive for METH compared to only 5.7% (n=20) of African-Americans. Subjects with positive urine tox have significantly lower mean TSH value compared to subjects

with negative test: TSH (mean ± SD): Any substance positive versus negative: 0.89 ± 2.39 vs. 1.09 ± 2.28 (P < 0.0002), cocaine positive: 0.86 ± 2.15 vs. 1.05 ± 2.37 (P<0.03), METH positive: 0.91 ± 2.39 versus 1.03 ± 2.33 (P < 0.04), either cocaine or METH positive: 0.87 ± 2.23 versus 1.08 ± 2.36 (P<0.0008,) other substances: 0.83 ± 2.85 versus 1.04 ± 2.24 (P<0.0002). Discussion: We found high prevalence of substance intoxication among PER patients. Ethnicity had a profound impact on the type of illicit drug used with almost half of African-Americans testing positive for cocaine.

NR7-21

BRAIN MECHANISMS OF DECISION MAKING DURING RECOVERY FROM METHAMPHETAMINE DEPENDENCE

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SUMMARY:

Abstract: The principal goal of this study was to examine the neural correlates of recovery of function during initial abstinence from methamphetamine (MA) addiction. Thirty recently (2 to 6 weeks) abstinent MA dependent patients and 18 age and gender matched controls (CS) were entered into a 6 month prospective study. To date, 17 MA subjects have been re-evaluated at 6 weeks and 10 MA subjects and 12 controls have been re-evaluated at 6 months. Subjects were studied with a battery of neuropsychological tests including a behavioral measure of impulsivity (area under individually determined delay discounting curve). At each evaluation visit, subjects' performance on a delay discounting and control task was evaluated with functional Magnetic Resonance Imaging (fMRI). MA subjects were cognitively impaired (global score, p < .05) and more impulsive (p < .05) compared to CS at the initial visit. Impulsivity (p < .05) and cognition (global score, p < .02) improved over 6 months. Examination of fMRI results indicated that both groups activated a decision network [anterior insula, dorsolateral prefrontal cortex (DLPFC), posterior parietal cortex (PPC) and dorsal anterior cingulate cortex (ACCd)] whose activity increased during harder (closer to the subject's indifference curve) versus easier discounting comparisons. The contrast between hard and easy trials was less pronounced in the more impulsive MA group. MA subjects (but not controls) showed an increase in the response in insula and DLPFC during hard comparisons (contrasted with a control task) after 6 weeks of recovery (Figure). Furthermore, the insular, DLPFC and ACCd activity in MA subjects was greater when they selected an immediate reward at their initial visit, but greater when they chose a delayed reward after 6 weeks. MA subjects become less impulsive with abstinence and their pattern of cortical activity during decision making becomes more similar to that of controls.

NR7-22

A REVIEW OF PANIC DISORDER/ATTACKS AND SUICIDAL ATTEMPTS IN THE ABSENCE OF MOOD DISORDERS

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SUMMARY:

Objective: Considerable evidence indicates that panic disorder and/or attacks comorbid with depression or bipolar disorder are associated with a higher risk for suicide attempts (reviews: Kilbane et al., 2009; Roy-Byrne et al., 2000). The association between panic and suicide in the absence of mood disorders is less clear. In this context, we have reviewed available literature on the possible association between panic disorder and/or attacks without comorbidity and suicide attempts. Method: We conducted PubMed and Medline searches for articles published between 1950 and 2009 using the key words "panic disorder," "attempted suicide," and "completed suicide." Articles were excluded if the primary focus was substance abuse, schizophrenia or psychotic disorders, mood disorders, personality disorders, medical disorders and insomnia. A total of seventeen articles, eight epidemilogical and nine clinical examined a relationship between panic and suicide attempts. Results: Results from all but one of the epidemiological studies suggested a positive association between uncomplicated panic disorder and suicide attempts. Clinical studies showed conflicting results, with the association between panic and suicide attempts being explained by comorbid depression. None of the seventeen studies suggested a negative association between panic disorder/attacks and suicide attempts. Alexithymia, anticipatory anxiety, attentional hypervigilance and avoidance of bodily sensations may be indicators of a higher risk of suicide attempt as suggested by clinical studies. Conclusion: Individuals with panic disorder and/or attacks without comorbid mood disorders may represent a high-risk group for suicide attempt, thus

requiring more aggressive treatment. An instrument that incorporates detailed assessment of panic states may help in assessment of suicidality in high-risk individuals.

NR7-23

DOES EARLY IMPROVEMENT PREDICT ENDPOINT RESPONSE IN GENERALIZED ANXIETY DISORDER (GAD) PATIENTS TREATED WITH PREGABALIN OR VENLAFAXINE-XR?

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SUMMARY:

Objective: There is a 3- to 6-week lag time in achieving a therapeutic response for many current treatments for GAD. Even after a full course of treatment, rates of partial or non-response are relatively high. Therefore, early identification of patients who are likely to respond to treatment may have important implications for treatment decision-making (Pollack 2008; Baldwin 2009). The goal of the current investigation was to determine which early improvement criteria optimally predict eventual response during short-term treatment of GAD. Methods: Data were analyzed from a double-blind trial in which adults with DSM-IV-defined GAD were randomized to 8 weeks of treatment with pregabalin (PGB; 300-600 mg/d; N=121), venlafaxine-XR (VXR; 75-225 mg/d: N=125), or placebo (N=128). Early improvement measures were analyzed, using both logistic regression models and receiver operator characteristic (ROC) curve analysis, in an attempt to predict endpoint response. Results: There was a significantly greater early improvement on the HAM-A at Day 4 (-5.2 vs. -3.9; P<0.05) and Week 1 (-6.9 vs -4.7; P<0.05) for PGB compared to VXR. The odds ratios for achieving endpoint response among patients showing early improvement were also higher on PGB versus VXR, whether using a global measure such as CGI-I or an illness-specific measure such as the HAM-A: for example, a 1-point improvement at Week 1 on the CGI-I (OR, 2.1 vs. 0.8); or a 4-point improvement on the HAM-A at Day 4 (OR, 1.4 vs 0.9) or Week 1 (OR, 2.5 vs 0.7). For VXR, evidence of an early improvement was not a reliable predictor of endpoint response: for example, a 4-point improvement on the HAM-A at both Day 4 (0.33; 0.65) and Week 1 (0.50; 0.41) was associated with a relatively low sensitivity and specificity for detecting endpoint response. Sensitivity and specificity were only modestly better at Day 4 (0.48; 0.61) and Week 1 (0.77; 0.42) for PGB.

Conclusions: In this study, an early improvement, especially for VXR, was not a useful predictor of the likelihood of endpoint response in GAD. This is in contrast to previous findings in GAD and for other anxiety disorders.

Funded by Pfizer Inc.

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NR7-24

EFFICACY OF PREGABALIN IN GENERALIZED SOCIAL ANXIETY DISORDER: RESULTS OF A DOUBLE-BLIND, PLACEBO-CONTROLLED, FIXED-DOSE STUDY

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SUMMARY:

Objective: To evaluate the efficacy and tolerability of pregabalin (PGB) for the treatment of generalized social anxiety disorder (SAD). Method: After a 1-week screening period during which eligibility was determined, patients with DSM-IV generalized SAD were randomly assigned to 11 weeks of double-blind treatment with fixed daily doses of either PGB 300 mg, 450 mg, 600 mg, or placebo. Primary efficacy outcome was an ANCOVA analysis of change from baseline to endpoint (LOCF) in the Liebowitz Social Anxiety Scale (LSAS) total score. Results: The intent-to-treat sample consisted of 328 patients, 59% male, with a mean (SD) age of 35 (11) years, and a baseline LSAS total score of 91.9 (20.5). Treatment with PGB 600 mg was associated with a significantly greater mean [SE] reduction in LSAS total score, from baseline to endpoint, compared to placebo (-29.8 [2.8] versus -19.7 [2.8]; p=0.0099), while reduction on PGB 300 mg (-20.2 [2.9]) and PGB 450 mg (-25.5 [2.7]) were not significant. Treatment with PGB 600 mg was also associated with a significantly greater improvement than placebo on the Fear and Avoidance subscales of the LSAS, as well as the majority of other secondary measures. Onset of improvement occurred by Week 1 in the PGB 600 mg dose group. The most common adverse events on all 3 doses of PGB were somnolence and dizziness. Discontinuation due to adverse events (AEs) occurred at a similar rate on PGB 300 mg (20.5%), 450

mg (14.0%), and 600 mg (17.1%), but at a lower rate on placebo (1.2%). Incidence of AEs rated as severe occurred at a higher rate on PGB 300 mg (10.3%) and 450 mg (8.1%) than on PGB 600 mg (4.9%) or placebo (3.7%). Conclusion: The results of the current study suggest that the 600 mg/day dose of PGB may be efficacious in the treatment of SAD. A previously reported trial (Pande et al, 2004) also reported efficacy for the 600 mg/day dose, but not a lower dose, providing additional support for the efficacy of PGB 600 mg/day in SAD.
Funded by Pfizer Inc.

