NEW RESEARCH

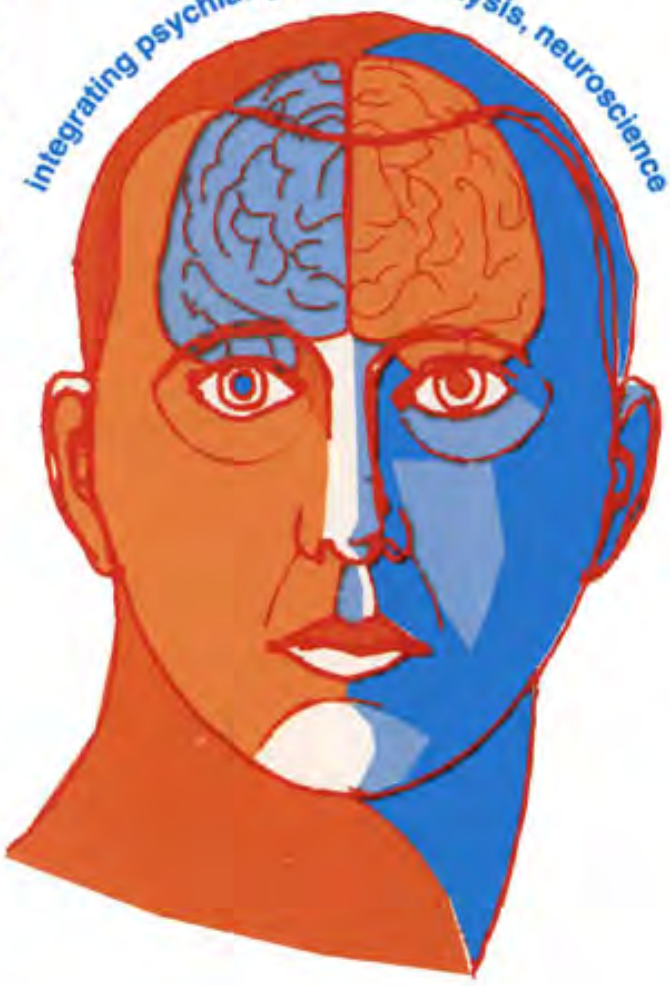
NEW RESEARCH ABSTRACTS

AMERICAN PSYCHIATRIC ASSOCIATION

2001 ANNUAL MEETING

mind meets brain

integrating psychiatry, psychoanalysis, neuroscience



New Orleans, LA ■ May 5-10, 2001

ABSTRACTS

NR1 Monday, May 7, 9:00 a.m.-10:30 a.m.

Topiramate Treatment of Bipolar Spectrum Disorders: A Retrospective Chart Review

S. Nassir Ghaemi, M.D., *Department of Psychiatry, Cambridge Hospital, 1493 Cambridge Street, Cambridge, MA 02139*; Sumita G. Manwani, M.D., Jacob J. Katzow, M.D., James Y. Ko, A.B., Frederick K. Goodwin, M.D.

Summary:

Objective: To determine if topiramate is effective as treatment for bipolar spectrum disorders in a naturalistic setting.

Method: All charts of outpatients treated with topiramate (N= 76) were reviewed, and clinical response was assessed retrospectively using the Clinical Global Impressions Scale for Improvement (CGI-I). This project was funded by a research grant from Janssen Pharmaceutica.

Results: Mild improvement was seen in 47% (N=36) and moderate to marked improvement in 13% (N=10). Responders received a higher mean dose (180mg/day) than non-responders (83.2 mg/day, p=0.002). Topiramate dose was also higher in those who lost weight (138.3 mg/day) than in those who did not (70mg/day, p=0.007). 50% experienced weight loss with a mean amount of 14.2 lbs. 82% (N=62) reported side effects including cognitive effects, sedation, parasthesias, nausea, insomnia, headache, and dizziness. 36% (N=27) of the total sample discontinued treatment because of adverse effects.

Conclusion: Topiramate led to significant weight loss in about half of this bipolar population, while also improving mood symptoms at least mildly in most patients. Topiramate response and weight loss were both dose related, with efficacy, in particular, associated with higher doses (mean 180 mg/day) than frequently used in current clinical practice.

NR2 Monday, May 7, 9:00 a.m.-10:30 a.m.

Opioid Hypothesis of Schizophrenia: A Genetic Evaluation

Gagandeep Singh, M.D., *Department of Psychiatry, Mayo Clinic, 200 First Street, SW, Rochester, MN 55905*; Vanessa F. Haluska, M.S., Orhun Kantarchi, M.D., Cynthia T. McMurray, Ph.D.

Summary:

Background: Family, adoption, and twin studies support a genetic component to pathogenesis of schizophrenia. Opioid peptides are neuromodulators that influence complex neurologic functions including behavior. Direct and indirect pharmacologic evidence supports their role in schizophrenia. Opiate precursors prodynorphin, preenkephalin A, and proopiomelanocortin are candidate genes for schizophrenia.

Objective: (1) Screen patients and controls for polymorphisms and missense mutations in the prodynorphin and preenkephalin genes. (2) To determine using a case control study design if these are associated with schizophrenia.

Method: Patient and control samples were collected by standard methods as described by Mickesell et al, 1997. Systematic search of the entire gene for variations was done using bi-directional deoxy finger printing method. This was confirmed by sequencing. Allele frequency will be calculated as a percentage of #of alleles/ total # of alleles x 100.

Results: Our group earlier described polymorphism and a missense mutation in the preenkephalin A gene. These studies revealed the presence of a single misense mutation in an African-American patient with severe hallucination phenotype. We have now identified four polymorphism in the promoter of the prodynorphin gene.

Conclusion: The prodynorphin gene has polymorphisms in the promoter region worthy of further study in schizophrenia.

NR3 Monday, May 7, 9:00 a.m.-10:30 a.m.

Development of Single Nucleotide Polymorphism Array for Prediction of Lithium Response in Bipolar Disorder

Gagandeep Singh, M.D., *Department of Psychiatry, Mayo Clinic, 200 First Street, SW, Rochester, MN 55905*; Jenny Ekholm, Ph.D., Tuula Kieseppa, M.D., Timo Partonen, M.D., Erkki Henriksson, M.D., Jouho Lonnquist, M.D., James T. McCracken, M.D., Nelson B. Freimer, M.D., Leena Peltonen, M.D.

Summary:

Background: Family, adoption, and twin studies support a genetic component to the pathogenesis of bipolar disorder (BD). The response to lithium has been suggested to be an endophenotype of this disorder. Variations in genes related to action of lithium (esp. the phosphoinositide and protein kinase C related pathways) are candidates for prediction of lithium response and could provide insights in BD.

Objectives: (1) To search and map single nucleotide polymorphisms (SNPs) in candidate genes for BD. (2) To determine wheter these SNPs are associated with lithium resistance in BD.

Methods: An extensive review of the literature was conducted to identify potential candidate genes. A systematic search of bioinformatics resources was used to search and map SNPs. These were confirmed by sequencing. An array technique based on Pastinen et. al. 2000, will be used to genotype. A case control study design will be used to look for an association in a Finnish bipolar disorder set.

Results: A total of 23 genes related to the phosphoinositide and protein kinase C pathways have been selected for initial evaluation. A comprehensive map of the SNPs has been developed for all the genes. The over 200 SNPs to be included in the microarray have been defined and confirmed.

Conclusions: The genes in this study are potential candidates for further functional studies of lithium response in BD.

NR4 Monday, May 7, 9:00 a.m.-10:30 a.m.

The Effect of Antipsychotics on Gene Expression in Hippocampus by DNA Chips

Eung-Seok Oh, *Department of Psychiatry, Han-Yang University, 17 Haengdang Dong Seongdong Ku, Seoul 133-792, South Korea*; Yun-Gyoo Cho, M.D., Byung-Hwan Yang, M.D., Yong-Sung Lee, M.D., Kyu-Yeong Lee, M.D., Hyun-Cheol Koh, M.D.

Summary:

Using 4,000 genes of which base sequences are already well known, we tried to identify and compare the effect of a typical antipsychotic (haloperidol) and an atypical antipsychotic (risperidone) on gene expression in the hippocampus of rats. Through this identification and comparison, we expected to understand the action mechanism of these drugs at the level of molecular genetics, get the basic materials for developing better antipsychotic drugs, and obtain basic information for identifying pathogenesis of schizophrenia at the level of molecular genetics.

Intraperitoneal injections of haloperidol (2mg/kg) and risperidone (0.5mg/kg) were done. One hour, 24 hours, and 60 hours after the injection we got the tissue preparations of the hippocampus of the rats. The process of total RNA extraction from the samples, microarray probe synthesis, and microarray hybridization were progressed favorably. Changes in gene expression significantly differend by drug and time passed after the injection. Detailed data will be presented.

In the near future, the study of the effect of various antipsychotics on numerous genes is essential for obtaining further information about antipsychotics and schizophrenia.

NR5 **Monday, May 7, 9:00 a.m.-10:30 a.m.**

Discrimination Through the MMPI-2 Between Self-Injured Inmates and the Rest of the Population in a Spanish Youth Prison

Leopoldo Ortega-Monasterio, M.D., *Department of Justice, Clinica Forense, Travesera de Garcia 14 3, Barcelona 08021, Spain*; Susana Mohino, Ph.D.

Summary:

Introduction: In the field of forensic and penitentiary psychiatry one of the more typical clinical problems is the risk of self-injuries among inmates (suicide attempts, manipulative behavior, or histrionic conduct.) In 1998 in the prisons of Barcelona (Spain) the Ministry of Justice of Spain collected 854 incidents of self-injury behavior in Barcelona, 71 of them were from youth inmates. The authors' goal was to predict the risk of self-injuries (independent of the different nosological subtypes, in which every behavior can be included). Using the MMPI-2 they discriminated between self-injured youth inmates and the other inmates.

Procedure: The random sample in this research was 107 male subjects between the ages of 18–25 years old. These inmates were in the Trinidat prison (Barcelona, Spain) in 1999. Subjects diagnosed with psychosis and severe disorders were already excluded. The recollected data of self-injury behaviors was from the emergency services of the Trinitat prison. With the MMPI-2 the authors identified a variety of psychopathological factors. Discriminant function analysis and other statistical techniques were used to determine scales of MMPI-2 that discriminated the self-injured inmates from the sample.

Results: Some scales of MMPI-2 classified 90% of the cases correctly. The results supported the use of MMPI-2 for the assessment of these problematic behaviors.

Conclusions: It is possible to identify some of the risk variables through the MMPI-2. These variables can facilitate the detection of the cases of self-injured inmates. The results can help to prevent these behaviors and aid in the adjustment to prison.

NR6 **Monday, May 7, 9:00 a.m.-10:30 a.m.**

Assessing Capacity Instruments in Inpatient Legal Proceedings

Robert B. Gilman, M.D., *Department of Psychiatry, St. Vincent's Hospital, 144 West 12th Street, Room 179, New York, NY 10011*; Stephen B. Billick, M.D.

Summary:

Introduction: Psychiatrists are required to assess inpatients who request early discharge from the hospital or inpatients who are refusing prescribed medication. Standardized instruments may be helpful in presenting data for judicial review.

Methods: The Competency Questionnaire (CQ) is a 15 item instrument that has been shown to be both reliable and valid in assessing psychiatric inpatient capacity to consent to hospitalization and treatment. The MacArthur Competency Assessment Tool (MacCAT-T) is a more complex interview instrument that has had excellent correlation in capacity assessment. Both instruments were administered to 13 psychiatric inpatients requesting premature discharge or refusing medication.

Results: All were found on clinical assessments to lack capacity for decision making regarding hospitalization and treatment. All 13 patients were retained or medicated by judicial order. Total CQ scores correlated well ($p = < .05$, $r = .76$) with total MacCAT-T scores. Both instruments were helpful in assessing capacity.

Discussion: The MacCAT-T provided a broader, more in depth assessment of the patient's capacity, but was more subjective. The CQ was quick and easy but was less discriminate in assessing the higher functioning patients.

NR7 **Monday, May 7, 9:00 a.m.-10:30 a.m.**

Feasibility of Health Care Proxy Counseling Among Geropsychiatric Inpatients

Marcus Tjia, B.S., *Department of Psychiatry, Mt. Sinai Medical Center, 50 East 98th Street, # 9E4, New York, NY 10029*; Margaret C. Sewell, Ph.D., Rachel Z. Goodman, Ph.D., Sean R. Chappin, B.A., Deborah B. Marin, M.D.

Summary:

Objective: To determine feasibility of health care proxy (HCP) counseling and formally measure capacity among geropsychiatry inpatients.

Methods: Sixty-six admissions to a geriatric psychiatric unit were screened for capacity to understand the consent process. Consented patients were administered the Mini-Mental Status Exam (MMSE) and the MacCat-T (MacArthur, Capacity Assessment Tool).

Results: Mean age was 75 (51% female; 49% Caucasian). Diagnoses: mood disorders (46%), dementia (33%), and thought disorders (11%). Thirty-three of the 66 admissions were approached. Those not approached were more likely to have dementia or thought disorders (χ^2=11.86, df=3, p=.008). Nineteen (mean MMSE=23) of the 33 participated. The most basic legal standard—ability to evidence a logical choice—was used to define capacity. Of 19 interviewed, 53% had capacity to assign an HCP. Those with capacity had a significantly higher MMSE (F=8.49, p=.012). Of those who had capacity, 11% assigned an agent.

Conclusions: Results suggest that most geropsychiatric inpatients do not have capacity to assign an agent. Few with capacity actually designated agents. Inpatient psychiatric settings may not be the appropriate arena in which to address this issue, which underscores the importance of proactive counseling before acute illness or during outpatient follow up.

NR8 **Monday, May 7, 9:00 a.m.-10:30 a.m.**

Personality Characteristics of Female Pathological Gamblers

Silvia S. Martins, M.D., *Department of Psychiatry, University of Sao Paulo, Rua Ovidio Peres Campos, S/N, Sao Paulo, SP 05403-010, Brazil*; Shelia C. Caetano, M.D., Hermano Tavares, Ph.D., Daniel Fuentes

Summary:

Objective: Describe personality characteristics of female pathological gamblers (PG).

Method: Comparison of 30 female PG with 35 well-matched male PG, regarding personality characteristics according to the Temperament and Character Inventory and controlling for depression and anxiety. Sample selection by the South Oaks Gambling Screen followed by a sociodemographic questionnaire and a psychiatric diagnosis questionnaire-SCAN.

Results: Women had higher Harm Avoidance I (p=0.03), lower Self-Directedness I (p=0.05) and lower Cooperativeness IV (p= 0.007) compared with male PG. Female subjects were more depressed than males (p=0.008).

Conclusions: Female PG differ from their male counterparts regarding personality characteristics. They are more pessimistic, blame others more, and are more revengeful than male PG. Clinicians should take into account that females may need different treatment approaches than those applied for males. Future research regarding how personality characteristics related to gender can influence clinical aspects, treatment, and prevention of pathological gambling are needed.

NR9 Monday, May 7, 9:00 a.m.-10:30 a.m.

Informed Consent: Psychiatrists' Background in Predicting Use in Practice

Matthew E. Kleban, M.D., *Department of Psychiatry, St. Vincent's Hospital, 153 West 11th, Reiss 172, New York, NY 10011*; Stephen B. Billick, M.D., James R. Roney, M.A.

Summary:

Objective: With the rise of different specific types of psychotherapy and biological treatments, psychiatrists often differ in their opinion as to what constitutes appropriate informed consent. In this study, the authors attempted to quantify the amount of informed consent given to patients and whether any correlation exists between informed consent and individual background of the treating psychiatrist.

Method: A simple questionnaire was developed incorporating the essential elements of informed consent for psychiatric treatment. An additional informational questionnaire was developed for assessing training and competence in various treatments. The questionnaires were administered to practicing psychiatrists. Demographic data were collected.

Results: Neither age, length of time since residency training, or gender were significant in correlating with the degree of informed consent given to patients. A direct effect of age was found, but this effect dropped out when other variables were controlled. History of past training in forensic psychiatry was significant in correlating with informed consent (p=0.01).

Conclusions: Many psychiatrists are not yet providing full informed consent. Training in forensic psychiatry helps clinical psychiatrists provide informed consent, providing a higher standard of care in their practice.

NR10 Monday, May 7, 9:00 a.m.-10:30 a.m.

Cancer Incidence in a Cohort of Schizophrenic Patients

Francoise Casadebaig, Ph.D., *Unite 513, Inserm, 8 Rue du General Sarrail, Creteil 94010, France*; Bernard Lachaux, M.D., Alain Philippe, Ph.D.

Summary:

The basis of this study is a cohort of 3,473 schizophrenic patients (ICD-10 criteria; 64% were men, 36% were women), monitored in France since 1993. The patients were treated in community psychiatric units (N=122), which provide similar health care facilities nationwide. A large majority of the patients were outpatients (63%). The mean age of the patients on inclusion in the study was 39.4 years (42.2 for women versus 37.8 for men). Patients who died from cancer (N=27), including lung cancer (N= 9), were matched with non-deceased patients (three non-deceased patients were matched with each deceased patient) by sex, age (within 4–5 years), and place of health care. The expected number of cancer-related deaths was 19.3 (SMR=1.4), and the expected number of deaths from lung cancer was 5.1 (SMR=1.8). The patients who died from lung cancer were more often smokers (100% versus 54%). No other statistically significant characteristics were associated with cancer-related deaths. This poster discusses the implications of these findings.

NR11 Monday, May 7, 9:00 a.m.-10:30 a.m.

Patients at Screen in a Psychiatric Research Center: Clinical and Demographic Features

Flavia C. Campos, *Psychiatric Institute, Fed University of Rio De Janeiro, Visconde de Piraja 407/702 Ipanema, Rio de Janeiro, RJ 22410-003, Brazil*; Antonio E. Nardi, M.D.