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NR7-25

FUNCTIONAL AND HEALTH-RELATED QUALITY OF LIFE OUTCOMES IN PATIENTS WITH OBSESSIVE-COMPULSIVE DISORDER: RELATIONSHIP TO TREATMENT RESPONSE AND SYMPTOM

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SUMMARY:
Objective: Data were analyzed from two long-term prospective double-blind placebo-controlled trials of escitalopram in obsessive-compulsive disorder (OCD) to characterize the baseline levels of functional disability and impairment in health-related quality of life (HRQoL) and to assess the relationship between treatment outcomes (response or relapse) and disability or HRQoL. Methods: Data from a 24 week, placebo-controlled, fixed-dose trial of escitalopram (10-20 mg/day) or paroxetine (40 mg/day), and from a 40 week, flexible-dose (escitalopram 10-20 mg/day), placebo-controlled relapse-prevention trial were analyzed. OCD symptoms were assessed using the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), functioning was assessed using the Sheehan Disability Scale (SDS), and HRQoL was assessed using the SF-36. Baseline data were pooled for patients across both studies. For patients in the fixed-dose study SDS and SF-36 scores were compared for patients receiving escitalopram, paroxetine or placebo and for responders versus non-responders. In the relapse-prevention trial, SDS and SF-36 scores were compared for relapsed versus non-relapsed patients. Results: Patients with more severe baseline symptoms reported significantly greater impairment on the SDS ($p<0.001$) and SF-36 ($p<0.01$ except for bodily pain). Patients receiving escitalopram or paroxetine reported significant improvements on most SF-36 dimensions and on the SDS, however improvements in work-related functioning were seen earlier for patients receiving escitalopram (20 mg/day). At the study endpoints, SDS and SF-36 scores were significantly better for patients who were responders (versus non-responders), and for patients who did not relapse (versus relapsers). Conclusion: OCD is associated with significant impairment in functioning and HRQoL. Significant differences in disability and HRQoL between responders and non-responders or relapsers and non-relapsers suggest a relationship between symptomatic and functional outcomes.

NR7-26

SWITCHING FROM LONG-TERM BENZODIAZEPINE THERAPY TO PREGABALIN IN PATIENTS WITH GENERALIZED ANXIETY DISORDER: A DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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SUMMARY:
Objective: To evaluate the efficacy of pregabalin in enabling patients to taper from long-term benzodiazepine therapy and to maintain a benzodiazepine-free state. Method: Adults with a primary lifetime diagnosis of GAD treated for 8-52 weeks with a benzodiazepine at doses of 1-4 mg/day (in alprazolam dose equivalents) were enrolled. All patients completed a 2-4 week, open-label, alprazolam Stabilization Phase prior to randomization to 12 weeks of double-blind treatment with either pregabalin 300-600 mg/d or placebo. During the 3-6 week Taper Phase patients were tapered off of alprazolam at a dose reduction rate of 25% per week, and then continued on double-blind treatment during a 6-week Benzodiazepine-free phase. Outcome measures included ability to remain benzodiazepine-free (primary) as well as changes in HAM-A and Physician Withdrawal Checklist (PWC). Results: 106 patients met entry criteria,

completed the alprazolam stabilization phase, and were randomized to pregabalin (N=56; mean HAM-A, 9.1) or placebo (N=50; mean HAM-A, 10.4). At endpoint, a non-significantly higher proportion of patients remained benzodiazepine-free on pregabalin compared to placebo (51.4% vs 37.0%; odds ratio, 1.39). Treatment with pregabalin was associated with significantly greater last observation carried forward (LOCF)-endpoint reduction in the HAM-A total score versus placebo (-2.5 vs +1.3; P<0.001), and lower endpoint mean PWC scores (6.5 vs 10.3; P=0.012). Conclusion: Approximately 50% of patients treated with pregabalin successfully discontinued chronic daily use of benzodiazepine. The results of the current study suggest that switching to pregabalin may be a safe and clinically preferable treatment option in patients with GAD.
Funded by Pfizer Inc.

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NR7-27

EFFICACY OF PREGABALIN IN PREVENTING RELAPSE IN GENERALIZED SOCIAL ANXIETY DISORDER: RESULTS OF A DOUBLE-BLIND, PLACEBO-CONTROLLED 26-WEEK STUDY

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SUMMARY:

Objective: To evaluate the efficacy and safety of 26 weeks of pregabalin (PGB) in preventing relapse among patients with generalized social anxiety disorder (SAD) who initially responded to open-label (OL) PGB. Method: Patients with SAD who met responder criteria after 10 weeks of OL treatment with a fixed daily dose of PGB 450 mg were randomly assigned to 26 weeks of double-blind (DB) treatment with either PGB 450 mg or placebo. The primary outcome of time-to-relapse was analyzed using the Kaplan-Meier method and the log-rank test. Relapse was defined as either 1) a CGI-C score of >=6 or more (worse/very-much worse) compared with DB baseline; and a CGI-Severity score equal to or greater than the OL baseline score on 2 consecutive visits, or 2) worsening of symptoms per the clinical judgment of the investigator. Results: 348 patients entered the OL phase and 153 (44%) responded to OL treatment and were randomized to the relapse prevention phase. In these 153 patients, the mean Liebowitz Social Anxiety Scale (LSAS) total score improved during OL treatment from 90 to 35. Fifty-four (15.5%) patients discontinued due to an adverse event in the OL phase. DB treatment with PGB was associated with a significant delay in time-to-relapse (p=0.035) versus placebo. Treatment with PGB was also associated with significantly greater maintenance of symptomatic improvement over 26 weeks on the LSAS total score (p=0.012), on all LSAS subscale scores, and on the Marks Fear Questionnaire total phobia (p=0.0095) and social phobia scales (p=0.014). PGB was generally well-tolerated. During DB treatment, 3.8% of PGB-treated patients discontinued due to adverse events vs 8.2% on placebo, and 2.6% of PGB-treated patients experienced a weight gain of >=7% vs none on placebo. Conclusion: The results of the current study suggest that PGB 450 mg/day is safe, well-tolerated, and has significant relapse prevention efficacy over 26 weeks in SAD subjects who have responded to an initial course of PGB treatment.
Funded by Pfizer Inc.

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NR7-28

THE USE OF THE INTERNET BY SOCIAL PHOBICS TO SEEK HEALTH INFORMATION

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SUMMARY:

Objective: The internet is commonly used as a tool for finding health information. Internet users are able to obtain anonymous information on diagnoses and

treatment, seek confirmatory information and are able to self-diagnose. We hypothesized that individuals with social phobia (SP) use the internet for health information more frequently than those with other anxiety disorders. Method: The MACSCREEN is a validated self-report screening tool, which screens for all anxiety disorders, as well as mood, substance use and psychotic disorders. It was posted online and was completed by 272 individuals in the general population. For those who qualified for a DSM-IV disorder, self-report symptom severity measures were completed. Information including demography and details of individuals' use of the internet for health information was collected. Results: Sixty-seven point two percent met DSM-IV criteria for SP. SP individuals were more likely to be single (51.9% versus 34.8%, p< .01) and have a lower level of education (37.2% versus 23% had high school education only, p<0.05), a younger mean age of 32.9 ±12.9 (SP) versus 38.5 ± 14.6 years (p<0.01), more comorbid diagnoses (3.1 versus 1.4, p<0.001), and higher rates of depression (42.6% versus 22.5%, p<0.001). Significantly more SP individuals reported searching for information due to concern that they had an anxiety problem (73.2% versus 56.2%, p<0.01), were more uncomfortable speaking to their doctor than those without SP (23.5% versus 4.5%, p<0.001) and were less likely to report seeing their family doctor "often" (p<0.05). Social phobics more often reported wanting to seek further assessment (70.5% versus 52.8%, p<0.01) and were less likely to report planning to "do nothing" with the information they received (12.6% versus 23.2%, p<0.05). Conclusion: Using the internet to seek information about anxiety appears to be common in individuals with social phobia. Implications of these findings for clinicians and afflicted individuals will be discussed.

NR7-29

HARM AVOIDANCE AND INCOMPLETENESS IN A CLINICAL SAMPLE OF OCD

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SUMMARY:
Objectives: The heterogeneity of Obsessive-Compulsive Disorder (OCD) is well documented in terms of both symptom presentation and treatment outcome. One approach to conceptualizing this heterogeneity is to focus on the underlying motivation driving the urge to perform compulsions. The role of harm avoidance (HA) as the motivating drive has received considerable attention. The role of the need to do things "just right" to prevent a sense of incompleteness (INC) has not been examined as systematically. Although these concepts have been described by a number of investigators, few studies have examined them empirically in clinical samples. A 20-item self-report measure, the Obsessive Compulsive Trait Core Dimension Questionnaire (OC-TCDQ; Summerfeldt et al., 2001), has been developed as a tool to assess these core hypothesized dimensions of OCD. In non-clinical samples, a small number of studies using the OC-TCDQ have found that the two dimensions of HA and INC, while correlated with each other, have unique relationships with a number of features of OCD. The primary aim of this study was to use this measure to investigate the underlying core features of harm avoidance and incompleteness in a well-characterized clinical sample of individuals with primary OCD. Method: 109 participants who were enrolled in a naturalistic, prospective study of the course of OCD completed the OC-TCDQ as part of their comprehensive diagnostic assessment battery. A series of analyses were conducted to evaluate the relationship between the constructs of HA and INC and a number of clinical features of OCD. Means and standard deviations on the HA (mean = 29.44, SD = 9.81) and INC (mean = 31.42, SD = 9.28) subscales of the OC-TCDQ were higher than those reported by previous researchers in several non-clinical samples and one clinical sample, indicating that these are frequently occurring phenomena. The predictive value of HA and INC on course, severity, and a range of clinical features in the current sample will be presented, and the implications for clinical practice will be discussed.

NR7-30

INSOMNIA AND GENERALIZED ANXIETY DISORDER (GAD): CLINICAL PRESENTATION AND DIFFERENTIAL RESPONSE TO THREE DRUG CLASSES

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SUMMARY:
Objective: Insomnia is one of the defining DSM-IV criteria for GAD. However, relatively little information is available on the proportion of GAD patients reporting early and/or middle and late insomnia, or on the differential response to treatment with classes of drugs with different mechanisms of action; or the extent to which improvement in insomnia

is a direct or indirect effect of different drugs. Methods: Data were pooled from 4 double-blind, placebo-controlled, 6-8 week trials of outpatients with DSM-IV GAD. Treatment response was analyzed for 3 classes of drugs: pregabalin (alpha2delta), alprazolam (benzodiazepine), and venlafaxine-XR (SNRI). The 3-item HAM-D insomnia factor was used to characterize insomnia status. A mediation model was used to estimate, for each active drug, the direct and indirect treatment effects on sleep disturbance. Results: Seven hundred fifty-two patients were treated with pregabalin 300-600 mg/d, 88 patients were treated with alprazolam 1.5 mg/d, 120 patients were treated with venlafaxine-XR 75-225 mg/d, and 394 patients were treated with placebo. At baseline, 28.7% of patients reported experiencing severe early insomnia, 24.0% reported severe middle insomnia, and 13.7% reported severe late insomnia. Two or more insomnia complaints were also commonly reported. Significant endpoint improvement in the HAM-D insomnia factor occurred after treatment with pregabalin ($P<0.0001$) and alprazolam ($P=0.0007$) but not venlafaxine-XR ($P=0.2752$). Results of mediational modeling found differential effects by drug class. For example, 48.2% of the effect of pregabalin on sleep disturbance was due to a direct effect, and 13.8% was due to an indirect effect, mediated through reduction in anxiety symptom severity. Conclusion: Results for this treatment sample suggest that insomnia is a very common occurrence in GAD, and is not limited to problems with sleep onset. There appear to be between-class differences in the sleep effects of various anxiolytics.

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NR7-31

EFFECTS OF ORAL RIVASTIGMINE ON SUBSCALES OF THE SEVERE IMPAIRMENT BATTERY (SIB) IN PATIENTS WITH SEVERE ALZHEIMER'S DISEASE

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SUMMARY:

Objective: Rivastigmine capsule has demonstrated overall effects in patients with mild-to-moderate Alzheimer's disease (AD) in numerous clinical trials. It has also shown effects in patients with severe AD, using the Severe Impairment Battery (SIB). In the current analysis, scores on the three higher-order subscales of the SIB, memory, language and praxis, were used to further evaluate the specific effects of rivastigmine in patients with severe AD. Methods: This retrospective analysis used data from a 26-week, randomized, placebo-controlled trial (CENA713BES02) that evaluated rivastigmine 3–12 mg/day capsules in Spanish patients with severe AD. Baseline to Week 26 changes in SIB subscale scores (memory, language, praxis) were calculated for the intent-to-treat last-observation-carried-forward population. Treatment differences were assessed using ANCOVA with treatment and center as factors and baseline as a covariate. Results: In total, 104 patients receiving rivastigmine capsules and 106 patients receiving placebo provided SIB data. At Week 26, significant improvements with rivastigmine compared with placebo were seen on memory (-0.38 versus -1.50, $p = 0.010$) and language (-1.01 versus -2.90, $p = 0.045$). A trend towards significance was observed on the praxis subscale (-0.35 versus -1.36, $p = 0.051$). Conclusions: Significant benefits of rivastigmine on memory and language in patients with severe AD were observed using subscales from the SIB. The results of this post-hoc analysis suggest that the memory and language subscales may have a stronger influence on overall SIB scores than the praxis subscale. This study and the presenting author's travel expenses were funded by Novartis Pharmaceuticals Corporation.

NR7-32

BECK DEPRESSION INVENTORY (BDI) AS A SCREENING TOOL FOR DEPRESSION: A POPULATION-BASED FINNISH COHORT STUDY

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SUMMARY:

Objective: As depression is a prevalent disorder, its recognition and diagnostic evaluation are important.

The present study assesses the effectiveness, usefulness and validity of the Beck Depression Inventory (BDI) as a screening tool for depression in a Finnish general population sample. Method: The original study population consists of 2840 randomly selected 45-74 year-old men and women. They were invited to health check-ups for evaluation of the effect of Finnish diabetes prevention programme (D2D) performed in primary health care between 2003-2007. A subsample of 432 persons scoring = 10 point on the BDI was identified. A comprehensive diagnostic evaluation including M.I.N.I. interview was performed on 162 participants and the optimal cut-off point for major depression was calculated. Results: A cut-off score of 15 simultaneously maximized both sensitivity and specificity of BDI. Conclusions: The Beck Depression Inventory with a cut-off score of 15 is a valid instrument for the diagnosis of major depression within the general population. FIN-D2D was supported by financing from hospital districts of Pirkanmaa, Southern Ostrobotnia, North Ostrobotnia, Central Finland and Northern Savo, the Finnish National Public Health Institute, the Finnish Diabetes Association, the Ministry of Social Affairs and Health in Finland and Finland´s Slottery Machine Association in cooperation with the FIN-D2D Study Group, and the Steering Committee: Huttunen J, Kesäniemi A, Kiuru S, Niskanen L, Oksa H, Pihlajamäki J, Puolakka J, Puska P, Saaristo T, Vanhala M, and Uusitupa M.

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NR7-33

WITHDRAWN

NR7-34

INPATIENT PSYCHIATRIC TREATMENT OF DEAF AND SEVERELY HARD-OF-HEARING ADULTS: DEMOGRAPHIC AND DIAGNOSTIC COMPARISONS WITH HEARING INPATIENTS

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SUMMARY:

Objective: This study examines the diagnostic and clinical features of deaf psychiatric inpatients. Methods: Archival clinical data of deaf and severely hard-of-hearing adults (N = 30) was compared with a random sample of hearing adults (N = 60) admitted to a state psychiatric hospital from 1998-2008. Results: Significant differences were found between deaf and hearing inpatient groups in the frequency of impulse control disorders (23% versus 2%), pervasive developmental disorders (10% versus 0%), substance use disorders (20% versus 45%), mild mental retardation (33% versus 3%) and personality disorders (17% versus 43%). The deaf group had more psychotic disorder not otherwise specified diagnoses (39% versus 3%). Deaf inpatients had longer hospitalizations than the hearing inpatients (17 months versus 10 months). Conclusions: Clinicians working with deaf and hard-of-hearing psychiatric patients should be aware of the cultural and linguistic differences in assessment and treatment of this population. Lack of experience with Deaf culture and American Sign Language makes assessment more challenging for clinicians, contributes to less specificity in diagnostic assignment and increases the potential for misdiagnosis. Understudied deaf and hard of-hearing patients should be the focus of additional research to develop appropriate assessment measures and treatment strategies designed for the deaf population.