Summary:

Objective: Describe the clinical and demographic profile of patients attending a screening at the Psychiatric Research Center in Rio de Janeiro, Brazil.

Method: The patients were interviewed on arrival and diagnosis was made by the structured Clinical Interview for DSM-IV. We also administered a questionnaire for demographic data, the self-rating SCL-90, and the Sheehan Incapacity Scale.

Results: 120 patients were interviewed between March and May/2000. Major depression (38, 4%), generalized anxiety disorder (25%), social anxiety disorder (10%), panic disorder (20%), and dysthymia (6,6%) were the most frequent diagnoses. The SCL-90 scores were higher in depression (mean=2.34), anxiety (mean=1.80), somatization disorder (mean=1.49), and interpersonal sensitivity (mean=1.77). The group was 38% men and 62% women; the mean age was 37.983. 63.4% of them had a least a high school level education.

Conclusion: The sample who characterized mostly with anxiety and mood disorders. The most frequent diagnosis was recurrent depression in single women. Higher incapacity was reported in social functioning (6.2, SD=2.9) than in family (5.3, SD=3.3) or occupational (5.9, SD=3.0) functioning. The description of clinical and demographic data of a specialized research center could be useful for comparing to non specialized centers in general hospitals and primary care units.

NR12 Monday, May 7, 9:00 a.m.-10:30 a.m.

Cigarette Smoking and Panic: The Role of Neuroticism

Renee Goodwin, Ph.D., *Department of Psychiatric Epidemiology, Columbia University, 1051 Riverside Drive, Unit 43, New York, NY 10032*; Steven P. Hamilton, M.D.

Summary:

Objective: To determine the role of neuroticism in the relationship between panic attacks and cigarette smoking among adults in the community.

Methods: Data were drawn from the Midlife Development in the United States Survey, a representative household survey of the adult population of the United States (N=3, 032). Multivariate logistic regression analyses were used to determine the association between cigarette smoking and panic attacks after adjustment for the effects of neuroticism, to test for evidence of interaction, and to determine whether neuroticism is an independent predictor of co-occurring cigarette smoking and panic.

Results: Individuals who smoke cigarettes were significantly more likely to have panic attacks (OR=1.9, 95% CI=1.3–2.9). This relationship remained significant after controlling for demographic characteristics and comorbid mental disorders (OR=1.7, 95% CI= 1.1–2.8), but was no longer evident after adjusting for neuroticism. Results of stratified analyses revealed that there was a significantly increased risk of panic attack associated with cigarette smoking among those with high neuroticism (OR=5.5, 95% CI= 1.6–18.8), but there was no significant relationship between cigarette smoking and panic among those with low neuroticism (1.2, 95% CI=0.7–2.1). Neuroticism independently predicted co-occurring cigarette smoking and panic but was not associated with panic or cigarette smoking in the absence of the other.

Conclusions: These data are preliminary but if replicated suggest that neuroticism may reflect a shared vulnerability for the co-occurrence of cigarette smoking and panic. Future studies are needed to further explore the mechanism of this association.

NR13 Monday, May 7, 9:00 a.m.-10:30 a.m.

Cellular Phone Calls Received and Hopelessness in the General Population

Kaisa Haatainen, M.H.S.C., *Department of Psychiatry, University of Kuopio, P O Box 1777, Kuopio 70211, Finland*; Antti Tanskanen, M.D., Kirsi Honkalampi, Ph.D., Paivi Maaranen, M.D., Heimo Viinamaki, M.D.

Summary:

Objective: Insufficient social contracts are associated with hopelessness. Cellular phones make social contacts possible and easy without personal face-to-face contact. It is not known whether there is any association between use of cellular phone and hopelessness.

Method: A large survey of psychosocial risk factors among Finnish adults was carried out in 1999. A total of 1,722 subjects responded. The level of hopelessness was estimated with the Beck Hopelessness Scale. A cutoff score of 9 or more was used to define at least moderate hopelessness (n=193, i.e. 11%). The users of cellular phones (n=1181, i.e. 69%) were divided into those who received few calls a day (i.e. insufficient social contact) and others (i.e. sufficient social contact).

Results: After adjustment for gender, age, marital status, education, work ability, place of residence, economical status, subjective health, and alcohol intake of parents during childhood, the risk of at least moderate hopelessness was 1.79 (95% CI's: 1.14–2.83, p=0.012) among those who received few cellular phone calls a day compared with others in the logistic model.

Conclusion: This study shows that insufficient social contacts estimated even by cellular phone calls received are associated with hopelessness in the general population.

NR14 Monday, May 7, 9:00 a.m.-10:30 a.m.

Incidence of Schizophrenia in Surinam

M. Hanoeman, M.D., *Koetshuis, St. Adhesie, Postbus 5003, Deventer GC-7400, Netherlands*; J. P. Selten, Ph.D., R. S. Kahn, Ph.D., L. Timmerman

Summary:

Background: More than one-third of the population of Surinam migrated to the Netherlands in the 1970s and 1980s. The incidence of schizophrenia in these immigrants has been found to be about three times higher than in their Dutch-born peers. If selective migration explains these findings, one expects to find a very low incidence of the disorder in Surinam. A study of the Dutch psychiatric registry found a relative risk of about 3 to 4, a first contact incidence study in de The Hague a relative risk of three.

Objective: To determine the rate of first admissions for schizophrenia in Surinam in the 1990s.

Method: Investigation of the medical records of the sole psychiatric hospital in Surinam.

Results: The mean annual rate of first admissions for schizophrenia or schizophreniform disorder (DSM-III-R criteria) in 1992 and 1993 was 1.61 per 10,000 (95% C.I. interval: 1.24–1.98 per 10,000). This is a normal figure. The proportions for each ethnic group (Afro-Surinamese 37/73 [50.7%], Hindustanis 23/73 [31.5%], others 13/73 [17.8%]), did not differ much from the proportions in the general population.

Conclusion: Since the incidence of schizophrenia, narrowly defined, is one to two per 10,000, we conclude that large-scale migration to the Netherlands did not lead to a decreased incidence in Surinam. The findings in the Netherlands and Surinam constitute a challenge to the hypothesis that selective migration explains the increased incidence in the immigrants.

NR15 Monday, May 7, 9:00 a.m.-10:30 a.m.

Psychiatric Morbidity in a Community Four to Six Months Postearthquake in Taiwan

Frank H.C. Chou, M.D., *Department of Psychiatry, Kai-Suan Psychiatric Hospital, 1301 Kai-Suan 2nd Road, Kaohsiung 802, Taiwan*; Tung-Ping T. Su, M.D., Wei-Tsuen Soong, M.D., Pesus Chou, Ph.D., Wen-Chen Ou-Yang, M.D., Ming-Kan Lu, M.D., I-Ju Jen, M.D.

Summary:

Objective: The prevalence and comorbidity of psychiatric disorders after 4–6 months were studied in a community situated near the epicenter of a severe earthquake that occurred in Taiwan in 1999.

Method: This was a community-based population survey. The target population was 772 residents (383 men and 389 women) who were ≧ 16 years of age. Trained lay interviewers collected their statements and background information from local government registries. Psychiatrists interviewed 442 subjects (213 men and 229 women) using the Mini-International Neuropsychiatric Interview. The adjusted response rate was 73.4%.

Results: DSM-III-R diagnoses found in the respondents included posttraumatic stress disorder (7.9%), current major depression (9.5%), panic disorder (1.6%), generalized anxiety disorder (4.8%), suicide ideation (3.8%), alcohol abuse or dependence (5.7%), and drug abuse or dependence (2.7%). Women were 2.2–10.7 times more likely than men to have a particular psychiatric diagnosis except for alcohol or drug abuse/dependence. Subjects with PTSD were 3.9–17.4 times more likely to have a comorbid psychiatric illness.

NR16 Monday, May 7, 9:00 a.m.-10:30 a.m.

Coercive Treatment of Immigrants with Psychosis

G. Eric Jarvis, M.D., *Department of Psychiatry, McGill University, 4333 Cote Ste-Catherine Road, Montreal, QC H3T 1E4, Canada*; Laurence J. Kirmayer, M.D., Bernard Unger, M.D.

Summary:

Objectives: To determine whether the coercive emergency treatment of patients with psychosis varies with immigrant status and ethnicity.

Methods: Retrospective immigrant and ethnic data of all psychotic patients admitted in 1999 were extracted from hospital records in Montreal (N=188). Of these, 44.1% (N=83) were immigrants. Patient ethnicity was as follows: Caucasian (N=129), Asian (N=33), and black (N=23). Measures of coercive treatment included use of seclusion, restraints, and medication in the emergency department. Chi-square analysis and comparison of means were used to determine significant differences among the groups.

Results: No significant differences were found between the immigrant versus non-immigrant groups. Likewise, comparisons between the Asian and Caucasian subsamples yielded no significant differences. Black subjects (mainly immigrants from Africa and the Caribbean) received significantly more seclusion (p=0.039), restraints (p=0.0063), and intramuscular (rather than oral) doses of antipsychotic medication (p=0.041) than Caucasians. Blacks also received a significantly higher mean dose of antipsychotic medication than Asians and Caucasians (p=0.01).

Conclusions: While rates of coercive treatment were similar between immigrant and non-immigrant groups, black immigrants with psychosis received more coercive treatment than their white and Asian counterparts. These results point to the need for training of emergency department staff to reduce potential bias in treatment.

Funding Source: The Metropolis Project.

NR17 Monday, May 7, 9:00 a.m.-10:30 a.m.

Global Assessment of Relational Functioning Scale: Portuguese Version

Andrea A.F. Mello, M.D., *R Urussut 71, CJ133, Sao Paulo, SP 04542-050, Brazil*; Sergio L. Blay, Ph.D., Renata D.G. Sommerman, Ph.D.

Summary:

Objective: To conduct a validity study of the Portuguese version of the GARF with families of depressive patients in Brazil.

Methodology: An experienced clinician in family therapy interviewed 34 families of patients with major depression, of recurrent type. Patients were recruited from three psychiatric inpatient units and two outpatient units. A semistructured family interview was used to classify family functioning as functional or dysfunctional. The semistructured interview was considered the gold standard. A trained psychologist, blind to the gold standard evaluation, used the GARF to assess family functioning.

Results: The best validity coefficients were obtained at a cutoff point of 70: sensitivity=78%, specificity=86%, positive predictive value=95%, and negative predictive value=50%. A regression analysis identified that some sociodemographic and clinical variables interfered with the assessment of the cutoff point.

Conclusion: This GARF validity study indicates that the validity coefficients were acceptable to assess family functioning for patients with major depression, recurrent type.

Financial support by a government agency: FAPESP

NR18 Monday, May 7, 9:00 a.m.-10:30 a.m.

Attitude of Nonpsychiatric Physicians Towards Mental Illness in Arab Communities

Tarek Assaad, M.D., *Department of Psychiatry, Ain Shams University, 14 Ali Algendi Street, Apt. 502, Nasr City-Cairo 11371, Egypt*; Fatmah Kaaki, A.B., Mustafa K. Saadani, M.D.

Summary:

Numerous studies conducted during the past decades indicate that the public attitude towards mentally ill patients is strongly "prejudiced." The aim of this study was to highlight the attitudes and orientation of nonpsychiatric doctors toward issues related to mental illness compared to those adopted by the close relatives of psychiatric patients in some Arab communities.

Methods: The study included 50 nonpsychiatric physicians from three general hospitals in Jeddah, Cairo, and Alexandria. A comparative group of 100 close relatives of psychiatric patients had been also randomly selected from the outpatient clinics of these three hospitals. This group was meant to be divided into two subgroups: The first subgroup included the relatives of 50 psychotic patients; the other subgroup included the relatives of 50 neurotic patients. Both physicians and relatives were asked to complete a questionnaire concerning "issues related to mental illness."

Results: Regarding the concepts about the possible etiological factors behind mental illness, there was no significant difference between the physicians and the relatives of psychotic and neurotic patients ($p > 0.05$). The same result was found for attitudes toward alternative medicine. Concerning the beliefs about psychotropic medications and electroconvulsive therapy, we found that a more negative attitude had been adopted by physicians toward psychotropics and ECT ($P < 0.01$) than was seen in the relatives of the patients.

Conclusion: A serious, nonobjective, nonscientific view has been adopted by physicians toward psychiatry and psychiatric treatment.

NR19 Monday, May 7, 9:00 a.m.-10:30 a.m.

Social Factors, Self-Care, and Well-Being in Diabetic Adolescents

Caridad Avedillo, *Department of Psychiatry, Hospital La Paz, Paseo Castellana 261, Madrid 28046, Spain*; Consuelo De Dios, M.D., Arancha Ortiz, M.D., Angela Palao, Jose L. Agud, M.D., Isabel Gonzalez, M.D.

Summary:

Introduction: Social support is an important although insufficiently studied issue to consider in the management of diabetic adolescents.

Objective: To evaluate social factors that influence well-being in diabetic adolescents.

Method: Self-reports were obtained from 55 adolescents using the following questionnaires: Well-being, Diabetic Care Health Professional Support, and Diabetic Care Friends' Support and Self-care. Metabolic control was measured by HbA_{1c}.

Results: Female patients perceived less professional support. Perceived support from health professionals was significantly correlated with energy (r=0.25), positive well-being. (r=0.40), and general (r=0.29) well-being. There were no significant correlations between specific friends' support and well-being. Self-care (as measured by a scale in which a low score means better care) was better in adolescents who perceived greater professional support (r=0.36, p=0.006). In hierarchical multiple regression analyses, self-care and adolescent's gender explained 49.7% of the variance in energy score, 66.3% of the variance in positive well-being, and 65.6% of the variance in general well-being. HbA_{1c} levels were not associated with well-being or any other psychosocial factors.

Conclusion: In this study, professional support was an important variable that determined patient's well-being, possibly through its effect on self-care. The strong negative impact of female sex on well-being, as well as this group's tendency to feel less support, suggests it could be a target for intensive psychosocial management.

Research support by Fondo de Investigaciones Sanitarias. Ministerio de Sanidad y Consumo. Spain. Grant n. 99/258.

NR20 Monday, May 7, 9:00 a.m.-10:30 a.m.

Weapon Screening and Safety Measures in New York Psychiatric Emergency Rooms

Maribel Abbate, M.D., *Department of Psychiatry, SUNY At Buffalo, 462 Grider Street, Buffalo, NY 14215*; Carolyn M. Young, M.D., Rajesh Narendran, M.D., Michelle T. Pato, M.D.

Summary:

Background: Weapon carrying among patients visiting a psychiatric emergency room has been estimated to be in the range of 4% to 8%. Previous studies have failed to demonstrate any demographic or diagnostic characteristics to identify weapon-carrying patients, which makes it difficult to identify these patients by suspicion. Currently no proposed guidelines exist for weapons screening procedures for psychiatric emergency rooms.

Objective: The purpose of this study was to collect data on the utilization of various weapons screening procedures and safety measures in New York psychiatric emergency rooms.

Methods: We conducted telephone interviews with either the clinical or administrative director of all the comprehensive psychiatric emergency programs (CPEPs) in the state of New York. The interview was conducted with a semi-structured questionnaire. Data collected included the number of patients seen per year; population treated; weapons screening methods in use such as electronic devices, physical padding, and verbal screening; and safety measures in place to reduce potential violence, such as hospital security, video monitoring, and panic buttons. We com-

pared the weapons screening methods and safety measures of the New York City (NYC) CPEPs vs Upstate New York (UNY) CPEPs as well as urban vs suburban settings.

Results: The data were obtained from 16 of the 17 New York State CPEPs. All of the CPEPs had a weapons-screening procedure in place. Seventy-five percent of the NYC CPEPs had electronic weapon-screening devices compared with only 62.5% of the UNY CPEPs. Among the CPEPs that lacked electronic screening devices, the preferred screening method was physical padding (25%) for NYC CPEPs as opposed to verbal screening (37.5%) for UNY CPEPs. Eighty-eight percent of the NYC CPEPs reported having at least one hospital security officer in the emergency room to protect their clinical staff from harm compared with only 37.5% of UNY CPEPs.

Conclusions: Weapons screening methods among psychiatric emergency rooms tend to be heterogeneous with safer measures in place in more urban settings despite the lack of evidence that non-urban settings are at reduced risk. Uniform guidelines regarding weapons-screening methods and safety measures in NY psychiatric emergency rooms should be made policy by establishments such as the New York State Office of Mental Health.

NR21 Monday, May 7, 9:00 a.m.-10:30 a.m.

Personality Traits and Global Function in Patients with Mitral Valve Prolapse

Jung-Chen Chang, Ph.C., *Nursing Department, University of Washington, No. 83 Nan-Chang Street, Lo-Tung I-Lan 265, Taiwan*; Chau-Shoun Lee, M.D.

Summary:

Objective: The study explored the personality traits and global function in patients with mitral valve prolapse (MVP).

Methods: A total of 28 MVP patients, ascertained by standard echocardiographic methods during a six-month period, rated by Global Assessment Scale (GAS), and completed Maudsley Personality Inventory (MPI). GAS measured level of psychopathology and social function in these patients and MPI comprised two personality dimensions, extroversion and neuroticism. Their mean age was 29.8 ± 10.4, 13 (46.4%) male, 12 (42.9%) married, 18 (64.3%) having Taiwanese folk belief, and educational years 12.7 ± 2.7.

Results: Eighteen MVP patients (64.3%) rated a score 6 or 7 in GAS, which meant mild to moderate level of psychopathology and social interference. There was no significant difference between neuroticism (23.5 ± 9.7) and extroversion (24.8 ± 8.3) scores among these patients. Neuroticism or extroversion score was not different between the groups of GAS score above 8 and below 7.

Conclusions: Most of MVP patients who come to hospital for echocardiographic exam have mild to moderate levels of psychiatric symptoms and social impairment, which does not related to a personality trait, such as neuroticism. Psychiatric consultation for these patients was advised to treat psychopathology and restore social function.