NR7-35

EFFECTIVENESS OF EATING DISORDER TREATMENT IN REAL WORLD SETTINGS: COMPREHENSIVE ASSESSMENT AND OUTCOME

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SUMMARY:

Objective: Most studies of patients with eating disorders (ED) derive from academic settings; little is known about real world results. We integrate comprehensive initial & outcome assessments of eating disorder (ED) symptoms, anxiety & depression, life functioning & eating behavior into private practice. Methods: At the Eating Disorder Center of Alabama [EDCA]), 21 ED patients (M Age = 30.0, range 16 – 55, 20 females, 1 male) with Anorexia

Nervosa (6), Bulimia Nervosa (7) & Eating Disorder NOS (8) received integrated individual and group therapy by a multidisciplinary team (CBT, DBT, groups, psychoeducation, nutritional counseling & medication); flexible 6-8 week treatment, goal: 2 weeks w/o symptoms. Scales: Eating Disorders Examination – Q [EDE-Q]; Beck Depression Inventory-II [BDI-II] and Anxiety Inventory [BAI]; Social Adjustment Scale – SR [SAS-SR]; rating hunger prior & fullness after test meals. Results: Significant pre- post-improvement (3 of 4 subscales of the EDE-Q & the Global score ($p < .001$). BDI-II and BAI scores decreased significantly ($p<.002$) from severe to mild (BAI) and minimal (BDI-II). Overall- and within-family-functioning: trend toward improvement ($p<.06$) & into normal range (SAS-SR). Test meal intake increased (75% to 95%, $p < .05$, hunger increased $p < .10$). Outcome was not predicted by readiness to change but lifetime weight fluctuations (>30%); external locus of control and greater illness duration predicted worse outcome/dropouts, identifying 70% dropouts and 82% completers. Conclusions: Dramatic improvements with our flexible treatment model were statistically and clinically significant across a range of psychosocial areas despite a small sample. External locus of control and greater duration of illness seem to indicate dropout risk, in line with prior studies. Since completers do well, we are developing a more aggressive intervention targeted at keeping the subgroup at risk of dropping out from doing so.

NR7-36

TESTS OF THE KOOB-KELLY-GOLD-VOLKOW-KESSLER HYPOTHESIS OF BMI INCREASES IN THE U.S.

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SUMMARY:

Objective: Why has the average Body Mass Index increased so dramatically since 1970 in the United States? Sugar and simple carbohydrates (Harrar, 2004; Adkins, 1992), fat consumption (Ornish, 2001; Pritikin, 1990), and palatability (Gold, 2003; Kelly and Berridge, 2002; Kessler, 2009; Koob 2003; Volkow, Fowler, & Wang, 2003) have been the most popular hypotheses implicated as causes of this increase. Method: Archival data on different kinds of food production available for consumption from the Department of Agriculture were used in quadratic equations to predict changes in Body Mass Index (BMI) from the Center for Disease Control and the U.S. Census Bureau. This was done from 1970 – 2007. All BMI and food availability data were converted to z-scores such that a common metric could be used for comparisons of food production and BMI increases. A z-score is a transformed score where it indicates how far and in what direction that item deviates from its distribution's mean, expressed in units of its distribution's standard deviation. Results: In line with the major physiological theories emphasizing palatability, the additives of fat and sugars in combination best predicted increases in BMI accounting for 98% of the variance in the quadratic equations. Popular diet hypotheses emphasizing only fats, sugars, or carbohydrates were not strongly supported. Conclusions: These data at the macro level of US food production and BMI statistics converged on the theories and data from the physiological level, and showed that additives for increased palatability best predicted increases in BMI. Furthermore, these results pointed to clear advice in terms of diets that can potentially work.

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NR7-37\

PSYCHOTROPIC DRUG USE IN OLDER PEOPLE AND RISK OF DEATH DURING HEAT WAVES: A FRENCH POPULATION-BASED CASE-CONTROL STUDY

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SUMMARY:

Objectives: To assess the risk of death associated with the use of psychotropic drugs during a heatwave in older people. Design: Population-based matched case-control study. Setting: French social security insurance national database. Participants: 12434 cases aged 70 to 100 who died in August 2003; 12434 controls alive at April 2004, matched on age, gender and presence of chronic illness. Main outcome measure: Exposure to psychotropic drugs, in subjects who died in the periods preceding and during the August 2003 heatwave, compared to survivors. Results: The association between exposure to

psychotropic drugs and risk of death was modified by the level of external temperature (Chi2=13.1, df=1, p<0.001). The increased risk of death associated with use of any psychotropic drug was restricted to the heatwave period, with a significant dose-response relationship between the number of psychotropic drugs and the risk of death (adjusted odds ratio (aOR) for linear trend 1.25, 95% Confidence Interval (95%CI) 1.21 to 1.29). During the heatwave, using antidepressants (aOR 1.71, 95%CI 1.57 to 1.86) or antipsychotics (aOR 2.09, 95%CI 1.89 to 2.35) was independently associated with an increased risk of death, while anxiolytics/hypnotics use (aOR 0.85, 0.79 to 0.91) was associated with a decreased risk. Findings were unchanged after adjustment for cardiotropic, anti-dementia or anti-parkinsonian drug use. Conclusion: The risk/benefit of psychotropic drugs should be carefully assessed in older people during a heatwave.

NR7-38

12-MONTH OUTPATIENT PSYCHOTHERAPY USE IN SÃO PAULO, BRAZIL: FINANCIAL PATTERNS

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SUMMARY:
Introduction: Utilization of outpatient mental health services is unevenly distributed in the general population. Amongst them, psychotherapy services are used annually by approximately 3% of the adult population. However, little is known about their patterns of utilization, including costs and financing sources. In the United States, there was a total of 79.5 million outpatient psychotherapy visits at a total cost of US$4.2 billion in 1987, which accounted for 8% of outpatient medical care costs. Ten years later, there was a total of 86.2 million visits at a cost of US$5.7 billion. Main source of payment was out-of-pocket payment, followed by private insurance and federal insurance. In Brazil, there is no similar data available. In a moment of economic pressure to contain health care expenditures, understanding psychotherapy utilization, costs and financing becomes of relevance. Objective: This study aims to investigate the financial sources of psychotherapy treatment in São Paulo, Brazil, given the 12-month prevalence of outpatient psychotherapy use by residents aged 18 to 65 years old. Method: In this cross-sectional study, randomized population–based sampling was composed by 2000 household residents aged 18 to 65 years old. Prevalence of 12-month outpatient psychotherapy use, user's sociodemographic characteristics and financing sources of treatment were assessed through a structured interview in a face to face procedure. The main outcome measure of the investigation is the financial patterns of 12-month use of outpatient psychotherapy services. Results: In 2000, the overall prevalence of 12-month outpatient psychotherapy use in São Paulo, Brazil was 4.6% (males 3.4%, females 5.6%). Federal financing accounted for 52.7% of costs (males 45.5%, females 56.9%), while out-of-pocket payment accounted for 30.8% (males 39.3%, females 25.9%) and private insurance accounted for 16.5% (males 15.2%, females 17.2%). Conclusion: The overall prevalence of 12-month outpatient psychotherapy use was 4.6%, similar to other investigations of this kind. Financing of outpatient psychotherapy treatment was unevenly distributed between sources and did not follow the patterns of similar studies, once federal payment was responsible for almost half of total costs, which could be a result of both Brazilian economic and public health characteristics.

NR7-39

CHANGES IN REGIONAL VARIATIONS IN LEADING SUICIDE METHOD IN TAIWAN: A SURGE OF CHARCOAL BURNING FROM 2002 TO 2008

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SUMMARY:
Background: Leading suicide method differed between countries, but little was known about whether the differences existed across regions within one country. This information is relevant in designing relevant suicide prevention programs in different regions. This study aimed to examine if there were changes in regional variations in leading suicide method in Taiwan from 2002-04 to 2006-08. Methods: Mortality data for all deaths classified as suicide or undetermined intent for years from 2002 through 2008 were extracted for analysis. Number of deaths and proportion (%) of four main suicide methods (such as hanging, charcoal burning, pesticide poisoning, jumping from a height) were calculated to identify leading suicide method in each city/county. Results: Of 22 cities/counties, hanging was the predominant suicide method in 18 cities/counties in 2002-04 and decreased to 11 cities/counties in 2006-08. For deceased aged 25-44 years old, charcoal burning had already been the leading suicide

method in 14 cities/counties in 2002-04 and increased to 21 cities/counties in 2006-08. However, for elderly in each city/county, charcoal burning has never been a preferred suicide method during the study period. Furthermore, jumping was the most popular suicide method for young female deceased in 7 cities/counties in 2002-04 and remained so in Taipei City in 2006-08. Pesticide was still the preferred suicide method for elderly deceased in five agricultural rural counties in 2006-08. Conclusion: Large changes in regional variations in leading suicide method in Taiwan support that the choice of suicide method depends on the socio-cultural acceptability of the method and its availability. Regional suicide prevention programs should take into account these differences.