NR22 Monday, May 7, 9:00 a.m.-10:30 a.m.

The Relation of Family Support to Psychopathology and Global Function in Patients with Mitral Valve Prolapse

Chau-Shoun Lee, M.D., *Department of Psychiatry, Poh-Ai Hospital, No. 83 Nan-Chang Street, Lo-Tung I-lan 265, Taiwan*; Jung-Chen Chang, Ph.C.

Summary:

Objective: This study explored the relation of family support to psychopathology and social function in patients with mitral valve prolapse (MVP).

Methods: Consecutive MVP patients confirmed by standard echocardiographic methods were recruited. A total of 33 MVP patients were interviewed to make clinical diagnoses according to DSM-IV criteria and to decide family support by family APGAR index. Global Assessment Scale (GAS, score 0-10) was used to measure the patients' psychopathology and social function. Their mean age was 32.2 ± 12.6, 13 (39.4%) male, 16 (48.5%) married, 24 (72.7%) employed, and educational years 11.9 ± 3.7.

Results: Of the 33 MVP patients, 14 (42.4%) had panic disorder. Twelve (36.3%) patients were rated as a low GAS score group (6 and below, at least moderate impairment) and 21 (63.7%) rated as a high GAS score group (7 and above, mild impairment to healthy life). High GAS group was more likely to have higher Family APGAR score (i.e., better family support, 8.5 ± 3.1) than low GAS group (6.5 ± 2.65) ($Z = 2.05$, $p = 0.04$).

Conclusions: Comorbidity with panic disorder was common in hospital-based MVP patients. The severity of psychopathology and impairment of social function might be related to their family support.

NR23 Monday, May 7, 9:00 a.m.-10:30 a.m.

Psychiatric Aspects of Hyperthyroidism in Stable Remission

Vladimir M. Diligenski, M.D., *Department of Psychiatry, KBC Dr Dragisa Misovic, NH Milana Tepica 1, Beograd, YU 11000, Yugoslavia*; Zorica Caparevic, Ph.D., Sinisa Dimkovic, Ph.D., Nada Kostic, Ph.D., Svetlana Jelic, Ph.D., Natasa Sikanic, M.D.,Slobodan Ristic, M.D.

The aim of our study was to evaluate the psychiatric status in patients with hyper-thyroidism. In order to establish the type and degree of psychiatric disorders we have examined 60 patients with hyperthyroidism in stable remission by using DSM-IV classification of mental disorders and psychological instruments: semi-structured psychiatric interview, MMPI, Zung depression scale, and a list of panic symptoms. The parameters that we observed included age, sex, marital status, social economic status, clinical examination, and the serum levels of total T_3 total T_4, TRAb, and TSH. All patients exhibited hyperthyroidism in stable remission with mean T_4=113.12 nmol/liter (SD=9.8), and TSH values also were in normal range: 1.99 mU/liter (SD=1.04).

Results: We found that 82% of the patients had anxiety, 28% met DSM-IV criteria for partial or complete panic disorder with or without agorophobia. Most frequent symptoms were shortness of breath, trembling or shaking, sweating, fear of doing something uncontrolled, excessive guilt, fatigue, or loss of energy. In conclusion we found that psychiatric evaluation is unavoidable for good assessment, choice of treatment, and prognosis of hyperthyroidism. Patients need psychotherapeutic and psychopharmacological treatment.

NR24 Monday, May 7, 9:00 a.m.-10:30 a.m.

Patterns of Illicit Substance Knowledge and Use by Adolescents

Israr A. Abbasi, M.D., *Department of Child Psychiatry, University of Texas at Houston, 1300 Moursund, Houston, TX 77030*; Michael G. Berno, M.D., Kathy Scott-Gurnell, M.D., Andrew Harper, M.D.

Summary:

Objective: To study the patterns of illicit substance knowledge and use by adolescents admitted to a psychiatric hospital.

Method: The participants, adolescents ages 13–17 years old admitted to Harris County Psychiatric Center, were asked to participate in two activities. The first was to list the illicit substances that they had knowledge of and access to. The second was to complete a questionnaire about their lifetime and current patterns of use of illicit substances, grouped into related categories.

Results: A total of 35 patients completed the study. Tobacco, marijuana, alcohol, and cocaine were identified most often, both for having knowledge of, and access to as well as usage.

Conclusions: There exists a stepladder pattern between knowledge, access, and usage in that order. Substance abuse evaluation and treatment should take that into account, and a new treatment paradigm is suggested.

NR25 Monday, May 7, 9:00 a.m.-10:30 a.m.

Depression and High-Risk Behavior in Suburban Homeless Adolescents

Jill H. Maddox, A.B., *School of Medicine, SUNY at Stony Brook, PO Box 59, Miller Place, NY 11764*; Robin B. McFee, D.O., Joyce Sprafkin, Ph.D., Christina Yambo, B.A., Rachel Boykan, B.A.

Summary:

Purpose: Past research has demonstrate increased rates of both depression and risk-taking in homeless adolescents. We examined psychiatric diagnosis, demographic data, and risk-taking behavior among adolescents at a temporary, emergency residence.

Methods: 29 consecutive residents (21 females, and 8 males; mean age=15.3 yr; 57% Caucasian, 19% Hispanic, and 24% African American) completed the following validated assessments: 1) Child Depression Inventory (CDI), 2) Structured Clinical Interview for DSM-4 (SCID), 3) Risk Assessment Battery, and 4) Youth's Inventory-4 (YI-4). Subjects were assigned to depressed (N=14) and non-depressed (N=15) groups based on major depressive disorder/dysthymia scores on the SCID and YI-4. T tests and Chi Square analyses were used to compare groups.

Results: The depressed group had significantly higher CDI scores than the non-depressed group ($p<0.005$), but the groups did not differ in mean age or gender composition. Hispanics were less likely to be depressed than Caucasians or African Americans ($p<0.05$). Results suggested that depressed adolescents engage in more risk-taking behavior ($p<0.09$) and are more likely to have comorbid psychiatric diagnoses ($p<0.07$).

Conclusion: These pilot data compel aggressive screening in this population, especially among non-Hispanics. Intervention programs should also address the possibility that concomitant diagnoses and risk-taking behavior may be more prevalent in the context of depression.

NR26 Monday, May 7, 9:00 a.m.-10:30 a.m.

Clinical Correlates for the Use of Restraints and Seclusion in Adolescents

Siham Muntasser, M.D., *Department of Psychiatry, Emory University, 2280 Desmond Drived, Decator, GA 30033*; Julie Kable, Ph.D., Lee Matthews, Ph.D., James W. Lowe, M.D., Daniel K. Winstead, M.D.

Summary:

The use restraints and seclusion in psychiatry, particularly in children and adolescents, has become subject of concern.

Objective: The present study looks at the relationship between the use of restraints and/or seclusion with psychopathology on an acute adolescent unit during a 24-month period.

Methods: Participants were 400 adolescents, males and females, between the ages of 12 and 18, hospitalized in an acute psychiatric unit from January 1, 1998, through December 31, 1999.

Results: Logistic regression analyses were performed using SAS to assess the relationships between the use of restraints and seclusion with various demographic and clinical variables. The likelihood of the use of restraints was increased with prior histories of physical and sexual abuse and of involvement with child protective service, after controlling for pertinent demographic characteristics. Length of hospitalization, possibly a marker of severity of pathology, was also positively associated with the use of restraints. By contrast, the use of seclusion was negatively associated with general intellectual functioning and specific verbal intellectual functioning. No relationship was found between the use of restraints or seclusion and age, sex, race, suicidality, history of violence or substance abuse, treating psychiatrist, or levels of depression or anxiety.

Discussion: Our data indicate that restraints and seclusion correlate with different clinical variables. The use of seclusion correlates with low intellectual functioning. Whereas, the use of physical restraints correlates with a history of abuse, a very interesting finding in light of the known susceptibility of this population to episodes of reinactment and to revictimization. These findings have important implications not only with regard to diagnosis and management, but they also highlight the importance of adequate staff training, particularly on issues of milieu and countertransferrance.

Conclusions: This study emphasizes the need for careful psychiatric and psychological evaluation of hospitalized children and adolescents, appropriate use of behavioral plans and adequate staff training to avoid further emotional damage of this very vulnerable population.

NR27 Monday, May 7, 9:00 a.m.-10:30 a.m.

Headache and Comorbid Psychopathology in Adolescent Inpatients

Lynnea T. Carder, M.D., *Department of Psychiatry, MCO, 3120 Glendale Avenue, Toledo, OH 43614*; David P. Bellian, M.D., Wun-Jung Kim, M.D., Michael P. Carey, Ph.D.

Summary:

Objective: This study examines the prevalence of clinically significant headache in adolescent psychiatric inpatients. The study also attempts to identify characteristics of psychiatric inpatients with clinically significant headache compared with a control group.

Method: A sample of 179 consecutive admissions of adolescents age 13–18 was screened for clinically significant headaches using a semistructured interview. The headache patients were then compared with psychiatric inpatients without headache using DSM III-R multiaxial diagnosis, scores from psychological tests, and demographic variables using chi square and t-tests as measures of significance.

Results: Findings indicated that the inpatients with headache were significantly more likely to report anxiety symptoms, oversensitivity, depression, despondency, active suicidal ideation, and general distress. The patients with headache also showed statistically significant higher rates of comorbid social phobia, overanxious disorder, major depression, and double depression.

Conclusion: Headaches were overrepresented in adolescent psychiatric inpatients with internalizing disorders such as depression, anxiety, and suicidality, and underrepresented in patients with externalizing disorders such as conduct disorder and oppositional defiant disorder.

NR28 Monday, May 7, 9:00 a.m.-10:30 a.m.

Weight Changes in Children and Adolescents on Atypical Antipsychotics

Jimmy O. Ibikunle, M.D., *Department of Psychiatry, Penn State University-Hershey Medical Center, 500 University Drive, H073, Hershey, PA 17033*; Eric K. Bonsall, M.D.

Summary:

Objective: A retrospective analysis of children and adolescents taking atypical antipsychotics was performed to determine weight changes and compliance of these patterns with earlier reported pharmacodynamic characteristics.

Method: Baseline and six consecutive monthly weight and height measurements of children (N=26, mean age 11.92 years, SD=2.61) receiving atypical antipsychotics were examined. Final weight and body mass index (BMI) changes were calculated and data analyzed for differences between subjects given risperidone (N=14), quetiapine (N=8) and olanzapine (N=4).

Results: Repeated measures analyses of variance controlling for age, sex, initial weight, duration of treatment, and placement on a weight reduction program revealed statistically significant difference between the groups in final weight change ($F=5.04$; df 2, 18; $p=0.018$). Mean weight change was highest in the olanzapine group (+6.53 kg) and lowest in the quetiapine group (–0.21 kg).

Conclusion: Atypical antipsychotics cause weight gain in children and adolescents. Weight gain patterns seem to correlate with previously described differential affinity for histamine H_1 receptors in adult males.

NR29 Monday, May 7, 9:00 a.m.-10:30 a.m.

Weight Gain with Clozapine in Patients with Childhood Psychotic Disorders

Peter A. Gochman, M.A., *CHP, NIH-NIMH, Building 10, Room 3N202, 10 Center Drive, Bethesda, MD 20892*; Alexandra L. Sporn, M.D., Kristin Janson, A.B., Judith H.L. Rapoport, M.D.

Summary:

Clozapine, remains a "gold standard" treatment for schizophrenia, however, adverse effects such as weight gain present a health risk to the patient. We studied weight gain in 22 patients with childhood-onset psychoses treated with clozapine after a follow-up period of between 1.3 and 7.7 years (mean=3.9 years). Clozapine doses ranged between 162.5 mg and 675 mg.

The mean weight gain at follow-up was 41.7 lbs., the mean increase in body mass index (BMI) was 4.8 kg/m^3. None of the studied variables (initial weight, BMI, treatment response, dose, or such laboratory values as glucose level, cholesterol, triglycerides) appeared to be associated with weight gain while taking clozapine.

Interestingly, for patients who were treated additionally with a beta-blocker for tachycardia or ADHD did not present with weight gain at the follow-up. The BMI change in these patients was significantly different from the rest of the group (0.7 kg/m^2 versus 5.6 kg/m^2, $p=0.03$). There was no difference between this group and the rest of the patients on any laboratory value, initial heart rate, increase in heart rate with clozapine, or any other studied measures. The significance of these findings may warrant further evaluation.

NR30 Monday, May 7, 9:00 a.m.-10:30 a.m.

The Naturalistic Study of Late-Adolescent-Onset Schizophrenia in Psychiatric Inpatients

Bahn Geon-Ho, M.D., *Department of Psychiatry, Kyunghee University, 1 Hoegi-dong, Dongdaemun-ku, Seoul 130-702, Korea*; Rho Bong-Keun, M.D., Yoon Doh-Joon, M.D., Yoo Hee-Jung, M.D., Kim Ki-Tae, M.D.

Summary:

Objectives: This retrograde study examined the naturalistic characteristics of late-adolescent onset of schizophrenia.

Method: The authors examined the charts of 148 inpatients admitted to the psychiatric ward at KyungHee University Hospital from 1988 to 1999. Diagnosis was based on DSM-III-R.

Results: 1) Age at admission: 218 months (SD=21.6); 2) age at onset: 201.9 months (SD=24.0); 3) sex: M:F=61.5%:38.5%; 4) SES: II=4.1%, III=46.6%, IV=43.2%, V=2%; 5) type of onset: acute=48.6%, chronic/delayed=51.4%; 6) IQ: total=90.8 (SD=16.7), verbal=94.1 (SD=16.7), performance=87.3 (SD=17.3); Verbal-performance IQ≥10=54/91 (59%); 8) main symptoms: delusions=82.4%, negative symptoms=70.9%, hallucinations=66.9%, aggressiveness/violence=43.2%; 9) premorbid characteristics: introverted=68.2%, extroverted=16.9%, nervous/impatient=4.7%, perfectionistic=2.0%, naive=7.4%; 10) medication dosage (in chlorpromazine equivalents): 715.4 mg (SD=477.8); 11) treatment received: chlorpromazine (N=86), haloperidol (N=85), thioridazine (N=23), risperidone (N=13), perphenazine (N=10), pimozide (N=7), clozapine (N=1), ECT (N=3).

Conclusions: About half of the subjects revealed symptoms acutely. The prominent symptoms besides psychotic symptoms were aggressiveness and violent behaviors. In the intelligence tests, they showed statistically significant difference between verbal and performance IQ. These results suggests that these patients may have some brain dysfunction.

NR31 Monday, May 7, 9:00 a.m.-10:30 a.m.

Bupropion Sustained Release for Substance Abuse, ADHD, and Mood Disorders in Adolescents

Ramon Solhkhah, M.D., *Department of Psychiatry, New York University Medical Center, 550 First Avenue, NB20N29, New York, NY 10016*; Timothy E. Wilens, M.D., Jefferson B. Prince, M.D., Jeanine Daly, B.A., Joseph Biederman, M.D.

Summary:

Objective: Few studies exist on pharmacological interventions for adolescents with substance use disorders (SUD). To this end, we evaluated the response of bupropion sustained release (SR) in SUD adolescents with comorbid psychopathology (both ADHD and a mood disorder).

Method: 14 adolescent outpatients were treated naturalistically and followed openly for 6 months. Adolescents were rated using the Drug Use Screening Inventory-Revised (DUSI-R), ADHD Symptom Checklist, and the Hamilton Rating Scale for Depression (HAM-D). Clinical Global Impression (CGI) scale scores were obtained for substance abuse, ADHD, anxiety, and depression. The ratings were completed at baseline, at month 3, and at the 6-month endpoint. Bupropion SR was initiated at 100 mg once daily and titrated naturalistically to a maximum dose of 400 mg/day.

Results: Of the 14 subjects followed, 13 subjects completed 6 months of treatment. At the 6-month endpoint compared to baseline, treatment with bupropion was associated with clinical and significant reductions in scores on the DUSI-R (–39%, $p<0.05$), ADHD symptom checklist (–43%, $p<0.001$), and HAM-D (–76%, $p\leq0.001$) as well as reductions in the CGIs for ADHD ($p\leq0.001$), depression ($p\leq0.001$), and substance abuse ($p<0.05$). The mean daily dose of bupropion SR was 315 mg (in divided doses). No significant adverse events were noted during the follow-up period.

Conclusions: These open data suggest that bupropion is well tolerated and may be an effective medication for the treatment of substance abusing adolescents with comorbid ADHD and mood disorders.

NR32 Monday, May 7, 9:00 a.m.-10:30 a.m.

Suicidal Youth with First Emergency Presentations: Six-Month Outcome Predictors

Ian G. Manion, Ph.D., *Department of Mental Health, CHEO, 401 Smyth Road, Ottawa, ON K1H 8L1, Canada*; S. Evelyn Stewart, M.D., Simon Davidson, M.B., Paula F. Cloutier, M.A.

Summary:

Objective: To examine the risk of future documented suicide attempts and emergency department (ED) returns among children and adolescents with first suicidal ED presentations.

Method: A total of 548 consecutive ED presentations of suicidal 7–19 year olds (mean age-14.6, SD-2.1) over a 1-year period were studied. Multiple logistic regression among 224 first-time presenters was used to predict ED return and future suicide attempts.

Results: At 6-month follow-up, 32.6% (N=73) had returned to the ED, 24.1% (N=54) had attempted suicide, and 14.3% (N=32) required psychiatric admissions. Predictors of ED return were child welfare guardianship (odds ratio [OR]=3.12; 95% CI=1.31–7.45), age ranged 15 to 19 years (OR=2.34; 95% CI=1.19–4.58), and mood disorder (OR=2.03; 95% CI=1.05–3.90). Past foster or group home placement (OR=3.66; 95% CI=1.54–8.77), mood disorder (OR=3.84; 95% CI=1.79–8.24), and age range of 15 to 19 years (OR=2.20; 95% CI=1.04–4.64) predicted future suicide attempts. Substance abuse at presentation was associated with fewer ED returns (OR=3.09; 95% CI=1.33–7.13) and attempts (OR=3.24; 95% CI=1.22–8.59).