NR7-40

MELANCHOLIA IN PATIENTS WITH PSYCHOTIC DEPRESSION: A 10-YEAR ANALYSIS OF CLINICAL SEVERITY AND OUTCOME

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SUMMARY:
Objective: In spite of ongoing interest in the syndrome of melancholia, little is known about its rate, relative clinical severity, or diagnostic stability. This longitudinal study determined whether individuals who met DSM-IV criteria for melancholic features formed a distinct subgroup among patients initially diagnosed with psychotic depression. Method: Data were derived from the Suffolk County Mental Health Project, a naturalistic study of individuals in Suffolk County, NY with a first-admission for psychotic illness who were interviewed face-to-face at baseline, and after 6-months and 2, 4, and 10 years. The 87 respondents who received a 2-year best estimate consensus DSM-IV diagnosis of Major Depressive Disorder (MDD) with psychotic features were divided into two groups based on the presence (N=34; 39.1%) or absence of DSM-IV-defined melancholic features. Statistical comparisons used t-tests for continuous variables and chi-square analysis for categorical data. Results: Compared to the non-melancholia patients, the melancholia group had significantly ($p<0.05$) greater depression severity on the Hamilton scale (24.0+/- 6.0 vs 18.4+/-8.5) and Brief Psychiatric Rating Scale Depression/Anxiety subscale (4.0+/-1.0 vs 3.3+/-1.1) at baseline. At 10-year follow-up, the melancholic subgroup was also more likely to persist in having a mood disorder diagnosis (e.g., MDD with psychotic features) and less likely to transition to a diagnosis of psychosis NOS or schizophrenia ($p<0.10$). Conclusion: Among patients hospitalized with psychotic depression, those with melancholia were more severely depressed at baseline and more likely to exhibit a stable diagnosis over 10 years of follow-up. The small sample size made statistical significance difficult to achieve, but the trend was consistent with other reports on the course and outcome of melancholia. Our results suggest that psychotic and melancholic subtypes of depression are distinct categories.

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NR7-41

FREQUENT VERSUS INFREQUENT VISITORS TO A PSYCHIATRIC EMERGENCY SERVICE

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SUMMARY:
Introduction: A subgroup of patients makes frequent use of hospital emergency departments, accounting for 30% of all visits to psychiatric emergency services (1). This phenomenon has been reported from many countries, irrespective of the prevailing health care system. It has been suggested as a consequence of deinstitutionalization, increasingly limited outpatient resources, and an increase in substance abuse (2). We have conducted a case-control study in a general hospital psychiatric emergency room to clarify the risk factors for repeat visits to psychiatric emergency services. Methods: We collected data from psychiatric emergencies in a 3 months period. Frequent visitors definition: patients with visits at least 2 standard deviations above the mean number of visits. On each visit clinicians completed an assessment form, providing demographic, clinical and psychosocial information. The study occurred at the psychiatric emergency service for a 500,000 people catchment area of Madrid, Spain. Bivariate analyses were conducted by using t tests and chi square tests. Odds ratios were calculated to summarize the magnitude

of the association. Results: A total of 105 patients (11.5 %) were identified as frequent visitors. The median number of visits was four and the mean (SD) number of visits 3.75 (1,041). Frequent visitors were more likely ($p<0.05$) than the infrequent visitors to be males, to be unemployed or receive Social Security Disability Income, to have been admitted to a psychiatric hospital (mean admissions 4.20 versus 1.04), to be admitted after the actual emergency visit, and to report substance abuse. Frequent visitors were less likely ($p<0.05$) to have been brought to the psychiatric emergency service under petition or certification. There was no difference between frequent and infrequent users in the clinician impression of the presentation being real. Risk factors identified for frequent visitors included: treatment adverse effects (OR=2,838); personality disorder (OR=2,108); previous suicide attempts (OR=1,846); psychotic disorder (OR=1,483); substance abuse: Alcohol (OR=1,109) and Cannabis (OR=1,619). Discussion: Risk factors associated with frequent visitors paint a picture of resource-poor mentally ill persons who rely on the psychiatric emergency service for support.

NR7-42

ETHNIC SELF-IDENTITY AND SUICIDAL IDEATION: RESULTS FROM THE NATIONAL COMORBIDITY SURVEY REPLICATION

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SUMMARY:
Objectives: Ethnic Self-Identity is an increasingly important concept given the demographic shifts taking place nationally. Studies on the impact of having a negative self-identification with one's own ethnic group with suicidality have produced inconsistent results. We investigated whether level of ethnic self-identity was correlated to report of suicidal ideation. Methods: The National Comorbidity Survey Replication (NCS-R) is a probability sample of the US population designed to constitute a nationally representative sample (N=9,882). In the suicidality section subjects were asked, "Have you ever seriously thought of committing suicide?" In the adult demographic section subjects were asked: "How close do you feel in your ideas and feelings about things to other people of the same racial and ethnic descent?" The answer was recorded in Likert scale format: very close, somewhat, not very, or not at all. Results: On the question of ethnic self-identity, 26% reported feeling very close, 56% somewhat close, 11% not very close, and 7% not close. This distribution varied by race, with African-Americans more likely to report feeling close or somewhat close to their own descent (Chi-square test of homogeneity of proportions =29.15, $p<.001$). After adjusting for sex, age, depression, work and marital status, in a weighted multiple logistic regression, reporting lower level of ethnic self-identity was associated with increased risk of suicidal ideation (odds ratio 1.64, 95% C.I. 1.31-2.05, $p<.001$). Conclusion: In this population-based study, having a lower level of ethnic self-identity was associated with a statistically significant elevated risk for suicidal ideation across all the ethnic groups. Our findings signify that assessing level of ethnic self-identity may be a valuable part of suicide risk-evaluation.

NR7-43

NON-MEDICAL USE SURVEILLANCE AND SIGNAL IDENTIFICATION OF LISDEXAMFETAMINE DIMESYLATE: A PRO-DRUG STIMULANT FOR THE TREATMENT OF ADHD

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SUMMARY:
Objective: To identify signals of misuse, abuse, diversion and intentional overdose (non-medical use) of the pro-drug stimulant lisdexamfetamine dimesylate (LDX), during its first 30 months of approval in the US. Methods: Data relevant to LDX non-medical use were collected from DAWN Live!, Internet and media monitoring, supply chain monitoring, and postmarketing adverse event reports (all ending August 2009), and Drug Diversion and Poison Centers studies from the RADARS® (Research Abuse, Diversion and Addiction-Related Surveillance) System (Q3 2007-Q2 2009). Results: Internet postings about LDX discussed potential methods of tampering, liking/disliking, and polydrug use. No exceptional orders were identified in supply chain monitoring nor did product quality complaints suggest diversion. From market launch to August 2009, 7,385,712 prescriptions were filled for LDX. During the respective analysis periods there were 54 postmarketing adverse event reports of non-medical use and 73 DAWN Live! mentions. As of Q2 2009, RADARS System Drug Diversion rates for LDX

were 0.027/1,000 Unique Recipients of Dispensed Drug (URDD, to account for product availability), compared to total extended-release amphetamines at 0.037/1,000 and total extended-release methylphenidate at 0.037/1,000. Likewise, RADARS System Poison Center call rates were 0.207/1,000 URDD, versus 0.170/1,000 and 0.228/1,000, respectively. RADARS trend data will be presented for Q3 2007-Q2 2009. We anticipate having an additional 6 months of data to present. Conclusions: Non-medical use of LDX was minimal during its first 30 months of marketing, based on data from DAWN Live!, Internet and media monitoring, supply chain monitoring, postmarketing adverse event reports, and RADARS.

NR7-44

NEUROCOGNITIVE PREDICTORS OF LAMOTRIGINE TREATMENT FOR PATHOLOGIC SKIN PICKING: A DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

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SUMMARY:
Background: Although a relatively common behavior, treatment data for pathologic skin picking (PSP) are limited. The current study sought to examine the efficacy and tolerability of lamotrigine in adults with PSP and to examine neurocognitive predictors of treatment response. Method: Thirty-two subjects (29 females [90.6%]; mean age 32.8 ± 13.3 years) with PSP were treated in a 12-week randomized, double-blind, placebo-controlled trial of lamotrigine as monotherapy. Baseline cognitive assessment comprised the Stop-signal and Intra-dimensional/Extra-dimensional (ID/ED) set shift tasks. Lamotrigine dosing ranged from 12.5mg/day to 300mg/day. The primary outcome measure was picking symptoms measured by the Yale Brown Obsessive Compulsive scale Modified for Neurotic Excoriation (NE-YBOCS). Subjects were also assessed with measures of psychosocial functioning. Analyses were performed on all available data using an intent-to-treat population (LOCF). Results: No significant overall differences were noted between lamotrigine and placebo on the primary or secondary endpoints. Seven subjects assigned to lamotrigine (43.8%) were considered responders (defined as =35% n the NE-YBOCS) compared to 5 (31.3%) assigned to placebo. Those who ultimately responded to lamotrigine exhibited impaired cognitive flexibility (ED shifting) at baseline compared to lamotrigine non-responders. Conclusions: These findings suggest that, although safe and well tolerated, lamotrigine treatment may not be efficacious in patients with PSP as a whole, compared to placebo. However, these neurocognitive data suggest that lamotrigine may be valuable in a subset of patients who exhibit relatively impaired cognitive flexibility.

NR7-45

EKG ABNORMALITIES DURING ECT: A MATCHED CONTROLLED STUDY

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SUMMARY:
Introduction: Electroconvulsive therapy (ECT) has been an effective treatment for mood and psychotic disorders over 70 years and has been considered a safe procedure (1). Though pre-ECT consultation and medical workup are keys to improve the safety, electrocardiogram (EKG) abnormalities are commonly seen during the treatment (2). This study was conducted to explore the frequency of EKG abnormality and factors associated with it. Methods: Retrospective review of ECT treatments for 8 patients (M=4, F=4) with normal baseline EKG before treatment - matched with age (46.88 ±16.91) and gender for patients with abnormal baseline EKG (N=16). Ten randomized treatments were selected from a total number received for each patient. Thymatron DGx machine and Bi-frontal placements were used in all cases. All patients received either Thiopental Sodium, Propofol or combination of both as an induction agent in each treatment. Recorded EKG tracings were reviewed for 30 sec prior to ECT and up to 90 sec after ECT. Variables of interest included energy used, duration of EEG and EMG, body weight, number of psychotropic medications used, type and timing of EKG abnormalities, and vital signs pre-, during and post-ECT. General Linear model was used to determine association among variables. Results: Premature atrial contractions are commonly seen (12.5%) among others. Body weight ($p<0.01$), pre-treatment heart rate ($p=0.05$), pre-treatment EKG abnormalities ($p<0.01$) and peak heart rate during the treatment ($p<0.001$) are significantly associated with development of post-ECT EKG abnormalities – regardless of baseline EKG status, number of current medications and energy used. Conclusions: Pre-treatment

EKG status and cardiovascular responses during the treatment are important factors in developing post-ECT EKG abnormalities. The clinician must consider factors associated with development of EKG abnormalities and closely monitor EKG tracing during treatment to safely administer the treatment.

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NR7-46

LONG-TERM DURABILITY OF ACUTE RESPONSE TO TRANSCRANIAL MAGNETIC STIMULATION (TMS) IN THE TREATMENT OF PHARMACORESISTANT MAJOR DEPRESSION

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SUMMARY:

Objective: TMS is an effective acute treatment for depressed patients who fail initial pharmacotherapy. We describe TMS' durability of effect for up to 24 weeks under a protocol-specified regimen of maintenance antidepressant monotherapy. Methods: Patients with pharmacoresistant major depression (N=301) were randomized to receive active or sham TMS in a 6-week controlled trial. Patients who failed to receive benefit from their blinded treatment assignment could subsequently enroll in a 6-week, open-label extension study. A total of 142 patients achieved at least partial acute response with active TMS in these two studies, and 99/121 successfully transitioned to antidepressant monotherapy and agreed to enter a 24-week durability of effect study. During follow-up, the initial antidepressant medication could not be changed. Up to 6 weeks of open-label TMS could be administered for patients who met criteria for symptom re-emergence. Relapse was defined as a recurrence of major depression for at least two weeks, or failure to receive adequate benefit from TMS reintroduction. Outcomes were assessed using the MADRS, HAMD-24, HAMD-17, IDS-SR, and CGI-S. Results: Across 24-weeks, 10/99 (10%; Kaplan-Meier survival estimate=12.9%) patients who had previously benefited from TMS relapsed on maintenance antidepressant monotherapy. Thirty-eight (38.4%) had symptom worsening, and 32/38 (84.2%) re-achieved symptomatic benefit when TMS was reintroduced. Patients with full response after acute treatment with TMS had the most durable long-term outcome. Conclusions: Durability of the acute response to TMS is excellent when followed by antidepressant medication and access to TMS reintroduction. Posted on www.clinicaltrials.gov, Listing No. NCT 00104611.
Supported by a grant from Neuronetics, Inc.

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NR7-47

EFFECT OF MILNACIPRAN TREATMENT ON FATIGUE IN PATIENTS WITH FIBROMYALGIA: POOLED ANALYSES FROM 3 RANDOMIZED, PLACEBO-CONTROLLED CLINICAL TRIALS

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SUMMARY:

Introduction: Fibromyalgia (FM) is a chronic disorder that includes symptoms beyond widespread musculoskeletal pain. In addition to pain, fatigue is one of the most commonly reported symptoms in patients with FM. Milnacipran, a dual reuptake inhibitor of serotonin and norepinephrine, is approved by the US FDA for the management of FM. This analysis uses pooled data from 3

clinical trials to further evaluate the effect of milnacipran on fatigue in patients with FM. Methods: Fatigue data were pooled from 3 phase III studies in FM patients randomized to receive placebo (n=1133), milnacipran 100 mg/day (n=1139), or milnacipran 200 mg/day (n=837). After a dose escalation phase, patients underwent 12 weeks of stable dose treatment. Fatigue was measured by using the Multidimensional Fatigue Inventory (MFI) total and subscale scores and the Fibromyalgia Impact Questionnaire (FIQ) fatigue items (6 and 7). Results: At the 3-month endpoint, significant improvements over placebo with both doses of milnacipran were observed in MFI total score and in FIQ fatigue items 6 and 7 (P<.01). Milnacipran 200 mg/day treatment resulted in significant improvements in all MFI subscale scores versus placebo (P<.05); milnacipran 100 mg/day significantly improved general fatigue, physical fatigue, and reduced motivation subscale scores versus placebo (P<.05). In milnacipran-treated patients, improvements in MFI total score correlated only moderately well with improvements in VAS pain (r=0.451) and Patient Global Impression of Change (PGIC; r=0.507), indicating that these domains provide additional contributions to FM symptomatology. Conclusion: Among patients with FM, milnacipran treatment resulted in significant improvements relative to placebo in multiple dimensions of fatigue. Milnacipran may be effective in treating symptoms of fibromyalgia beyond pain, including fatigue.

Supported Statement: Supported by Forest Laboratories, Inc. and Cypress Bioscience, Inc.

NR7-48

MILNACIPRAN IMPROVES PAIN, PGIC, PHYSICAL FUNCTION, AND DEPRESSIVE SYMPTOMS IN FIBROMYALGIA: RESULTS FROM A PLACEBO-CONTROLLED MILNACIPRAN TRIAL

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SUMMARY:

Introduction: The management of fibromyalgia (FM) is complicated by multiple symptoms, including pain, fatigue, stiffness, physical dysfunction, and depressive symptoms. Milnacipran is a serotonin and norepinephrine reuptake inhibitor approved in the US for the management of FM. This clinical trial evaluated the effect of milnacipran 100 mg/day in FM patients on the multidimensional symptoms of FM, including depressive symptoms. Methods: In this phase 3 trial, FM patients were randomized to milnacipran 100 mg/day (n=516) or placebo (n=509) for 12 weeks of stable-dose treatment. Primary endpoints included 2 composite responder analyses. A 2-measure analysis required individual patients to have >/=30% improvement from baseline in pain VAS scores and a rating of "much improved" or "very much improved" on the Patient Global of Impression of Change (PGIC); a 3-measure analysis also required a >/=6-point improvement in the SF-36 Physical Component Summary score. Depressive symptoms were assessed by using the Beck Depression Inventory (BDI). Results: Treatment with milnacipran versus placebo resulted in a significantly higher proportion of composite responders (2-measure: 42% versus 26%; 3-measure 30% versus 16%; both P<.001). At endpoint, LS mean changes from baseline in BDI scores were significantly greater with milnacipran versus placebo (-2.12 vs -1.24; P=.008). In a post hoc analysis, small but statistically significant correlations were found between changes in BDI in the milnacipran group and changes in pain VAS (r=0.210) and PGIC (r=0.309) (both P<.001). However, pain and PGIC improved regardless of changes in BDI. The most common adverse event was nausea. Conclusion: In FM patients, treatment with milnacipran 100 mg/day significantly improves multiple domains, including pain, global status, physical function, and depressive symptoms.