Conclusion: Clinicians should be aware of the above risk factors when assessing and managing suicidal youth at their first ED presentation.

Funding source: CHEO Mental Health Research.

NR33 Monday, May 7, 9:00 a.m.-10:30 a.m.

State-Specific rCBF Changes in Acute Catatonia

Ruben A. Miozzo, M.D., *Department of Psychiatry, Beth Israel Medical Center, First Avenue at 16th Street, New York, NY 10003*; Eleonora Rubin, M.D., Milica Stefanovic, M.D., Lillian Belman, M.D., Igor I. Galynker, M.D., Lisa J. Cohen, Ph.D.

Summary:

Background: Brain imaging studies demonstrate fronto-temporal and parietal abnormalities in patients with catatonia. However, these studies lack consistency with regard to location of these abnormalities and on whether they reflect "state" or "trait" phenomena. The purpose of this study was to evaluate regional cerebral blood flow (rCBF) in patients during an acute catatonic state and after resolution of catatonic symptoms.

Methods: A 99Tc-HMPAO SPECT was used to assess rCBF in five subjects hospitalized on an acute psychiatric unit in the acute catatonic state and in the post-acute state after treatment. Their rCBF patterns were compared to those of five non-catatonic psychiatric control subjects using independent t-tests.

Results: Patients in the acute catatonic state compared to control subjects had broadly decreased perfusion in the parietal cortex bilaterally (five out of six ROIs; p=0.02–0.03), in the right occipital cortex (p=0.03), and in the right thalamus (p=0.045). Except for decreased rCBF in the right thalamus (p=0.004), these abnormalities were absent in the post-acute state. Compared to the control subjects, rCBF in the post-acute state was decreased in the left inferior temporal cortex (p=0.02) and right basal ganglia (p=0.02).

Conclusion: The results of our study replicate findings of decreased perfusion in the parietal cortex of catatonic patients. This abnormality could be either state-specific for catatonia or accentuated by an acute catatonic state. Decreased perfusion in the inferior temporal cortex, right basal ganglia, and right thalamus present in the post-acute state could be related to a number of factors, including a trait predisposition to catatonia.

NR34 Monday, May 7, 9:00 a.m.-10:30 a.m.

Prefrontal Subregion Abnormalities in Patients with Bipolar Disorder

Melissa P. Lopez-Larson, B.S., *Department of Psychiatry, University of Cincinnati, 231 Albert Sabin Way, Cincinnati, OH 45267-0559*; Melissa P. DelBello, M.D., Molly E. Zimmerman, B.A., Stephen M. Strakowski, M.D.

Summary:

Objective: Previous MRI studies indicate that compared with healthy volunteers (HV) patients with bipolar disorder (BPD) have abnormalities in the prefrontal cortex. The aim of this study was to investigate differences in specific prefrontal subregions between BPD and HV.

Method: BPD hospitalized for a manic episode (n=17), and HV (n=13) matched for age, sex, and race were recruited. Contiguous 1 mm coronal T1-weighted MRI slices were obtained using a Picker 1.5 Tesla scanner. The gray and white matter volumes of five prefrontal subregions of interest were measured: superior, middle, inferior, cingulate, and orbital.

Results: Multivariate analyses of covariance (MANCOVAS) covarying for substance duration, education, and total brain volume revealed BPD patients had smaller left gray matter volumes (F= 3.26, df=5,20,p=0.03, effect size=0.34), specifically in the middle (p=0.04) and superior (p=0.03) regions; and smaller right gray matter volumes (F=3.71, df=5,20, p=0.02, effect size=0.36), specifically in the cingulate (p=0.03), inferior (p=0.003), orbital (p= 0.04), and middle (p=0.003) regions. No white matter differences were found.

Conclusion: These results suggest that BPD patients have global decreases in gray matter volumes in the prefrontal cortex compared with HV. Further investigation into the role of the prefrontal cortex in BPD appears warranted.

NR35 Monday, May 7, 9:00 a.m.-10:30 a.m.

ECT and CBF in a Patient with Refractory Schizophrenia

Clarissa S. Gama, M.D., *Department of Psychiatry, UFRGS-Faculty of Medicine, Rua Pedro Ivo 767, Porto Alegre, RS 90450-210*, Brazil; Maria I. Labato, M.D., Marcelo T. Berlim, M.D., Paulo Abreu, Ph.D., Betina Matevi, M.D.

Summary:

The basic approach to refractory schizophrenia (Kane JM, 1988) is centered on either modifying doses of conventional antipsychotics, use of new neuroleptics (e.g., risperidone, olanzapine, and clozapine) or using adjunctive agents (e.g., as anticonvulsivants, lithium, and benzodiazepines). For some patients with refractory schizophrenia eletroconvulsive therapy (ECT) is an effective treatment. Its mechanism of action is unknown, but since schizophrenics present with abnormalities in the regional cerebral blood flow (rCBF), one may presume that it is related, at least in part, with an interference in the brain blood flow. However, few studies focus on the effects of ECT in the rCBF and its relationship with clinical condition. Here is discussed a case of a 32-year-old male with schizophrenia (DSM-IV) refractory to typical antipsychotics (e.g., haloperidol and chlorpromzine in full doses), whose symptomatology became worse despite medication. He presented predominantly with auditory hallucinations and persecutory delusions. Because of the symptoms' severity, ECT was administered three times a week for four weeks (i.e., 12 treatments). Single photon emission computed tomography (SPECT) images were made before and after the ECT series, and when compared showed a

great increase in the rCBF in the temporal and frontal brain areas, both correlated with clinical improvement.

NR36 Monday, May 7, 9:00 a.m.-10:30 a.m.

Brain White Matter Changes on Diffusion Weighted MRI in Bipolar Patients

Narayanan Ramesh, M.D., *Department of Psychiatry, University of Maryland, 22 South Greene Street, Box 351, Baltimore, MD 21201*; William T. Regenold, M.D., Rao Gullapalli, Ph.D.

Summary:

T_2-weighted MRI is typically used to identify subcortical white matter lesions in patients with bipolar disorder. MR diffusion-weighted imaging (DWI) is a newer technique that provides unique information regarding the structural characteristics of tissue by detecting the molecular motion of water. We have performed a pilot study to determine the utility of DWI in assessing the structural integrity of subcortical white matter, which appears normal by T_2-weighted MRI, in patients with bipolar disorder. We analyzed the DWIs of eight bipolar inpatients, eight patients who had DWI to rule out a recent stroke, and five normal control subjects. The average apparent diffusion coefficient (ADC_{av}), which is inversely proportional to tissue structural integrity, was calculated for tissue in six subcortical regions of interest (ROI): right and left frontal, temporal and occipital legions. Data analysis showed no significant differences among groups in any of the six ROIs with the exception of the left frontal ROI, where median ADC_{av} values were 750.1, 793.0, and 852.8 mm/s^2, respectively, for normal control subjects, stroke patients, and bipolar patients (χ^2=7.0, df=2, p= 0.031). These preliminary results are consistent with other reports implicating left frontal cortex dysfunction in mood disorders and suggest the utility of DWI in assessing subcortical white matter in mood disorder patients.

NR37 Monday, May 7, 9:00 a.m.-10:30 a.m.

TC(99m) HMPAO SPECT in Depressed Bipolar I Patients

Antonio Benabarre, M.D., *Department of Psychiatry, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain*; Eduard Vieta, M.D., Francisco Lomena, Ph.D., Anabel Martinez-Aran, Ph.D., Francesc Colom, Ph.D., Maria Reinares, Ph.D., Francisco Martin, M.D.

Summary:

Objective: Several neuroimaging techniques have shown functional abnormalities in bipolar patients during acute depressive episodes. In this study, the regional cerebral blood flow of 17 bipolar I depressed patients (DSM-IV criteria) were studied by single-photon computed emission tomography (SPECT). SPECT was performed in a doubled-headed gammacamera (Helix, GEMS) fitted with high-resolution fan beam collimators, 20 minutes after endovenous injection of 20 mCi of HMPAO-Tc^{99m} (Nycomed-Amersham). In order to demonstrate the clinical value of SPECT findings, only visual analysis of SPECT images was done. SPECT revealed no abnormality in eight patients and abnormal findings in nine patients, who exhibited regional decreases of HMPAO uptake (four in frontal region, two in basal ganglia, and three in frontal and basal ganglia). There was no statistical differences in sex and age distribution between the two groups. The group with abnormal SPECT results had statistically (p<0.002) higher scores on the Hamilton Depression Rating Scale (HDRS) than patients group with normal SPECT results (21.22, SD=3.19 versus 17.62, SD=0.9).

Conclusions: Tc^{99m}HMPAO SPECT can be visually normal in depressed bipolar I patients. This technique can show perfusion deficits in frontal lobe and/or basal ganglia in the most clinically depressed patients.

NR38 Monday, May 7, 9:00 a.m.-10:30 a.m.

Arylsulphatase A Activity in the Development of Depression

Alma Mihaljevic-Peles, Ph.D., *Department of Psychiatry, KBC Rebro, Kispaticeva 12, Zagreb 10000, Croatia*; Miro Jakovljevic, Ph.D., Ivica Kracun, Ph.D., Zeljko Milicevic, M.D., Marina Sagud, M.D.

Summary:

Relatively little attention has been paid to the role of neurodegenerative processes in the pathophysiology of depression. It is an open question whether low ASA activity could be connected with the development of depressive symptoms. The hypothesis underlying this work is that there is a subclass of depressed patients whose symptoms are at least partly caused by abnormal arylsulphatase Activity. Metachromatic leukodystrophy (MLD) is a disease caused by deficiency of the enzyme arylsulphatase A. Clinically, adult MLD may present as a schizophrenia-like psychosis, deterioration of cognitive functions, personality changes, depression, or dementia. Depression has been relatively rarely described. However, there are individuals with low ASA activity without clinical symptoms of MLD. This state is described as ASA pseudodeficiency. It remains controversial whether low ASA activity predisposes or influences in the development of depression symptoms. The purpose of this particular study was to determine whether abnormal ASA activity could be detected in major depressed patients. There were 59 patients with DSM-IV major depression. In the control group were 102 healthy volunteers. Leukocyte ASA activity was determined from blood samples using p-nitrocatechol sulphate as substrate. Our results showed that low ASA activity was more frequently found in depressed patients than in control subjects. Our findings indicate that clinical types of major depression could be in connection with low ASA activity. The presence of decreased ASA activity in depressed patients points to the conclusion that enzyme deficit could play a role in the pathophysiology of depression.

NR39 Monday, May 7, 9:00 a.m.-10:30 a.m.

Increased Serum S100B Protein in Drug-Free Bipolar Patients

Flavio Kapczinski, Ph.D., *Department of Psychiatry, Bioquimica ICBS, Ramiro Barcelos 2600 Anexo, Porto Alegre, RS 90035-003, Brazil*; Rodrigo Machado-Vieira, M.D., Diogo R. Lara, Ph.D., Luiz V.C. Portela, Ph.D., Carlos A. Goncalves, Ph.D., Jair C. Soares, M.D., Diogo O. Souza, Ph.D.

Summary:

S100B protein is a calcium-binding protein mostly derived from glial cells that exerts trophic or toxic effects on neural cells depending on its concentration. Serum S100B level has been used as a marker of brain injury in neuropsychiatric disorders. Since glial alterations and structural abnormalities have been recently associated with bipolar disorder, this study assessed whether S100B serum levels were increased in the first manic episode of drug-free bipolar patients. Mean serum concentration of S100B protein were significantly higher (p=0.014) in 20 manic patients (0.065 ng/ml, SD=0.068) compared to healthy control subjects matched for age and gender (0.018 ng/ml, SD=0.029). No correlation with psychopathology scales was observed. These results support the hypothesis of glial abnormalities in bipolar disorder, with a possible role of elevated S100B in the trophic activity or induction of neural damage during acute mania.

NR40 Monday, May 7, 9:00 a.m.-10:30 a.m.

Effects of Chronic Treatment with the Novel Metabotropoc Glutamate Receptor Agonist LY354740 in Nonhuman Primates: Evidence for Uncoupling of the HPA Axis and Noradrenergic System

Sanjay J. Mathew, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive, Box 84, New York, NY 10032*; Eric L. P. Smith, Ph.D., James A. Monn, Ph.D., Darryle Schoepp, Ph.D., Jack M. Gorman, M.D., Leonard A. Rosenblum, Ph.D., Jeremy D. Coplan, M.D.

Summary:

Background: We hypothesized that chronic attenuation of glutamatergic transmission would blunt hypothalamic-pituitary-adrenal (HPA) axis and noradrenergic (NE) system responsivity. To test this, we measured the effects of chronic treatment with the metabotropic glutamate (mGlu 2/3) agonist LY354740 (Eli Lilly and Company) on plasma cortisol and 3-methoxy-4-hydroxyphenylglycol (MHPG) in bonnet macaques.

Methods: Two subjects were treated for six weeks with oral LY354740 (1.5 mg/kg/day), and were compared with untreated controls (n=10) on baseline measures of plasma cortisol and MHPG. The LY354740-treated subjects subsequently underwent yohimbine (cumulative dose=2.75 mg/kg) infusions, which were compared with non-treated subjects undergoing yohimbine and saline infusions.

Results: Subjects treated with LY354740 showed markedly lower baseline cortisol levels (mean=33.78 ug/dl, sd=1.35) compared with untreated controls (mean 65.29 ug/dl, sd=14.92; F (1,10)=8.24; p=.016), while there were no significant differences in baseline MHPG (p=.94). Yohimbine-induced MHPG values were increased in the LY354740-treated group compared with the untreated saline- and yohimbine-alone groups (F(2,9)=8.59; p=.008).

Conclusion: Chronic treatment with a mGlu 2/3 agonist failed to attenuate one measure of locus ceruleus (LC)/NE function, though there was a reduction of the "set point" of the HPA axis. HPA axis and LC/NE systems normally work in tandem, but treatment with this glutamate antagonist selectively "uncoupled" the systems, with a possible protective mechanism for the HPA axis. The ability of LY354740 to modulate the HPA axis suggests a potential therapeutic action in stress related conditions such as anxiety and depressive disorders.

Funding: Eli Lilly, NARSAD.

NR41 Monday, May 7, 9:00 a.m.-10:30 a.m.

Autonomic Evaluation of Panic Disorder Versus Postural Orthostatic Tachycardia Syndrome (POTS)

Gustavo D. Kinrys, M.D., *Department of Psychiatry, Mayo Foundation, 200 First Street, SW, Rochester, MN 55905*; Teresa A. Rummans, M.D., Donald E. McAlpine, M.D., Lisa M. Benrud-Larson, Ph.D., Tonette L. Opfer-Gehrking, Stacy M. Hines, Phillip A. Low, M.D.

Summary:

Objective: To compare the autonomic response of patients with panic disorder to patients with postural orthostatic tachycardia syndrome (POTS) and control subjects.

Design/Methods: Seven patients with panic disorder (PD; 4 F, 3 M), five patients with both POTS and panic disorder (MIXED, 5 F), 16 healthy controls (CONTROL; 12 F, 4 M), and 13 POTS patients (7 F, 6 M) underwent head-up tilt test (HUT) for autonomic function. Changes in HR and BP values from baseline to 30 seconds, and to 1, 3, 5, 7, and 10 minutes were measured.

Results: POTS patients had significantly greater HR change from baseline than did the PD and CONTROL groups. The MIXED group, however, had an initial HR response from baseline similar to the POTS group, and then a decline, resembling the pattern seen in the PD and CONTROL groups. For all other time points, the POTS group showed a significantly greater HR response to HUT than did the other three groups.

Conclusions: In this pilot study, individuals with POTS differed significantly from patients with panic disorder and controls with regard to autonomic alterations in response to head-up tilt. However, individuals with both panic disorder and POTS experienced autonomic alterations in a mixed pattern, initially similar to POTS patients and subsequently consistent with panic disorder patients and controls.

NR42 Monday, May 7, 9:00 a.m.-10:30 a.m.

HPT Axis Dysregulation and Response to Antidepressant Treatment in Resistant Depression

David Mischoulon, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114*; Stella Bitran, B.A., Kathryn A. Bottonari, B.A., John J. Worthington III, M.D., Jonathan E. Alpert, M.D., Maurizio Fava, M.D., Andrew A. Nierenberg, M.D.

Summary:

Objective: To assess a relationship between TSH response patterns to TRH stimulation in treatment-resistant depressed patients, and response to antidepressant treatment.

Methods: Forty-four patients, ages 18–65, diagnosed with treatment-resistant major depressive disorder (MDD) by SCID-P and having a Hamilton D-17 score ≥ 18 were recruited into a study using open-label nortriptyline. Prior to entering the study, patients underwent challenge with thyrotropin releasing hormone (TRH) at the MGH General Clinical Research Center (GCRC). Response patterns to thyroid stimulating hormone (TSH) were assessed at times 0, 10, 20, 30, and 60 min. Patients were subsequently started on nortriptyline 50–150 mg/d for a period of six weeks, with flexible dosing schedules.

Results: Treatment response (defined as ≥ 50% decrease in HAM-D-17 score) rates were 34% (20/59) for study completers. Peak TSH times in response to TRH stimulation were either 20min (n=14) or 30min (n=16) for 30 participants for whom data were available (mean age=41.5 ± 11.2; 50% female). We found a statistically significant association between earlier response to TRH stimulation (at 20min) and percent change in HAM-D-17 score following antidepressant treatment (p=0.05), even after adjusting for age and gender (p<0.05).