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NR7-49

FUNCTIONALITY AND QUALITY OF LIFE ARE IMPROVED IN FIBROMYALGIA PATIENTS TREATED WITH SODIUM OXYBATE: RESULTS FROM A PHASE 3 INTERNATIONAL TRIAL

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SUMMARY:

Background: While fibromyalgia (FM) is classified by pain and tenderness, many other clinical features are present, including functional disability, fatigue, sleep disturbance, and psychological distress. This constellation of symptoms impairs patient function and health-related quality of life (HRQoL). Objective: The effects of sodium

oxybate (SXB) on FM symptomatology were assessed in a 14-week randomized, double-blind, parallel, placebo controlled international trial. Methods: A total of 571 patients in 8 countries meeting the American College of Rheumatology criteria for FM were randomized equally to SXB 4.5g/night (SXB4.5g), 6g/night (SXB6g), or placebo (PBO). The primary outcome was the percent of patients reporting a >=30% reduction in Pain VAS (PVAS) scores from baseline to Week 14. Function and HRQoL were evaluated using the Fibromyalgia Impact Questionnaire (FIQ) and the Short Form-36 Questionnaire (SF-36). Other assessments included: percent reporting >=30% reduction in total FIQ total score, change from baseline to Week 14 in FIQ subscales, SF-36 physical component summary (PCS), and SF-36 subscales. Results: Compared to PBO, treatment with SXB4.5g or SXB6g resulted in significantly more patients (42.0% and 51.4%, respectively, vs 26.8%) reporting a reduction of >=30% in PVAS (p<=0.002) and >=30% in FIQ (both p<0.001). Statistically significant improvements with both SXB doses were noted on FIQ subscales for pain, stiffness, tired upon awakening, fatigue, functionality, difficulty with work, and did not feel good. No significant differences were noted in work missed, anxiety, or depression subscales. Both doses demonstrated improvements versus PBO in the SF-36 PCS (p<=0.003). Both SXB doses showed significant improvements in the following SF-36 subscales: physical functioning, social functioning, bodily pain, and vitality. Significant improvement in role-physical and general health was noted with SXB6g only compared to PBO. No significant difference was noted in the two remaining SF-36 subscales. Adverse events with SXB (>=5% and 2X PBO) were nausea, dizziness, vomiting, insomnia, anxiety, somnolence, fatigue, muscle spasms, and peripheral edema. Conclusion: The results from this Phase 3 international trial confirm the findings of previous clinical trials demonstrating clinically relevant improvements in pain, stiffness, fatigue, function and HRQoL in FM patients treated with SXB.

Disclosures: This study was sponsored by Jazz Pharmaceuticals.

NR7-50

INFLUENCE OF PARENTING STYLES ON TEMPERAMENT, NORMAL PERSONALITY TRAITS, AND PERSONALITY DISORDERS

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SUMMARY:

Objective: Despite much research there has not been a clear consensus on the nature and extent of the association between parenting styles of mothers and fathers and adult temperament and personality traits. The aim of this study was to further examine this question using a dimensional approach to personality and temperament which is under growing consideration in the development of DSM-V. Methods: We utilized the Parental Bonding Instrument (PBI) and the Schedule for Nonadaptive and Adaptive Personality 2nd Edition (SNAP-2) to assess a community sample of forty-two females aged 18 to 30. We assessed the relationship between participants' recollections of their parents' parenting behaviors during childhood, and their traits, temperament, and DSM-IV personality disorders. Linear regressions were conducted to explore which parenting styles (maternal and paternal care and protectiveness) were predictive of each temperament, trait, and personality disorder. Results: Forty-two point nine percent of the participants completed both measurements. Maternal care was found to predict exhibitionism, entitlement, and narcissistic personality. Paternal care was found to positively predict disinhibition, histrionic personality, and antisocial personality, and negatively predict dependent personality. Lower paternal protectiveness predicted low self-esteem as well as depressive and schizotypal personality. Conclusion: Our study found that for women both maternal and paternal behaviors predicted their adult temperament, personality traits, and personality disorders. Further research is needed to understand how parenting styles may influence adult characteristics.

NR7-51

POSTTRAUMATIC STRESS DISORDER: CLINICAL PERSONALITY DISORDERS THAT CORRELATE WITH THE ONSET OF COMBAT STRESS

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SUMMARY:

Objective: Why do some soldiers returning home from combat have post traumatic stress disorder (PTSD) and others do not? It is estimated that PTSD affects 1 in 5 combat veterans today. A significant but underappreciated study in our understanding of the development of PTSD

came from one conducted by Dieperink, Leskela, Thuras, & Engdahl, (2001). They found that veterans classified as insecurely attached were 5.8 times more likely to have PTSD than those classified as secure (Dieperink et al., 2001). However, their measure used the Experiences in Close Relationships Questionnaire (ECR), which contains two major scales, anxiety and avoidance in relationships (Brennan, Clark, & Shaver, 1997). It has been shown that this measure does not measure attachment, but rather generalized psychopathologies centering on anxiety and avoidance, principal defining characteristics of PTSD (Lindberg, 2008; Lindberg & Thomas, 2007). The present study attempted to correct this flaw in methodology. Method: Veterans from Iraqi Freedom (N=44, 33 male and 11 female) were given the Attachment and Clinical Issues Questionnaire (ACIQ) along with the PCL-S, the military scale of PTSD; the CES or combat exposure scale, the CAGE, a measure of alcohol consumption; and the M-Mast/F-Mast, measures of parental alcohol consumption. The ACIQ is a well-validated measure of attachment and clinical issues that contains 29 scales. Results: Along with Combat and Post Combat exposure scales, the ACIQ scales of Control, Family Rigidity versus Chaos, and Perfectionism were found to be significant predictors of PTSD symptoms. We are currently further analyzing these and other relevant data. Summary: It was found that the clinical issues along with the combat exposure scales combined to provide a good model of the development of PTSD. The results will be discussed in terms of further research and potential clinical implications.

NR7-52

FACIAL AFFECT RECOGNITION IN NARCISSISTIC PERSONALITY DISORDER

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SUMMARY:
Background: Although most experimental studies on narcissistic personality disorder (NPD) have focused on the concept of self-esteem by measuring the reactions to provoked self-esteem instability, other studies are emerging that examine the concept of narcissism from a different viewpoint. An important element of narcissistic behaviors is the presence of affective deficits, illustrated by the lack of empathy, or the recognition of emotions in others. In the present study, possible affective deficits will be measured by administering a facial recognition task among individuals with NPD. Methods: A facial affect recognition task (FEEST) was administered to 30 participants (10 NPD, 10 Cluster C patients and 10 healthy men). Participants were asked to choose the adequate emotional expressions out of six categories (anxious, angry, happy, neutral, disgust and sad). Results: Overall, patients with NPD were significantly worse at recognizing emotional expressions compared to other patients with personality disorders and normal controls. More specifically, narcissistic men were worse at recognizing fear in men and anger and disgust in females. Conclusions: It is shown that men with NPD are worse in facial affect recognition compared to other patients with personality disorders and a normal control group. This is in line with earlier facial affect recognition studies among psychopathic individuals.

NR7-53

EFFECT OF ARMODAFINIL ON PATIENT FUNCTIONING AND FATIGUE IN PATIENTS WITH RESIDUAL EXCESSIVE SLEEPINESS ASSOCIATED WITH TREATED OSA AND COMORBID MDD

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SUMMARY:
Background: As previously reported, the current study showed that armodafinil, the longer-lasting isomer of modafinil, improved overall ES-related clinical condition in patients with residual ES associated with CPAP-treated OSA who had a comorbid depressive disorder. Armodafinil also improved wakefulness compared with placebo although the difference was not statistically significant. The objective of the current analysis was to assess the efficacy of armodafinil for improving patient functioning and reducing fatigue in these patients. Methods: In the 12-week, multi-center, randomized, double-blind, placebo-controlled, parallel-group study, 249 patients with residual ES associated with CPAP-treated OSA and a comorbid major depressive or dysthymic disorder requiring antidepressant monotherapy were randomized to armodafinil 200 mg or placebo once daily at 8 am. Effects on patient functioning and fatigue, secondary outcomes of the study, were assessed using the Functional Outcomes of Sleep Questionnaire (FOSQ) and the Brief Fatigue Inventory (BFI) at weeks 2, 4, 8, 12 or final visit. Tolerability was also assessed. Results: Demographic and clinical characteristics were similar between groups at

baseline. The mean change from baseline to final visit for total FOSQ score was 2.2 for patients receiving armodafinil and 1.7 for patients receiving placebo (nominal P=0.0308). A greater proportion of patients administered armodafinil (45%) were responders (>17.9 on the total FOSQ score) at final visit than patients administered placebo (28%) (nominal P=0.0100). Improvement in total FOSQ score and proportion of responders was observed at week 4 and maintained through week 12. Patients in the armodafinil group reported a greater reduction in fatigue than patients in the placebo group, according to the change from baseline in global BFI score at weeks 2, 8, and 12 (nominal P=0.0349) but not at week 4 (nominal P=0.1272) or final visit (nominal P=0.0523). Similar results on the BFI scores for worst fatigue and interference of fatigue with daily activities were observed. Armodafinil was generally well tolerated. Conclusions: Armodafinil 200 mg/day improved patient functioning versus placebo as assessed by the FOSQ in patients with residual ES associated with CPAP-treated OSA and a comorbid depressive disorder. Fatigue also improved at weeks 2, 8, and 12 as assessed by the BFI in patients who received armodafinil.
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NR7-54

"WHAT A DIFFERENCE A KID MAKES": HOUSEHOLD DEMOGRAPHICS AND SLEEP IN THE U.S.