Conclusion: A pattern of early TSH peaking following TRH stimulation may correlate with a more robust response to antidepressants in treatment resistant depressed populations.

This study was supported by a grant from the NIMH (5 R29 MH46952-05).

NR43 Monday, May 7, 9:00 a.m.-10:30 a.m.

Repetitive Transcranial Magnetic Stimulation as Adjunctive Antidepressant Therapy in Treatment-Resistant MDD

Jorge Gonzalez-Olvera, M.D., *Service Clinicos, INPRF, Calzada Mexico Xochimilco 101, DF 14370, Mexico*; Ariel Graff-Guerrero, M.S.C., Alejandro Jimenez-Guenchi, M.D., Yazmin Mendoza-Espinosa, M.D., Patricia Martinez-Medina, M.D., Jose Garcia-Marin, M.D., Gerhard Heinze-Martin, M.D.

Summary:

In this study the effects of repetitive transcranial magnetic stimulation (rTMS) as adjunctive therapy in treatment-resistant major depressive disorder (MDD) were assessed. Seven patients diagnosed with treatment-resistant MDD were studied. The patients had been resistant to at least two pharmacological treatments at therapeutic dosages administered for 6 weeks. The Hamilton (21-

item) baseline was score ≥20 (mean 25.4 points) without suicidal risk. The patients received one daily session of rTMS in the left prefrontal cortex for 10 days. The stimulation parameters were: 20Hz, 15 daily trains of 2 sec, 80% of the motor threshold and inter-train interval of 58 sec. The study design was single blind, and the patients received their last pharmacological treatment without dosage variation. Hamilton and Beck depression scales evaluated the efficacy endpoints. The patients had an average reduction of 11.6 points on the Hamilton scale and 12.6 points on the Beck scale at the end of the rTMS sessions. The mean reductions after 8 weeks of follow-up were 16 points on the Hamilton scale and 16 points on the Beck scale. It is concluded that rTMS improves the depressive symptoms in patients with treatment-resistant MDD.

NR44 Monday, May 7, 9:00 a.m.-10:30 a.m.

The Clinical Response of Mood Disorders According to the Gene Polymorphisms

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Summary:

The serotonin transporter (5HTTLPR) is a compelling candidate gene in mood disorders and a prime target for SSRIs. A number of association studies have investigated the role of the monoamine oxidase A (MAOA) gene in the susceptibility to mood disorders. We investigated a genetic association between mood disorders and genotype of 5HTTLPR and MAOA. In addition, we evaluated the therapeutic response according to genotype. 5HTTLPR and MAOA gene polymorphism was studied in 191 mood disorder and 80 control subjects. Subjects were rated using the CGI (Clinical Global Impression). There was statistically no difference between mood disorder patient and healthy control subjects in genotype frequency. There was statistically no difference between the genotype and subdiagnosis of mood disorders. The subjects with *ls* or *ss* genotype of 5HTTLPR had a higher relapse rate and lower CGI scores, but they were much more improved based on CGI scores. These differences were not significant. The 12 or 22 genotype of MAOA gave similar results. Our results suggest there is no association between mood disorders and the polymorphism of the serotonin transporter gene and monoamine oxidase A gene. Even though other factors may be implicated, genotyping at serotonin transporter gene and MAOA gene may play some role in determining clinical response to antidepressants.

NR45 Monday, May 7, 9:00 a.m.-10:30 a.m.

Ethnicity and Rates of Follow-Up Among Dual-Diagnosis Patients

Timothy W. Fong, M.D., *Department of Psychiatry, University of California at Los Angeles-NPI, 6221 Orange Street, #3, Los Angeles, CA 90048*; John T. Tsuang, M.D., Andrew P. Ho, M.D., Carol Giannini, R.N.

Summary:

Results: Complete follow-up data was collected on 394 patients. Of those, 225 were given either a psychiatric appointment or referral. 38% (21/56) of Caucasian patients showed up to a mental health referral compared to 57% (37/65) of non-Caucasian (Black, Hispanic, and Asian) patients. Chi-square value for attendance rates between groups was 4.54, $p<0.05$. Among those given a psychiatric appointment, 42% (24/57) of Caucasian patients and 39% (19/49) non-Caucasian patients showed up.

Conclusions: Ethnicity appears to be a significant factor in determining follow-up rates for dual diagnosis patients who are given psychiatric referrals but not appointments.

NR46 Monday, May 7, 9:00 a.m.-10:30 a.m.

Unexpected Delirium in Rapid Opioid Detoxification (ROD)

Duru Sakhrani, M.D., *St. Francis Medical Center, 6350 Marchand Street, #3, Pittsburgh, PA 15206-4312*; Scott A. Golden, M.D.

Summary:

Rapid opioid detoxification (ROD), using a combination of the long-acting opioid antagonist naltrexone and the alpha 2 agonist clonidine is a method to detoxify patients on a regimen of methadone maintenance. The daily administration of naltrexone in increasing dosages decreases the duration of the withdrawal syndrome associated with methadone.

Objective: To ascertain the frequency with which delirium occurs during the ROD of methadone-maintained patients.

Method: A chart review was conducted with 20 consecutive patients who received inpatient ROD from methadone maintenance from January 1999 to December 1999. Patients were receiving varying amounts of methadone (max=40 mg) on admission with varying lengths of methadone taper (range 6–450 days, mean=62.35 days) prior to ROD. Methadone was discontinued on admission, and naltrexone was administered in increasing daily doses. Withdrawal symptoms were treated with clonidine and lorazepam.

Results: Five patients developed delirium on the first day of the procedure. Fourteen patients completed the protocol. One patient discontinued the ROD on the second day.

Conclusion: We found a significant incidence of delirium after ROD in methadone-maintained patients.

NR47 Monday, May 7, 9:00 a.m.-10:30 a.m.

High-Dosage Risperidone Treatment of Acute Psychoses: A Case Series

Alessandro Lenzi, *Department of Psychiatry, University of Pisa, Via Rome 67, Pisa 56100, Italy*; Letizia Tiano, M.D., Elisabetta Coli, M.D., Enzo Poggi, M.D., Alessandro Nassimbeni, M.D.

Summary:

Risperidone, a novel antipsychotic medication with a different receptor profile, has proven effective in treatment-refractory or intolerant schizophrenia. We report a case series where risperidone, was used in the treatment of acute psychosis in a psychiatry emergency unit.

Method: A total of 29 acute psychotic patients were treated with 6–9 mg/day risperidone; the drug was rapidly titrated to the maximum dose (12 mg/day) until symptom remission, and then gradually reduced to the commonly advised one. Concomitant treatment, except conventional neuroleptic medication, was continued. Response to treatment and tolerability were measured on days 2, 4, 6, 8, 12, 15, and 45 of the trial.

Results: Diagnoses according to DSM-IV were the following: schizophrenia (n=9), substance-induced psychotic disorder (n=7), manic episode (n=6), schizophreniform disorder (n=5), and schizoaffective disorder (n=2). Drop-out rate (21%) was due to low compliance (n=3), hospitalization (n=2), and severe side effects (n=1). The course of the disorder was progressively improving in 91% of the patients, with a significant decrease in BPRS score in the first week onward ($p<.05$). Risperidone was generally well tolerated: though 40% of the subjects reported extrapyramidal side effects in the first week, those were substantially decreased in the following weeks.

Conclusion: Results from this naturalistic outcome study highlight the double nature of risperidone, which, according to the dosage, shows conventional high-potency antipsychotic properties, and atypical features, with substantial implications on long-term compliance.

NR48 Monday, May 7, 9:00 a.m.-10:30 a.m.

Predictors of Multiple Admissions to the Maricopa County Psychiatric Center

Thomas P. Tarshis, M.D., *Maricopa Medical Center, 2601 East Roosevelt, Phoenix, AZ 85008*; Jacob J. Venter, M.D.

Summary:

Introduction: In 1999, there were 2,086 admissions to the Maricopa Medical Center Psychiatric Facility. Of these admissions, 572 were for repeat patients. Factors that predispose individuals to multiple admissions were investigated in this study.

Methods: A retrospective case-control study was performed. 100 psychiatric patients (54 with multiple admissions and 46 with a single admission) were used for the analysis. Predictors tested included substance abuse, medications, family involvement, discharge site, legal status, education, prior admissions, sex, race, age, and diagnosis.

Results: Patients were less likely to have multiple admissions if 1) their discharge site was to home versus elsewhere (p=0.038), 2) they had no previous admissions at least 6 months prior to the current admission (p=0.046), and 3) their court-ordered evaluation was dropped (p=0.026). Only legal status (OR=3.5, 95% CI=1.1 to 10.7) remained in a multiple variable logistic regression model.

Conclusions: Discharge site, prior admissions, and legal status may provide information on who is more likely to have multiple admissions. Patients with prior admissions and no family involvement have more risk for re-admission after discharge. People who have their court-ordered evaluation dropped are less likely to be re-admitted. Future studies are needed to investigate the reasons behind the high re-admission rate for psychiatric patients.

NR49 Monday, May 7, 9:00 a.m.-10:30 a.m.

Do Huntington's Disease and OCD Belong to the Same Spectrum?

Nicola de Marchi, M.D., *Department of Psychiatry, ASL NA4, Via Pirozzi 18, Pomigliano, NA 80038, Italy*; Maria A. Ragone, M.D., Rosa Fusco, M.D., Fabiana Daniele, M.D., Rosa Mennella, M.D., M. Grazia Ariano, M.D., Alfredo Dama, M.D.

Summary:

Introduction: There is increasing evidence that there may be a heightened risk for OCD in a variety of neurological conditions sharing an impairment of the basal ganglia. Recently, our group has described a nuclear HD pedigree with a striking excess of OCD in carriers of the HD mutation. We report here the results of a neurologic and psychiatric evaluation of an extended HD pedigree.

Methods: 43 individuals with HD or at 50% risk for the disease received a thorough neurological assessment to ascertain their HD status. They were also given a semistructured psychiatric interview (DEC), followed by administration of the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS). In 30 subjects we have been able to determine the mutation status. The prevalence of OCD in the patient sample was compared with that of a control population, composed of first-degree relatives of the probands' spouses (N=46).

Results: 15 subjects exhibited the full OC syndrome, whereas no OCD cases were found in the control population (p=0.00002). The Y-BOCS scores ranged from 2 to 29. 11 probands with OCD carried the HD mutation, and only one showed OCD (score=2) in the presence of a normal gene at the HD locus.

Discussion: This finding supports the initial hypothesis of a strong relationship between HD and OCD, at least in this sample. On a clinical ground, the basic clinical features of these two disorders (chorea and obsessions/compulsions) may be regarded as part of a continuum, although at two different levels of severity. This relationship seems to underlie an involvement of the basal ganglia and related fronto-thalamo-cortical circuits in the pathogenesis of both disorders. It is clear that the mutation carrier status greatly increases the risk for HD in this sample. The implications of these findings are discussed.

NR50 Monday, May 7, 9:00 a.m.-10:30 a.m.

Demographic and Clinical Features of 131 Adult Pathological Gamblers

Jon E. Grant, M.D., *Department of Psychiatry, University of Minnesota, 2450 Riverside Avenue, Minneapolis, MN 55454-1495*; Suck Won Kim, M.D.

Summary:

Purpose: This study was constructed to detail the demographic and phenomenological features of pathological gamblers as well as to assess psychiatric comorbidity in a sizeable study group.

Methods: One hundred thirty-one subjects with DSM-IV pathological gambling were administered a semistructured interview to elicit demographic data, diagnostic history of axis I disorders, and information on the phenomenology, age of onset, course, associated features, treatment history, and response to treatment of the pathological gambling, followed by the Structured Clinical Interview for DSM-IV (SCID).

Results: The majority of subjects were married (56%) and female (60%). Subjects gambled an average of 16 hours per week. Slot machines (65%), cards (33%), and blackjack (26%) were the most popular forms of gambling. Lifetime comorbid affective illness, or substance use were common disorders. Most gamblers had severe financial, social, and legal problems. The mean length of time between first gambling behavior and onset of pathological gambling was 6.3 (SD=8.9) years. Sixty-four (49%) of the subjects progressed to pathological gambling within 1 year of starting gambling.

Conclusion: Pathological gambling is a disabling disorder associated with high rates of social and legal difficulties and lifetime psychiatric comorbidity.

NR51 Monday, May 7, 9:00 a.m.-10:30 a.m.

Treating Patients with Fibromyalgia Using a Brief Interdisciplinary Program

Laura M. Worrel, B.A., *Department of Psychiatry, Mayo Clinic, 2225 Brook Lane, SW, Rochester, MN 55902*; Lois E. Krahn, M.D., Christopher D. Sletten, Ph.D., Gregory R. Pond, M.S.C.

Summary:

Objective: To evaluate the efficacy of a brief, interdisciplinary treatment program for fibromyalgia and determine which patient characteristics are associated with better treatment response.

Method: The study group consisted of 100 consecutive patients who met the American College of Rheumatology criteria for fibromyalgia and agreed to participate. These patients completed a 1 1/2 day outpatient treatment program at Mayo Clinic Rochester. Two self-report measures, the Fibromyalgia Impact Questionnaire (FIQ) and the Multidimensional Pain Inventory (MPI) were administered before treatment and 1 month later. 74% of patients completed the study.

Results: Patients were less restricted by fibromyalgia after participation in the treatment program. This is demonstrated by improvement in the FIQ score (p<0.001), the MPI Pain Severity score (p<0.001), and the MPI Interference score (p=0.014). The patient characteristic significantly associated with a better response was a high pretreatment level of impairment.

Conclusion: A brief, interdisciplinary treatment is effective at reducing fibromyalgia symptoms. This knowledge is useful to health care providers aiming to develop beneficial, convenient treatments for fibromyalgia. This study was funded by the Mayo

Medical School and the Mayo Department of Psychiatry and Psychology.

NR52 Monday, May 7, 9:00 a.m.-10:30 a.m.

The Pain in Psychiatric Patients: Cause or Effect?

Ariel Graff-Guerrero, M.S.C., *Service Clinicos, INPRF, Calzada Mexico Xochimilco 101, DF 14370, Mexico*; Alberto G. Lopez, M.D., Francisco Pellicer, M.D., Jose Garcia-Marin, M.D., Gerhard Heinze-Martin, M.D.

Summary:

Psychiatric patients present differences in the characteristics of pain perception in comparison to nonpsychiatric patients. In psychiatric clinics a dilemma in the treatment of the pain is whether to consider it as cause or an effect. An auto-applied survey was carried out in 210 consecutive patients that attended a first-time general psychiatric service. The survey evaluated the presence and general characteristics of pain. The psychiatric diagnosis was evaluated by DSM-IV criteria. Results showed that 77.5% of the patients presented some sort of pain complaint, and in 53.8% of the cases it was more than 6 months old. In 18.6% of the patients the pain was continuous, in 29.8% the pain almost totally incapacitated the patient, and in 33.2% the ache was from severe to unbearable. Half of the patients received some type of treatment for their pain complaints, and 61.9% described its pain by cognitive-emotional concepts. The main diagnosis of the sample was generalized anxiety disorder (GAD) (23%). The patients with GAD had the biggest number of pain complaints in comparison with the rest of the diagnoses (χ^2=30.2, $p < 0.05$). In all patients with GAD, the pain was more than 1 month old. We conclude that it is important to implement ad hoc evaluations for pain in patients with psychiatric disorders.

NR53 Monday, May 7, 9:00 a.m.-10:30 a.m.

Cataplexy Triggers

Ashwin Gowda, M.D., *Department of Psychiatry, Mayo Clinic, 200 First Street SW, Rochester, MN 55905*; Lois E. Krahn, M.D., Nancy L. Slocumb, James F. Lymp, Ph.D., Wendy R. Moore, Michael H. Silber, M.D.

Summary:

Objective: Narcolepsy typically includes symptoms of excessive daytime sleepiness, cataplexy, sleep paralysis, and hypnagogic hallucinations. Cataplexy is the most specific symptom of this disease and is characterized by muscular weakness following strong emotional stimuli. Cataplexy is usually determined based on patient history. This study will verify previous research regarding potential triggers, the most common parts of the body affected, and examine the risk of cataplexy during several activities, including driving.

Method: The Stanford cataplexy questionnaire was modified with the addition of several items. The Mayo Narcolepsy Diagnostic Criteria were used to determine that all patients had definite narcolepsy. Fifty-five patients with narcolepsy-cataplexy completed the questionnaire as did as 47 obstructive sleep apnea control subjects.

Results: Laughter, excitement, and surprise were the most important triggers of cataplexy. Involvement of the head was most strongly associated with cataplexy. There was a 12-fold increased odds of having muscle weakness while driving for narcoleptic patients.

Conclusion: Clinicians need to recognize the specific emotional triggers and weakness of facial muscles to differentiate cataplexy from other "spells." Safety concerns exist for patients with cataplexy who drive. Watching television was associated with cataplexy, which potentially can be incorporated into a provocative objective cataplexy test.

NR54 Monday, May 7, 9:00 a.m.-10:30 a.m.

Comparison of Sexual Dysfunction Between Geriatric Outpatients in Primary Care and Psychiatric Clinics

Ahsan A. Naseem, M.D., *Department of Psychiatry, Wayne State University, 2751 East Jefferson, Suite 400, Detroit, MI 48207*; Richard Balon, M.D.

Summary:

Only a few studies address the impact of psychiatric symptomatology on sexual functioning in geriatric population. We assessed the existence and severity of sexual problems in the selected populations using Golombok-Rusk Inventory of Sexual Satisfaction (GRISS). Two groups of geriatric outpatients were recruited for this study. These patients were 65 years of age or older, referred to psychiatric outpatient, or seen in primary care clinic. Subjects filled out the GRISS questionnaire in confidence, after a written consent was obtained.

Fifty-two patients participated in the psychiatric outpatient clinic and 57 patients at the primary care outpatient site. Following comparative analysis, male psychiatric patients showed a higher prevelance of the inability to be aroused during foreplay (73%) compared with 52% of the primary care population. Similarly, 62% of the psychiatric patients described usually losing their erection during intercourse compared with 39% of the primary care group. Interestingly, the women groups did not show any noticeable difference in sexual dysfunction.

Our results show that the psychiatric geriatric male differed in sexual dysfunction from the primary care patients. These results signify the need for closer assessment of sexual dysfunction in older adults, especially men, presenting to psychiatric settings.

NR55 Monday, May 7, 9:00 a.m.-10:30 a.m.

Influence of Age of Onset on the Course of Schizophrenia

Aida T. Ruiz, M.D., *Department of Psychiatry, University of Chile, Avenida La Paz 1003, Santiago 700-10, Chile*; Eduardo Miranda, M.D.

Summary:

Objective: It has been reported that age of onset of schizophrenia is one of the factors that determines the prognosis of illness. The objective of this study was to analyze the relationship between age at onset of schizophrenia and its course.

Method: A sample of 400 patients with DSM-III-R schizophrenia, was ascertained. Information about age of onset (first psychotic symptoms), course of symptoms, schizophrenic subtype according to Crow's classification, and the number of hospitalizations was obtained. Chi-square test was used in the statistical analysis of the data.

Results: The earliest onset schizophrenic patients had the highest number of rehospitalizations. They also showed a tendency of having a chronic course and were classified as mixed Crow's subtype; however, no statistical significant differences were found ($p>0.05$), either in the total sample or in the analysis by sex.

Conclusions: The results of this study showed no significant associations between age at onset and course of schizophrenia.

NR56 Monday, May 7, 9:00 a.m.-10:30 a.m.

Effects of Age at Onset of Schizophrenia on Familial Psychiatric Morbidity

Aida T. Ruiz, M.D., *Department of Psychiatry, University of Chile, Avenida La Paz 1003, Santiago 700-10, Chile*; Eduardo Miranda, M.D.

Summary:

Objective: It has been suggested that age of onset of schizophrenia is related to the risk of familial psychiatric morbidity. The objective of this study was to examine the possible association between age at onset of illness and familial risk.

Method: Four hundred patients with DSM-III-R schizophrenia were studied. Age of onset of schizophrenia (first psychotic symptoms) and psychiatric morbidity in relatives of schizophrenic patients were determined. Chi-square test was applied for the statistical analysis of the data.

Results: The earliest onset schizophrenic patients showed the highest familial aggregation of psychiatric disorders; however, no significant differences were found ($p>0.05$), either in the total sample or in the analysis by sex.

Conclusions: The results of this study were not conclusive and did not support an association between familial risk and age of onset of schizophrenia.

NR57 Monday, May 7, 9:00 a.m.-10:30 a.m.

Could the Hypofrontality Pattern Be Modified After Neuropsychological Rehabilitation in Schizophrenia Patients?

Rafael Penades, Ph.D., *Department of Psychiatry, Hospital Clinic, Villarroel 120, Barcelona, Spain*; Rosa Catacan, Teresa Boget, Francisco Corena, Cristobal Gasto, M.D., Nanel Saldnero

Summary:

Objective: To compare the resting and frontal activation SPECT before and after neuropsychological treatment in schizophrenic patients.

Method: Eight subjects (six men and two women) with persistent negative symptoms and cognitive impairments were evaluated with SPECT procedures before and after neuropsychological treatment.

Results: Changes were found after the neuroactivation condition but not in the control condition in the neuroimaging scans. Although the changes were small and non-specific, they appeared to show modifications in the pattern of brain perfusion. The activation score showed an increase over baseline levels and no cognitive-dependent hypofrontality after treatment.

Conclusion: Functional changes in frontal areas were found after neuropsychological treatment. The reduction of the hypofrontality improvement would be showing the functional nature of the hypofrontality hypothesis in schizophrenia and it would possibly be related with cognitive improvements.

NR58 Monday, May 7, 9:00 a.m.-10:30 a.m.

Brain Changes Associated with Linkage Marker for Schizophrenia

Serge A. Mitelman, M.D., *Department of Psychiatry, Mount Sinai, One Gustave Levy Place, Box 1505, New York, NY 10029*; Monte S. Buchsbaum, M.D., Bradley R. Buchsbaum, Lina S. Shihabuddin, M.D., Adam M. Brickman, B.A., Christopher Smith, M.A., Jeremy M. Silverman, Ph.D.

Summary:

Background: A large pedigree was identified with evidence of a genetic linkage marker for schizophrenia and related disorders. This marker is found on the short arm of chromosome 5 (5p14.1–13.1). We previously demonstrated that family members with this marker had significantly larger ventricle-to-brain ratios than those family members without the marker on computed tomography (CT) analysis.

Methods: In this study, the family sample was expanded to include six family members with the genetic marker and eight without the marker. Of those with the marker, five had a schizophrenia-related disorder (three with schizophrenia, two with schizotypal personality disorder), either by DSM-III-R or by a slight modification that emphasized the presence of negative social deficit symptoms. High-resolution magnetic resonance images (MRI) with SPGR anatomical sequence were obtained on each subject. Ventricle-to-brain ratios were calculated. Further analysis of the volumes of the frontal and temporal Brodmann regions, as well as the caudate and putamen, are underway.

Results: Family members with the marker had significantly larger ventricle-to-brain ratios than did family members without the marker.

Conclusion: This study, which used high-resolution MRI, replicates our earlier CT findings and suggests that within this pedigree, presence of the marker is associated with structural brain changes.

NR59 Monday, May 7, 9:00 a.m.-10:30 a.m.

Evaluation of Dimensions of Delusions in 57 Indian Patients

Subodh P. Dave, M.D., *Department of Psychiatry, Birmingham University, QEPH Edgbaston, Birmingham B15 2QZ, United Kingdom*

Summary:

Purpose: Kendler, Garety etc. have demonstrated the multidimensional nature of delusions in Western populations. This study assesses whether similar dimensions are seen in a sample of Indian patients.

Method: 57 patients with delusions as affirmed by two independent psychiatrists (irrespective of diagnosis) were recruited, after obtaining informed consent, from the psychiatry clinic of a teaching general hospital in Bombay. A principal delusion was elucidated in each participant. The participants were then asked to rate this belief on a scale comprising six items, (conviction, distress, obtrusiveness [preoccupation], concern [reassurance seeking], awareness of the absurdity of the belief, and interference with day-to-day activities) rated subjectively, from 1–100 using a visual analogue scale. The belief was also rated on three categorical items: reaction to hypothetical contradiction (RTHC), accommodation (awareness of events that were contradictory to the delusion), and assimilation (awareness of events that bolstered the delusion). The data obtained were analyzed using Pearson's correlation using SPSS.

Results: Preoccupation, concern, and distress showed a significant correlation as did conviction and awareness of absurdity. Three independent dimensions emerged, namely conviction, interference, and reassurance seeking.

Conclusions: While being multidimensional, delusions in this Indian sample possess fewer dimensions than reported in Western samples.

NR60 Monday, May 7, 9:00 a.m.-10:30 a.m.

Medical Comorbidity in Persons with Severe Mental Illness

Janine C. Delahanty, M.A., *Department of Psychiatry, University of Maryland, 685 West Baltimore Street, MSTF 300, Baltimore, MD 21201*; Faith Dickerson, Ph.D., Lorraine O'Donnell, M.S., Alicia Luckstead, Ph.D., Lisa B. Dixon, M.D.

Summary:

Objective: Persons with severe mental illness have a higher mortality rate than the general population that cannot be accounted for by suicide.

Methods: This study describes the comorbid medical conditions in a randomly selected sample of 200 outpatients (mean age = 44 years, SD=9), equally divided among schizophrenia, schizoaffective disorder, bipolar disorder, and major depression with half of each drawn from suburban and urban psychiatric clinics. Study participants completed an interview about their medical conditions with items drawn from the NHANES and NHIS national surveys.

Results: Approximately three-quarters (153/200) reported having one or more lifetime medical conditions, almost two-thirds (127/200) reported currently having a medical condition, and over half (107/200) were currently receiving treatment. Among the entire sample, the reported rates of ever receiving the following diagnosis were as follows: high blood pressure=31.5%; chronic bronchitis=19.6%; asthma=18.5%; diabetes=14%, and liver condition=8.5%. For six of 29 medical conditions, patients with major depression reported significantly higher rates than did persons with schizophrenia or schizoaffective disorder. The rates of illness in this population will be compared to published norms of age- and gender- and SES-matched persons in the general population.

Conclusion: These findings point to the high rate of comorbid medical conditions in persons with severe mental illnesses. Attention to these conditions is critical in order to increase patients' longevity and improve their quality of life.

NR61 Monday, May 7, 9:00 a.m.-10:30 a.m.

Gamma Band Evoked Potential in Schizophrenia Patients and First- Degree Relatives

Liyi E. Hong, M.D., *Department of Psychiatry, University of Maryland, 701 West Pratt Street, Baltimore, MD 21212*; Ann Summerfeld, Ph.D., Gunvant Thaker, M.D.

Summary:

This study's goal was to replicate the finding that schizophrenia patients have reduced 40-hz gamma band response (GBR) in a steady state evoked potential (SSEP) paradigm (Kwon, 1999). SSEP refers to the phenomenon that EEG synchronizes to repeated stimulations. SSEPs were recorded while subjects were listening to 20, 30, and 40-Hz click train stimuli. EEG power spectra from three frontal sites were examined in 14 patients taking olanzapine or clozapine, nine first-degree relatives with schizophrenia spectrum personality traits, and 13 normal subjects. There were significant effects of stimulus [$F(2,26)=3.8$, $p=0.02$] and group x stimulus interaction [$F(4, 54)=4.5$, $p=0.02$] on GBR. Post hoc analyses revealed that patients had higher 40-hz GBR than normal subjects ($p=0.035$) and relatives ($p=0.047$). Relatives did not differ from control subjects ($p=0.95$). We found increased 40-hz SSEP in patients taking olanzapine or clozapine and failed to replicate the previous findings, in which reduced GBRs were found in patients taking typical/atypical neuroleptics. Possible effects of novel versus typical neuroleptics on GBR will be discussed. Data in relatives suggested that GBR is not a schizophrenia liability marker but may be a medication-sensitive state marker.

Supported in part by a NIMH training grant R25-MH60487

NR62 Monday, May 7, 9:00 a.m.-10:30 a.m.

A Knockout Mouse Model of Altered Neural Connections in Schizophrenia

Marcus Fauero, *Department of Psychiatry, MPRC/UMMS, 252 D. Rodgers Forge Road, Towson, MD 21212*;

Summary:

Objective: Pruning is a physiologic process in the maturation of the CNS in which target neuronal connections are formed. A deficit in afferent pruning may be responsible for neuroanatomical abnormalities underlying schizophrenia. In this study, we tried to model the effects unbalancing pruning by altering the afferent and target neuron development in the cerebellum of the Bax knockout mice. Bax is a pro apoptotic protein of the Bcl-2 family that is involved with neuronal death; the cerebellum was used for its simple afferent/efferent structure. Our study aim was to explore the alterations in the Purkinje cell tree caused by the absence of the Bax protein. Previous research has shown that the Bax knockout mutant has on average 30% more Pukinje cells, with a normal gross cerebella area. Our hypothesis is that the dendritic tree of Bax negative Purkinje cells will be affected by abnormalities in pruning; we predict a reduction in dendritic area in the knockout cerebellum.

Methods: 10 Golgi-stained Purkinje dendritic trees per cerebellum were measured in three control and three BAX knock out brains. Dendritic tree area, length, and branch-points were measured using NeuroZoom.

Results: Purkinje cell dendrites tended to be smaller in the BAX knockout cerebella, with a 15% and 25% reduction in overall dendritic area and length, respectively, but only 4% reduction in branch point numbers.

Conclusion: The reduction in dendritic area and length suggests that dendritic growth was altered by decrease in presynaptic input. Dendritic complexity was not altered. The implication for schizophrenia is that areas like the hippocampus and thalamus with multiple afferents may be altered in their dendritic growth due to imbalance between afferent and target neuronal populations. This model of research of dendritic structure will be repeated in a postmortem study of schizophrenia. Support provided by NS 34309

NR63 Monday, May 7, 9:00 a.m.-10:30 a.m.

Diet and Exercise Habits Among Persons with Severe Mental Illnesses

Karen A. Wohlheiter, M.S., *Department of Psychiatry, University of Maryland, 685 West Baltimore Street, MSTF Room 300, Baltimore, MD 21201*; Janine C. Delahanty, M.A., Lorraine O'Donnell, M.S., Faith Dickerson, Ph.D., Alicia Luckstead, Ph.D., Lisa B. Dixon, M.D.

Summary:

Objective: To describe the diet and exercise habits among persons with severe mental illnesses including schizophrenia, schizoaffective disorder, bipolar disorder, and major depression.

Methods: A random sample of 200 consenting patients (mean age=44 years, SD=9) equally divided among the above diagnoses, with 50% each from suburban and urban mental health clinics, participated in a survey of health behaviors and use of health services. Measures were drawn from national probability surveys including the NHIS and NHANES.

Results: A greater proportion of patients with affective disorders (72%) than patients with schizophrenia disorders (56%) reported wanting to weigh less ($p<0.05$). Overall, 58% of patients reported trying to lose weight in the last year; no group differences were observed. Only 18% of patients reported changing their eating habits due to being obese or overweight. Over half of patients reported that they were less active than they were a year ago and were less active than others their own age. The types of exercise reported by more than 10% of patients include walking (46%), dancing (12%), "exercise" (20%), gardening (17%), and lifting weights (11%).

Discussion: These findings demonstrate a high number of reported weight problems and limited exercise among persons with severe mental illness. Results also show that appropriate methods of weight loss need to be explored.

NR64 Monday, May 7, 9:00 a.m.-10:30 a.m.

Schizophrenia With and Without Comorbid Alcohol and/or Drug Abuse

Vishal K. Adma, M.D., *Department of Psychiatry, University of Kansas Medical Center, 3901 Rainbow Boulevard, Kansas City, KS 66160*; Elizabeth C. Penick, Ph.D., Elizabeth J. Nickel, M.A., Ekkehard Othmer, M.D., Cherlyn DeSousa, M.D., Marsha R. Read, Ph.D., Barry I. Liskow, M.D.

Summary:

Objective: To compare the family and clinical histories, social functioning, and treatment utilization of a large (N=192) carefully defined group of outpatients diagnosed with schizophrenia who did or did not satisfy criteria for comorbid drug and/or alcohol dependence.

Method: Over a five-year period, 1,458 consecutive patients completed the initial screening in the outpatient psychiatry clinic of a large, midwestern medical school. One-hundred ninety-two (13%) met inclusive Feighner/DSM-III criteria for schizophrenia. Of these, 66 or 34% satisfied diagnostic criteria for substance dependence while 126 or 66% did not. The initial screening included a structured interview, self-report tests, evaluations by a clinic physician, and prescribed treatments.

Results: Patients with schizophrenia and a comorbid substance dependence disorder were younger, more likely to be male, and reported an earlier onset of psychotic symptoms. Drug abuse, but not alcoholism, was more prevalent in the family histories of schizophrenic patients with comorbid substance dependence. A family history of schizophrenia, mania, and anxiety disorder was also more prevalent in this group. Schizophrenic patients with comorbid substance dependence reported higher degrees of psychopathology, more psychotic symptoms, and greater psychosocial dyfunctioning. Measures of past treatment utilization did not distinguish the two groups.

Conclusions: The results were highly consistent, suggesting marked clinical and historical differences between schizophrenic patients with and without a comorbid alcohol or drug problem. Patients with schizophrenia and substance dependence showed an earlier onset and more malignant course than those with no comorbid alcohol or drug abuse.

NR65 Monday, May 7, 9:00 a.m.-10:30 a.m.

Comorbid Anxiety and Treatment Among Outpatients with Schizophrenia and Bipolar Disorder

Michael S. Wilson, *Department of Psychiatry, Louisiana State University Health Science Ctr, 1542 Tulane Avenue, New Orleans, LA 70112-2822*; Mark H. Townsend, M.D.

Summary:

Objective: We conducted this study to determine anxiety disorder comorbidity among 23 outpatients with schizophrenia, schizoaffective disorder, and bipolar disorder with psychotic features. Furthermore, we hypothesized that those who had been prescribed divalproex sodium would have fewer diagnosable anxiety disorders and would have lower BPRS items that reflect agitation and anxiety.

Method: Each of 23 patients who attend a partial hospital program associated with a large, urban teaching hospital was administered the MINI International Neuropsychiatric Interview, and four BPRS items associated with anxiety were assessed: anxiety, hostility, excitement, and tension.

Results: Of the 23 patients, two qualified for obsessive-compulsive disorder (8.7%), four (17.4%) for panic disorder, five (21.7%) for posttraumatic stress disorder, and six (26.1%) for social phobia. Twelve were prescribed divalproex sodium. The use of divalproex sodium was not associated with a reduction in anxiety disorder comorbidity, however total BPRS agitation scores were reduced (p=0.07).

Conclusion: Anxiety disorders were common among our sample and had not been addressed as such. Patients taking divalproex sodium had lower BPRS anxiety scores, although the relation between divalproex sodium use cannot be determined.

NR66 Monday, May 7, 9:00 a.m.-10:30 a.m.

Tardive Dyskinesia in Chronic Schizophrenia in Hong Kong

Siu-Kau Leung, M.D., *Department of Psychiatry, Castle Peak Hospital, Tsing Chung Koon Road, Tuen Mun, Hong Kong*; Gabor S. Ungvari, M.D., Fung-Shing Ng, M.D.

Summary:

Objective: To determine the point prevalence of tardive dyskinesia (TD) in Chinese patients with chronic schizophrenia and its association with sociodemographic, clinical, and treatment variables and other movement disorders.