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SUMMARY:
Recent research has demonstrated the increased prevalence of insufficient sleep in the U.S. Notably, insufficient sleep has become increasingly associated with motor vehicle accidents, industrial disasters, and impaired academic and vocational performance. In the present investigation, we analyzed data from the 2008 Behavioral Risk Factor Surveillance Survey (BRFSS), a population-based telephone survey of U.S. adults (N=400,977) to examine the relationship between marital status (married, previously married, and never married) and the number of children in the household, to insufficient sleep. As part of the core BRFSS questionnaire in 2008, respondents were asked, "During the past 30 days, for about how many days have you felt you did not get enough rest or sleep?" Our results indicated that the number of days of insufficient rest or sleep was higher for married adults with any children in their household relative to married adults in households with no children. Among married respondents, we also found that women reported significantly more days of insufficient sleep than men did. In contrast, among previously married respondents, there was no significant gender-specific difference in insufficient rest or sleep, although an increase in reported insufficient rest or sleep associated with the presence of one or more children in the household remained significant. Among never married respondents, women with no children in the home reported more days of insufficient sleep than men, while there was no association between the presence of children in the household and insufficient sleep among never married men. These findings suggest that the presence of children in the household often increases the frequency of insufficient rest or sleep among the adults with whom they reside. Thus, clinicians may wish to consider the presence of children in the household as a possible "risk factor" for insufficient rest or sleep among adults and tailor screening and intervention efforts accordingly.

NR7-55

A RANDOMIZED, CONTROLLED TRIAL OF VIRTUAL REALITY EXPOSURE WITH AROUSAL CONTROL FOR ACTIVE DUTY SERVICE MEMBERS WITH COMBAT PTSD

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SUMMARY:
Post Traumatic Stress Disorder (PTSD) is a significant problem in Service Members returning from deployment to Iraq and Afghanistan, but no randomized controlled trials have been published for treatment of this population. Virtual Realty-based therapy has been emerging as a potentially useful modality for treating PTSD, but likewise no randomized controlled trials had previously been conducted. Objective: to study the effect of Virtual Reality Exposure with Arousal Control (VRE-AC) versus Treatment As Usual (TAU) for combat PTSD. Methods: Twenty active duty members with PTSD related to service in Iraq or Afghanistan were enrolled in a trial at two military hospitals in Southern California. Participants were randomly assigned to receive 10-weeks of treatment

with VRE-AC (n=10) or TAU (n=10). Outcomes were tracked using the Clinician Administered PTSD Scale (CAPS), with treatment considered successful if there was a 30% or greater response on the CAPS. Results: All 10 participants in VRE-AC returned for post-assessment, as did 9 of the TAU participants. Seven of 10 participants improved by 30% or greater while in VRE-AC, while only one of the nine returning participants in TAU showed similar improvement ($X2=6.74$, $p<0.01$). Participants in VRE-AC improved an average of 35 points on the CAPS, while those in TAU averaged only a 9 point improvement ($p < 0.05$). Conclusions: This result suggests that VRE-AC can be a useful modality in treating combat PTSD.

NR7-56

SCREENING FOR BIPOLAR POSTPARTUM DEPRESSION: VALIDATION OF THE MOOD DISORDER QUESTIONNAIRE

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SUMMARY:

Background: Despite the prevalent nature of postpartum depression in women with bipolar disorder, there are currently no screening instruments designed specifically for bipolar disorder in the postpartum period. Methods: Women with histories of major depressive disorder or bipolar disorder attending an outpatient perinatal clinic were administered the Mood Disorder Questionnaire during the first month after delivery. A research professional, blind to the Mood Disorder Questionnaire results, conducted a face to face diagnostic interview using the Structured Clinical Interview for DSM-IV. Results: A total of 36 women with bipolar disorder (31 with bipolar II disorder and 5 with bipolar I disorder) and 62 women with major depressive disorder completed the Mood Disorder Questionnaire between 2 to 4 weeks after delivery. The traditional scoring criteria yielded a sensitivity of 51.61% and a specificity of 82.61%. The optimal cut-off score was 8 or more endorsed symptoms without the supplementary questions (sensitivity of 87.10% and a specificity of 81.16%). Conclusions: The Mood Disorder Questionnaire with alternate scoring is a useful screening instrument for bipolar disorder in the postpartum period.

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NR7-57

CHILDHOOD ADVERSITY, MENTAL DISORDER COMORBIDITY, AND SUICIDAL BEHAVIOR IN SCHIZOTYPAL PERSONALITY DISORDER

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SUMMARY:

Background: Schizotypal personality disorder (SPD) is a serious psychiatric disorder, characterized by a pervasive pattern of social and interpersonal deficits and marked functional impairment. However, it remains understudied among the personality disorders and very little is known about the psychiatric correlates of SPD in the general population. Objectives: To examine whether SPD is associated with childhood adversity and suicidal behavior in a representative epidemiologic sample. Method: The current study utilized data from Wave 2 of the National Epidemiological Survey on Alcohol and Related Conditions (NESARC). The 2004-2005 Wave 2 NESARC dataset sampled the United States civilian adult population, surveying 34,653 individuals via in-person interviews. DSM-IV diagnoses were made using the Alcohol Use Disorders and Associated Disabilities Interview Schedule IV (AUDADIS-IV). Multiple logistic regression compared people with SPD to the general population across a broad range of childhood adversities, comorbid psychiatric disorders, and suicidal behavior. Results: SPD was strongly associated with many adverse childhood experiences, with physical abuse [Adjusted OR (AOR) = 4.43, 95% CI = 3.64-5.40] and sexual abuse (AOR = 4.67; 95% CI = 3.95-5.73) showing the highest odds ratio values. Even after adjusting for confounding factors, SPD was independently associated with major depression and several anxiety disorders, including posttraumatic stress disorder (AOR = 1.51, 95% CI = 1.23-1.87). Interestingly, SPD was more strongly associated with borderline (AOR = 6.89; 95% CI = 5.56-8.53) and narcissistic (AOR = 4.80; 95% CI = 4.00-5.76) personality disorders than Cluster A personality disorders. In adjusted models, individuals with SPD were also more likely to attempt suicide (AOR

= 1.34; 95% CI = 1.03-1.74) compared to those without SPD. Conclusions: SPD is associated with considerable negative consequences, including suicidal behavior. The surprising association with Cluster B personality disorders requires replication in future studies, and if consistent may have potential implications for the categorization of SPD.

NR7-58

CARCINOGENESIS OF PSYCHOPHARMACOLOGICAL TREATMENTS PRESCRIBED IN GENERAL PSYCHIATRY:A SYSTEMATIC REVIEW

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SUMMARY:
Introduction: The risk for carcinogenesis of psychotropic drugs in the market has been fairly understudied. Preclinical and epidemiological studies looking at these risk factors in specific clinical populations with major mental disorders are scarce. Most research includes small sample sizes, potential for confounding bias and methodological limitations. Objective: Systematic review of the available data regarding preclinical and epidemiological studies looking at the carcinogenesis of psychotropic medications used in psychiatry. Methods: We search the published scientific literature from 1965-2009 regarding preclinical and epidemiological studies on carcinogenesis for antidepressants, antipsychotics, benzodiazepines, psychostimulants, and mood stabilizers. Results: Two-thirds of psychotropic medications available in the market have some availability of data regarding carcinogenesis (Table 1). Amphetamines seem to produce a significant risk of hematologic and renal malignancies associated with frequency and dose-response. Methylphenidate exposure appears not to produce a long-term risk in children and adults with ADHD (Table 2). Most studies regarding antidepressants, antipsychotics and benzodiazepines report limited evidence against their long-term use (Table 3). Mood stabilizers such as lithium and valproate may have antineoplastic and chemopreventive properties inherent to their intracellular mechanisms of action (Table 4). Carbamazepine, newer antiepileptics and anti-dementia medications have not been adequately studied to date in terms of carcinogenesis (Table 5). Conclusions: There is a strong need for clinical trials including risk of carcinogenesis as their main outcome when evaluating psychotropic treatments used in psychiatry. In the meantime, issues regarding carcinogenesis in clinical practice should rely mostly on results and findings from preclinical studies of experimental models in animals and humans.

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