Method: A cross-sectional assessment of a randomly selected cohort of inpatients (n=225; mean age=42±7yrs) with DSM-IV schizophrenia employing standard rating instruments for TD and other drug-induced movement disorders, catatonia, and psychotic, negative, depressive, and obsessive-compulsive symptoms.

Results: Using Schooler and Kane criteria, 15 subjects (6.7%) had TD. Patients with TD were significantly older and significantly fewer of them were on antiparkinsonian medication than their non-TD counterparts. There were no significant differences between the two groups with respect to other demographic, clinical, and treatment variables including sex, age at onset, duration of illness, current antipsychotic dosage, negative symptoms, catatonia, and Parkinsonism.

Conclusion: The present study has replicated the association of TD in Chinese schizophrenia patients with older age but failed to demonstrate any association between TD and other demographic and clinical characteristics, including catatonia.

NR67 Monday, May 7, 9:00 a.m.-10:30 a.m.

Decreased Sensitivity But Preserved Vascular Response to Niacin in Schizophrenia

Erik Messamore, M.D., *Department of Psychiatry, OHSU, 3181 SW Sam Jackson Pk. Road, UHN-80, Portland, OR 97201*; Aaron Janowsky, Ph.D., William F. Hoffman, M.D.

Summary:

Objective: The blunted flush response to niacin is a sensitive marker of schizophrenia, but its mechanism is unknown. We investigated whether the mechanism involves decreased pharmacologic sensitivity to niacin or diminished ability of the vasculature to dilate.

Methods: We measured the dose-response relationship between topically applied niacin and cutaneous blood flow in 13 schizophrenic and 13 control subjects. Blood flow was quantified by laser Doppler flowmetry before and after application of increasing concentrations (10^{-5} to 10^{-1} molar) of niacin. To further assess cutaneous vascular function, blood flow changes in response to two other stimuli, heat and transient ischemia, were also measured.

Results: The dose-response curve was shifted to the right in subjects with schizophrenia. The EC_{50} value of niacin was significantly increased in the schizophrenia group; however, this was not associated with a significant decrease in the vasodilatory response to niacin. The vasodilatory response to heat and ischemic stimuli was similar in both groups. Reduced niacin sensitivity was noted in 85% of the schizophrenic patients but only 13% of the control subjects.

Conclusions: Blunted niacin-induced skin flushing is a sensitive marker of schizophrenia. Its mechanism involves selectively diminished pharmacological sensitivity to niacin and is not due to an impaired vasodilatory response.

(Supported by a grant from the Oregon Medical Research Foundation) Biological and research-oriented psychiatrists/neuroscientists.

NR68 Monday, May 7, 9:00 a.m.-10:30 a.m.

Treatment of Atypical Antipsychotic-Resistant Schizophrenia

Rajesh Narendran, M.D., *Department of Psychiatry, Suny at Buffalo, ECMC 462 Grider Street, Room 1184 A, Buffalo, NY 14215*; Carolyn M. Young, M.D., Antoinette M. Valenti, B.A., Dedenia D. Yap, M.D., Cynthia A. Pristach, M.D.

Summary:

Background: Treatment resistance in schizophrenia remains a public health problem. The seminal Kane et al. Study led to the breakthrough finding that clozapine is effective in about 30% of treatment-resistant schizophrenic patients. All studies of treatment-resistant patients using clozapine were done prior to the release of a new generation of atypical antipsychotic agents, such as risperidone, olanzapine, and quetiapine. An important clinical question is whether non-response to these new-generation atypical agents predicts nonresponse to the prototypical atypical antipsychotic clozapine.

Objective: To assess the efficacy and safety of clozapine therapy in a group of schizophrenic patients who have failed newer atypical agents.

Methods: Ten schizophrenic inpatients (four men, six women) who had failed at least two of the three new-generation atypical antipsychotics for adequate dosage and duration were given a 6-week open-label trial of clozapine. Structured rating scales were performed to assess efficacy and safety at baseline, week 3, and week 6.

Results: Six of the nine (66%) patients who completed the 6-week trial met a priori set response criteria of 20% reduction in the BPRS and a CGI $\leq$ 3 or final BPRS $\leq$ 30. The mean final dosage of clozapine was 344.4 mg/day.

Conclusion: This study demonstrates that failure to respond to risperidone, olanzapine, and quetiapine does not predict failure to respond to clozapine. Schizophrenic patients resistant to new-generation atypical antipsychotics may benefit from a trial of clozapine.

NR69 Monday, May 7, 9:00 a.m.-10:30 a.m.

Sexual Dysfunction in Schizophrenic Patients on Atypical Antipsychotics

Antoinette M. Valenti, B.A., *Department of Psychiatry, Suny at Buffalo, ECMC 462 Grider Street, Room 1184 A, Buffalo, NY 14215*; Alice R. Fass, B.A., Carolyn M. Young, M.D., Rajesh Narendran, M.D., Cynthia A. Pristach, M.D.

Summary:

Background: The incidence of sexual dysfunction in schizophrenic patients taking the 'typical' antipsychotic medications (haloperidol, fluphenazine, and others) has been reported to be as high as 42% (1, 2). Whether the 'atypical' antipsychotics (clozapine, risperidone, olanzapine, and quetiapine) also have sexual dysfunction as a common side effect is unknown.

Objective: The purpose of this study was to compare the sexual functioning between patients taking atypical antipsychotic medication and patients taking typical antipsychotic medication.

Methods: Male and female schizophrenic outpatients, taking either an atypical or typical antipsychotic medication for at least 3 months were administered the Changes in Sexual Functioning Questionnaire-I (CSFQ-I), a standardized semistructured questionnaire. Subjects suffering from medical conditions or taking medications (including antidepressants)/substances documented to affect sexual functioning were excluded from the study. The CSFQ-I assessed antipsychotic-induced sexual dysfunction in the following five dimensions: sexual desire, arousal, pleasure, orgasm, and overall sexual functioning.

Results: Significant overall sexual dysfunction was reported in 60% of patients currently taking typical antipsychotic medications in contrast to only 23.5% of patients taking atypical antipsychotic medications. A significant decrease in sexual desire was also noted in men taking typical antipsychotic medications compared to man taking atypical antipsychotic medications ($p \leq 0.05$). Differences among the atypical antipsychotic medications in the above five dimensions will be presented.

Conclusions: Atypical antipsychotics seem to have a lower propensity to induce sexual dysfunction than typical antipsychotics.

NR70 Monday, May 7, 9:00 a.m.-10:30 a.m.

Relationship Between Family History and Antipsychotic Response in Schizophrenia

S. Evelyn Stewart, M.D., *Department of Psychiatry, University of Ottawa, 1106-751 Parkdale Avenue, Ottawa, ON K1Y 1J7, Canada*; Alain Labelle, M.D., Sharman J. Robertson, M.D., Luc Boulan, M.A., Martin Alda, M.D., Rami Habib, M.D., Sandhya Patel

Summary:

Schizophrenia research is often hampered by the inherent heterogeneity of the disorder. Because the etiology of schizophrenia is most likely multifactorially based, and because subtyping schizophrenia on the basis of a single criterion has proven unfruitful, it has been suggested that a combination of factors be used to construct patients profiles—profiles that may improve the chances of identifying subgroups of schizophrenia.

Recent reports in the literature have suggested that a positive family history of schizophrenia tends to be related to a poor response to neuroleptic treatment. We hypothesized that these patients may represent a subgroup of persons with schizophrenia. We have examined the relationship between a family history of schizophrenia or schizophreniform disorders in first-degree relatives (N=115; assessed using the Family Interview for Genetic Studies, FIGS) and probands response to haloperidol or olanzapine treatment (N=27; response was defined as a >20% improvement on the Positive and Negative Syndrome Scale [PANSS]. Our pilot data suggest that there appears to be no significant relationship between treatment response and family history.

We are currently increasing our sample size to 1) determine the robustness of these findings, and 2) determine the utility of this approach in identifying subtypes of schizophrenia.

NR71 Monday, May 7, 9:00 a.m.-10:30 a.m.

Medical Students' Mental and Physical Health Promotion: A North American School Survey

S. Evelyn Stewart, M.D., *Department of Psychiatry, University of Ottawa, 1106-751 Parkdale Avenue, Ottawa, ON K1Y 1J7, Canada*; Paul K. Dagg, M.D.

Summary:

Objective: To investigate programs promoting the mental and physical health of North American medical students, to contrast American and Canadian schools, and to compare results with a 1988 survey.

Method: The 1999 Medical School Health Promotion Survey was designed, piloted, then mailed to 143 medical schools. An SPSS database was used for data analysis.

Results: Among respondent schools, 67 (69.1%) had a program, of which 60 (89.5%) were designed on-site, and 14 (20.9%) were mandatory. The most common components were stress (88.2%) and time management (77.9%). American programs were significantly older than Canadian ones (49% were older than 10 years) (p=0.017) and were less frequently initiated by students (43.5% versus 88.9%). A 46.6% program increase has occurred since 1988. The emphasis has shifted from physical to psychological well-being.

Conclusion: The prevalence of health promotion programs for medical students has markedly increased over the past decade. Most are moderately successful and have been designed on-site, although few have mandatory attendance. Significant differences between American and Canadian programs and between current and past programs exist. Standardized mental and physical health promotion programs should be integrated into medical school curricula.

Ongoing program accreditation and outcome studies are needed.

NR72 Monday, May 7, 9:00 a.m.-10:30 a.m.

Nicotine and Cotinine Levels in Schizophrenic Patients With and Without Substance Use Disorder

Marcelo R. Eizner, M.D., *Department of Psychiatry, University of New Mexico, 2400 Tucker, NE, Albuquerque, NM 87131*; Michael P. Bogenschutz, M.D., Juan R. Bustillo, M.D.

Summary:

Introduction: Few studies have examined the relationship between nicotine dependence and other substance use disorders in patients with schizophrenia. Here, we report nicotine, cotinine, and caffeine levels in schizophrenic patients with and without substance abuse disorder.

Methods: Subjects were 49 patients with schizophrenia or schizoaffective disorder. Twenty patients had active non-nicotine substance dependence, and 29 patients had no active non-nicotine substance use disorder. All diagnoses were made using the SCID for DSM-IV. Data collected for both groups included demographic data; SES (Hollingshead); smoking status; serum nicotine, cotinine, and caffeine levels; and scores on the PANNS, Barnes, Simpson Angus, and AIMS scales.

Results: Eighteen of the 20 substance-dependent subjects, and 25 of the 29 non-substance-involved patients were smokers. Nicotine and cotinine levels were significantly higher in the dually diagnosed subjects compared with the non-dually diagnosed (nicotine: t=2.251, df=47, p=0.029; cotinine: t=2.031, df=47, p=0.048). The difference remained significant after we excluded the non-smokers (nicotine t=2.344, df=41, p=0.024; cotinine: t=2.147, df=41, p=0.038). Caffeine levels did not significantly differ between the two groups but were positively correlated with age (r=.495, N=49, p,<0.0005).

Conclusions: Substance-dependent schizophrenic patients appear to smoke more intensively than those who do not have a substance use disorder.

NR73 Monday, May 7, 9:00 a.m.-10:30 a.m.

Adult Antisocial Personality Traits Are Associated with Experiences of Low Parental Care and Maternal Overprotection

Irving M. Reti, M.D., *Department of Psychiatry, Johns Hopkins University, 600 North Wolfe Street, Meyer 3-181, Baltimore, MD 21205*; Jack F. Samuels, Ph.D., William W. Eaton, Ph.D., Oscar J. Bienvenu III, M.D., Paul T. Costa, Jr., Ph.D., Gerald Nestadt, M.D.

Summary:

Background: Clinical studies have pointed to both genetic and environmental influences in the development of adult antisocial personality traits, and much interest has focused on the role of parenting in their development. Its role, however, remains poorly understood.

Method: A total of 742 community-based subjects, comprising the Hopkins Epidemiology of Personality Study, were assessed for adult DSM-IV antisocial personality disorder traits and for various measures of parental behavior experienced as children, including by the Parental Bonding Instrument.

Results: It was demonstrated that parental behavior can be described by three fundamental dimensions—care, behavioral restrictiveness, and denial of psychological autonomy—and that these dimensions significantly correlate with measures of parental behavior known to be influential in later antisocial behavior. Linear regression analysis indicated that adult antisocial personality traits in males are associated with low maternal care and high maternal behavioral restrictiveness, and that in females, adult antisocial traits are associated with low paternal care and high maternal denial of psychological autonomy. These dimensions do not, however, explain all the variance that parental behavior has on adult antisocial personality traits.

Conclusion: Adult antisocial personality traits are associated with experiences of low parental care and maternal overprotection. An understanding of how this association is mediated may shed further light on the etiology of adult antisocial personality traits.

NR74 Monday, May 7, 9:00 a.m.-10:30 a.m.

Persistent Expression of Narp Following Neuronal Stimulation

Irving M. Reti, M.D., *Department of Psychiatry, Johns Hopkins University, 600 North Wolfe Street, Meyer 3-181, Baltimore, MD 21205*; Jay M. Baraban, M.D.

Summary:

Background: A central focus of research in psychopharmacology is to understand the molecular alterations underlying the long-term effects of repeated stimulation. Recent studies have identified an immediate early gene, Narp, that has an atypical, sluggish time course and that clusters AMPA receptors at synapses. Narp, therefore, might be contributing to alterations in excitatory transmission induced by repeated neuronal stimulation. We examined this hypothesis in animal models of repeated electroconvulsive seizure (ECS) and repeated psychostimulant administration.

Method: Some rats were treated with acute ECS and killed eight, 24, or 48 hours after a single ECS. Others were treated chronically receiving ECS on alternate days, and were then killed 48 hours after five ECS or eight, 24, 48 hours or seven days after six ECS. Control animals received six sham treatments. Narp protein levels in hippocampus were examined by immunoblot. In the psychostimulant paradigm, all rats were pretreated with normal saline for seven days, i.p., and then some continued to receive saline while others received cocaine 20mg/kg, i.p., twice a day, for seven days. VTA Narp protein levels were examined by immunoblot.

Results: There was a significant increase in hippocampal Narp levels at 48 hours after five or six ECS compared with 48 hours after one ECS, and there was a significant increase in VTA Narp levels in animals treated with cocaine chronically compared with those treated acutely.

Discussion: Narp may play a role in the molecular alterations induced by repeated ECS and by repeated psychostimulant administration.

NR75 Monday, May 7, 9:00 a.m.-10:30 a.m.

Knowledge and Impressions of BPD Vary Among Groups of Providers

Stacy L. Volkert, M.D., *Mental Health Services, Naval Medical Center, 34800 Bob Wilson Drive, Suite 108, San Diego, CA 92134-1108*; James L. Spira, Ph.D.

Summary:

This project was developed to help providers identify the role of formal DSM-IV criteria and informal clinical impressions in assessing for borderline personality disorder (BPD). The presentation will be useful for all providers and students.

Background: It was hypothesized that ability to assess for the diagnosis of BPD would be partly based on provider type and/or level of training.

Method: 107 providers were administered a questionnaire designed by the authors to examine the providers' personal and clinical impressions about BPD and knowledge of the American Psychiatric Association's Diagnostic and Statistical Manual, 4th edition (DSM-IV) criteria. Various mental health professionals, transitional interns, and emergency medicine residents were studied.

Results: Significant differences were found between types of providers, both in their ability to correctly identify DSM-IV BPD criteria and in their association of non-DSM-IV clinical impressions with the diagnosis.

Conclusion: The study's implications are discussed, including the need to better acquaint mental health staff with DSM-IV criteria for BPD and the benefit of educating providers on the ramifications of making a diagnosis too quickly or in error. The richness and variation of the clinical impressions serve to indicate the complexity of working with this patient population.

NR76 Monday, May 7, 9:00 a.m.-10:30 a.m.

Convergence Between Clinicians and Researchers for Diagnosing Personality Disorders (PDs)

Holly Garcia-O'Hearn, Ph.D., *Department of Psychiatry, Yale University, P O Box 208098, New Haven, CT 06520-8098*; Charles A. Sanislow, Ph.D., Carlos M. Grilo, Ph.D., Sandra L.C. Young, Psy.D., Thomas H. McGlashan, M.D.

Summary:

Objective: To compare DSM-IV personality disorder (PD) diagnoses obtained by a semistructured diagnostic interview to those generated independently by clinical teams.

Method: Subjects were 62 adult psychiatric inpatients (mean age 30.9 years [SD=8.5]). Discharge diagnoses made by clinical teams in a university-based psychiatric teaching hospital were compared to those generated by the Diagnostic Interview for Personality Disorders-IV (DIPD-IV). The DIPD-IV was administered by Ph.D.-level research clinicians who were trained to reliable standards (median kappas for interrater reliability ranged from 0.58 to 1.0 for specific diagnoses).

Results: Number of PD diagnoses given by clinicians ranged from none to two (M=0.48, SD=0.57); for the DIPD-IV, they ranged from none to 10 (M=3.77, SD=2.62). For the presence of any PD, there was a 21% agreement (kappa=0.01); for individual PDs, agreement ranged from 0% (histrionic; kappa=–0.03) to 35.5% (BPD; kappa=0.31, $p<0.005$; "fair agreement" per Fleiss [1981]). BPD was the PD diagnosis most often assigned by both clinicians and researchers, given in 40.3% and 67.7% of cases, respectively. Avoidant, depressive, passive-aggressive, and obsessive-compulsive PDs were never diagnosed by the clinical teams.

Conclusions: Consistent with previous studies, convergence between clinician-generated diagnoses and those generated using diagnostic interviews was low. Clinicians diagnosed PDs less frequently than researchers using diagnostic interviews. When clinicians did diagnose a PD, they rarely diagnosed more than one and rarely diagnosed PDs other than BPD. Clinician-generated diagnoses demonstrated "fair agreement" with DIPD-IV-generated diagnoses only for BPD.

NR77 Monday, May 7, 9:00 a.m.-10:30 a.m.

Relationship of Kraepelinian Affective Temperaments (as Measured by TEMPS-I) to the Tridimensional Personality Questionnaire (TPQ)

Icro Maremmani, M.D., *Department of Psychiatry, University of Pisa, Via Roma 67, Pisa 56100, Italy*; Salvatore Signoretta, M.D., Antonia Liguori, M.D., Giulio Perugi, M.D., Hagop S. Akiskal, M.D.

Summary:

Background: There is considerable uncertainty in the present literature about the relationship between personality dimensions and affective temperaments.

Method: We compared—in a non-ill 14–26 year-old Italian student population of 1,010—the affective temperaments of classic psychiatry conceived as subaffective traits (and measured with the interview version of the Temperament Evaluation of Memphis, Pisa, and San Diego [TEMP-I]) with Cloninger's revised Tridimensional Personality Questionnaire (TPQ) deriving from the experimental psychology tradition.

Results: The depressive temperament (DT) and harm avoidance (HA) loaded positively on the same canonical variate, whereas the hyperthymic temperament (HT) strongly, and novelty seeking (NS) moderately, loaded negatively. By contrast, the cyclothymic temperament (CT) loaded highly positively on a second variate, on which both novelty seeking strongly and harm avoidance moderately loaded positively. Reward dependence (RD), persistence (P), and irritable temperament (IT) did not significantly relate to any temperamental or personality constructs. At a subdimensional level of TPQ "shyness with strangers," "stoic rigidity," "detachment," "fear of uncertainty," "reflection," and "anticipatory worry" correlated best with the DT. "Gregariousness," "exploratory excitability," "uninhibited optimism," "attachment," "confidence," "extravagance," "independence," "vigor," and "impulsiveness" correlated best with the HT. Lastly, "anticipatory worry," "disorderliness," "sentimentality," and "fatigability" correlated best with the CT.

Conclusions: The data provide concurrent validity to the TEMPS-I and, as earlier suggested by Cloninger, indicate that (as expected) HA and DT are related, NS is both related to the HT and CT, and (somewhat unexpectedly) the CT is related to HA. In a more theoretical vein, the hyperthymic-novelty seeker can be predicted to be over-represented among those with high achievement; on the other hand, a moody, restless disposition (a cyclothymic-harm avoidance type) may engage in outrageous behavior and be liable to negative affective arousal. We submit that these considerations could shed some light on the origin of socially adaptive behavior ("sunny" or sanguine types) on the one hand, and borderline, anxious, or dysphoric bipolarity ("dark" types) on the other.

NR78 Monday, May 7, 9:00 a.m.-10:30 a.m.

Affective Temperamental Traits (TEMPS-I), Personality Dimensions (TPQ), and Emotional-Behavioral Problems in Children, Adolescents, and Young Adults

Salvatore Signoretta, M.D., *Department of Psychiatry, University of Pisa, Via Roma 67, Pisa 56100, Italy*; Icro Maremmani, M.D., Antonia Liguori, M.D., Giulio Perugi, M.D., Hagop S. Akiskal, M.D.

Summary:

Background: It is widely believed, but still unproven, that extreme temperamental traits predispose individuals to the development of emotional and behavioral problems and/or neuropsychiatric conditions during their lifespan. We explored this question using our scale for Affective Temperaments (conceptualized as subclinical variants of the major affective disorders) relative to the Tridimensional Model of Personality (which quantifies differences among individuals in distinct, experimentally derived components of personality).

Methods: A non-clinical sample of 1,010 students (518 male and 492 female) without major psychiatric disorders were given psychometric assessment using TEMPS-I (The Italian semistructured interview version of the Temperament Evaluation of Memphis, Pisa, and San Diego), the TPQ (Tridimensional Personality Questionnaire), and the EBC (emotional and behavioral checklist in Infancy, Childhood and Adolescence).

Results: The prevalence of such problems, as well as gender differences in our sample, were consistent with those reported in the literature. As for affective temperaments, the cyclothymic disposition was significantly associated with anxiety-sleep disturbances, sensitivity to separation, eating disturbances (in females), and antisocial-aggressive behavior (in males). Among the TPQ dimensions only high HA was related to total number of emotional-behavioral problems during infancy and adolescence. In particular this relationship increased with age. Subjects with high NS presented more antisocial-aggressive behavior, while those with low NS reported more odd-schizoid behavior and identity problems. High HA was related to motor and vocal disturbances in the youngest subjects, with anxiety-sleep disturbances in the oldest subjects, and with sensitivity to separation. Interestingly, social inhibition was related to high HA and high NS.

Conclusions: Of all of the affective temperaments, the cyclothymic turned out to be the most morbid, while among the TPQ dimensions extreme variations in HA and NS correlated best with the disposition to emotional and behavioral problems. Prospective research is needed to verify this conclusion based on our correlational analyses, these data indicate that even within a juvenile population sample, extremes of emotionality and behaviors occur preponderantly in those with temperamental excesses in HA and NS along cyclothymic lines. Both internalizing and externalizing disturbances may thus belong to the realm of affectivity.

NR79 Monday, May 7, 9:00 a.m.-10:30 a.m.

Personality Disorders in the Offspring of Antenatally Depressed Mothers

P. Helena Maki, M.D., *Department of Psychiatry, University of Oulu, P O Box 5000, Oulu FIN-90014, Finland*; Juha M. Veijola, M.D., Matti Joukamaa, Ph.D., Paula Rantakallio, M.D., Jari Jokelainen, M.S.C., Liisa Kantojarvi, M.D., Matti K. Isohanni, M.D.

Summary:

Departments of Psychiatry and of Public Health Science and General Practice, University of Oulu, Finland

Objective: The aim was to evaluate the association between maternal depression during pregnancy and personality disorders of the offspring.

Method: At midgestation mothers of 12,058 babies in the Northern Finland 1966 Birth Cohort were asked at the antenatal clinic if they felt depressed. This general population birth cohort has been followed for 31 years. Offspring of the cohort who appeared on the Finnish Hospital Discharge Register between the years 1982–97 were identified. All psychiatric diagnoses were validated using DSM-III-R criteria.

Results: Of the mothers, 14% felt depressed during pregnancy. The cumulative incidence of hospital-treated personality disorders was 2.4% among sons of depressed mothers and 0.6% in sons of nondepressed mothers (OR=3.1, 95% CI=1.5–6.5; p<0.001) when adjusted for mother's marital status, place of residence, maternal smoking and age, parental socioeconomic status, desirability of pregnancy, and perinatal complications (low birth weight [<2500 g], short gestation time [<37 weeks], or perinatal brain damage). Corresponding figures for daughters were 0.8% and 0.3% (OR=2.3, 95% CI=0.8–6.9; p<0.05).

Conclusions: Mothers antenatal depression predicted severe personality disorders in their offspring.

NR80 Monday, May 7, 9:00 a.m.-10:30 a.m.

Psychotic Depression: Differences Between Delusional and Nondelusional

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Summary:

Objective: To examine patients with DSM-IV psychotic depression and identify differences between those with and without delusions.

Method: Inpatients consecutively admitted to Butler Hospital psychiatric units with a DSM-IV diagnosis of major depressive disorder with psychotic features at admission were reviewed. Those patients whose psychotic symptoms were not due to substance abuse or medical conditions were approached for the study. 10 patients entered, and eight completed the study. Diagnoses were confirmed with the SCID I and II. Main outcome measures included plasma dopamine-beta-hydroxylase level, comorbid diagnoses (PTSD, anxiety disorders, and borderline personality disorder), history of childhood trauma, and severity of hallucinations and delusions.

Results: Delusional subjects were defined by delusions with or without hallucinations. Non-delusional subjects lacked delusions, having hallucinations only. Both groups of patients reported auditory hallucinations. Non-delusional subjects had a higher rate of PTSD, borderline personality disorder, childhood trauma, and more severe auditory hallucinations.

Conclusions: Among psychiatric inpatients with DSM-IV psychotic depression, those with only auditory hallucinations had a higher rate of PTSD, borderline P.D., and childhood trauma. This, suggests that the occurrence of auditory hallucinations without delusions in depressed inpatients could be influenced by the presence of these factors.

NR81 Monday, May 7, 9:00 a.m.-10:30 a.m.

Is Normalization of DST an Indicator for Discontinuing the Pharmacological Treatment?

Rosa Catalan, M.D., *Department of Psychiatry, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain*; Rafael Penades, Ph.D., Cristobal Gasto, M.D., Ester Gomez, M.D., Julio Vallejo, M.D.

Summary:

Aim: This report attempted to evaluate the factors of recurrence in melancholic depression to focus attention on serial DST as a biological marker of recurrence during maintenance treatment with imipramine.

Patients and Methods: The study sample included 42 ambulatory patients with a diagnosis of melancholic depression (score≤6 on the Newcastle Endogenicity Scale and for DSM-IV criteria). We collected data corresponding to sociodemographic, clinical, and psychosocial variables and serial Dexamethasone Suppression Test (DST) during follow-up. DSTs were repeated bimonthly as a biological marker of recurrence. We examined for differences on neurohormonal measures using the log-rank test and assessed

Kaplan-Meier survival curves for differences in time to recurrence between groups and multiple logistic regression models.

Results: 29 (70% of subjects) patients finally met criteria for full remission (as least 24 consecutive weeks with HDRS≤6) and were further studied during maintenance phase of pharmacological treatment. We observed that 1/19 patients, who were persistent suppressors, presented recurrence versus seven of eight patients with one time of non-suppression in the serial DST previous recurrence (Log Rank 8.47, df 2, p=0.01).

Conclusions: DST results could be a good indication for continuing imipramine treatment because serial persistent suppression was related to a good long-term response to imipramine treatment.

NR82 Monday, May 7, 9:00 a.m.-10:30 a.m.

Reasons for Screen Failure in Bipolar Treatment Studies

Laura E. Oakley, B.A., *Department of Psychiatry, New York Hospital, 525 East 68th Street, New York, NY 10021*; Joseph F. Goldberg, M.D.

Summary:

Background: A recent, growing number of randomized drug trials in affective disorders have reported negative or failed results, prompting questions about the clinical characteristics and diagnostic accuracy of patients entering research studies. We evaluated the sociodemographic and clinical features of a consecutive series of patients contacting a tertiary treatment center for bipolar illness to determine the profile of potential bipolar patients in the community who enter a treatment protocol.

Method: 100 prospective subjects who contacted the Bipolar Disorders Research Clinic of New York Presbyterian Hospital underwent initial telephone screens to ascertain provisional diagnoses, define current psychopathology and psychiatric complexity, and assess interest and suitability for entry in one of several clinical drug trials for diverse phases of bipolar illness.

Results: 1) A likely provisional diagnosis of bipolar disorder was deemed applicable by initial screening in 80% of prospective subjects; 25% of this pool subsequently entered a treatment protocol (i.e., approximately one in five initial callers). 2) Only 35% of self-diagnosed patients screened positive for bipolar illness; clinician and subject agreement on bipolar illness was modest (k= 0.39, C.I.=0.19 0.58). 3) Reasons for exclusion from study entry in rank order included: lack of patient interest (29.3%), patient not bipolar (18.3%), or patient had concurrent medications (8.5%). 4) Study entrants were more likely than those excluded to be Caucasian, male, lacking a regular psychiatrist, and be depressed upon contact (p<0.05).

Conclusions: 90% of patients in the community who identify themselves as having bipolar illness either reject or are deemed inappropriate for entry in controlled pharmaceutical trials. 90% of patients who participate in clinical trials have a history of bipolar disorder prior to initial contact. Overall, men were more apt to participate in clinical research trials compared with women of the same sociodemographic background (male to female research participation was approximately 3:1).

NR83 Monday, May 7, 9:00 a.m.-10:30 a.m.

Prevalence and Prognostic Significance of Atypical Features in Bipolar Depression

Stephen M. Gray, B.A., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, Suite 580, Boston, MA 02114*; Roy H. Perlis, M.D., Leslie J. Yan, B.A., Caroline M.J. Orsini, B.S., Thilo Deckersbach, Ph.D., Gary S. Sachs, M.D., Andrew A. Nierenberg, M.D.

Summary:

Objective: To assess the prevalence and prognostic significance of the neurovegetative components of atypical depression among outpatients in a bipolar specialty clinic.

Methods: Fifty-three bipolar depressed patients were systematically followed for up to 3 years. DSM-IV features of major depression were assessed. Atypical depressive features included hypersomnia, increased appetite, and leaden paralysis/psychomotor slowing. Only the first depressive episode was analyzed for patients with multiple episodes. Duration of episodes were assessed with survival analysis.

Results: Mean age was 41.4 years, SD=13.0; 52.8% were female; 90.9% were bipolar I, and 9.1% were bipolar II. 30.2% exhibited two of more neurovegetative features of atypical depression. An additional 32.1% exhibited a single atypical symptom. Moreover, in a Kaplan-Meyer survival analysis, presence of any atypical feature was not associated with a difference in duration of depressive episode.

Conclusions: Atypical features of depression in bipolar disorder may be less frequent than previously reported and may not be a distinguishing characteristic of bipolar depression.

NR84 Monday, May 7, 9:00 a.m.-10:30 a.m.

Residual Symptoms in Recovered Bipolar Patients

Leslie J. Yan, B.A., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, Suite 580, Boston, MA 02114*; Roy H. Perlis, M.D., Stephen M. Gray, B.A., Louisa D. Grandin, B.A., Caroline M.J. Orsini, B.S., Andrew A. Nierenberg, M.D., Gary S. Sachs, M.D.

Summary:

Objective: To assess the prevalence of subthreshold affective symptoms in patients with bipolar disorder who recovered from an acute episode of either depression or mania.

Methods: We studied 64 bipolar I or II outpatients (mean age 44.3±14.2, 53% female, 86% bipolar I) assessed prospectively for DSM-IV features of depression and mania. We assessed the first recorded episode in which patients had been considered "recovered" (two or fewer DSM-IV criteria for depression or mania) for at least eight weeks.

Results: 33.3% reported no depressive symptoms, while 19.6% reported three or more symptoms. For the ten days preceding the visit, patients reported feeling depressed for a mean of 4.6% of days, elated for 2.3% of days, irritable for 9.3% of days, and anxious for 11.2% of days. 60.0% reported no hypomanic symptoms, while 6.0% reported two or more. Mean GAF (week) in those with and without residual depressive symptoms was 77.9±8.5 and 71.3±8.5, respectively (p<.05).

Conclusions: Most bipolar patients in this cohort who achieve episode recovery continue to show modest levels of depressive and hypomanic symptoms, as well as irritability and anxiety. Residual symptoms in bipolar disorder are frequent and warrant further study to determine their course and treatment.

NR85 Monday, May 7, 9:00 a.m.-10:30 a.m.

Migraine, Anxiety, and Depression: A Large Population-Based Study in Norway

Ketil J. Odegaard, M.D., *Department of Psychiatry, University of Bergen, Haukeland Hospital, Bergen N-5021, Norway*; John A. Zwart, Ph.D., Alv A. Dahl, Ph.D., Knut Hagen, M.D., Dag Neckelmann, Ph.D., Arnstein Mykletun, Ph.D., Oleb Fasmer, Ph.D.

Summary:

Objective: To study the prevalence of anxiety and depression in persons with migraine headache in a large population-based study.

Method: Data analyses of the Nord- Tronderlag Health Survey 1995–97 in Norway, where 51,365 people answered a questionnaire based on the diagnostic criteria for migraine and to the Hospital Anxiety and Depression scale (HADS).

Results: In this study, a total of 5,173 (10.1%) people met the criteria for migraine without aura, and 1,035 (2.0%) had a diagnosis of migraine with aura. A total of 5,396 (10.8%) persons had a depression and 7,503 (15.2%) suffered from anxiety. Both migraine with aura and migraine without aura are strongly associated with anxiety and depression, the association being stronger for migraine with aura than for migraine without aura. However, there is a significant gender effect of migraine without aura on anxiety and depression. Women who suffer from migraine without aura have a significantly lower risk for both anxiety (OR 2.24 for men and 1.59 for women) and depression (OR 1.84 for men and 1.37 for women) than men with the same disease. No significant gender effect of migraine with aura was found on anxiety (OR 1.86) or depression (OR 2.13).

Conclusions: Migraine headache is associated with anxiety and depression.

NR86 Monday, May 7, 9:00 a.m.-10:30 a.m.

A Naturalistic Study of the Use of Atypical Antipsychotics in the Treatment of Bipolar Disorder

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Summary:

Objective: To assess the frequency of atypical antipsychotics use in the treatment of bipolar illness during routine clinical practice at a bipolar specialty clinic.

Methods: We reviewed charts of bipolar patients in our clinic. Standardized assessments and charting techniques were used during routine, open treatment of patients between January 1, 1998, and December 15, 2000.

Results: A total of 164 individuals (43% male, 66% BPI, 9% BPII, 9% BPNOS, 26% unknown/other), were seen at least one time within the study period (mean 8 visits +/–7.8, median treatment time 227 days). Of these, 58 (35.4%) had taken an atypical antipsychotic at least once. The distribution of the antipsychotic type was as follows: risperidone 52.6%, olanzapine 31.5%, quetiapine 16.8%, and clozapine 2%. Those taking atypical antipsychotics were rated as "well" (two or fewer DSM-IV criteria for depression mor mania) at 27.6% of their visits; those without atypical antipsychotics, 42.1%. They were in the mood states in the following proportions: 7.7% mood elevation, 20.8% depressed, and 17.7% residual symptoms at the remainder of their visits.

Conclusion: Over a third of outpatients in our clinic were prescribed atypical antipsychotics and those on atypicals were well less than a third of the time. Long term use of antipsychotics is common and warrants further study.

NR87 Monday, May 7, 9:00 a.m.-10:30 a.m.

Episode Length and Determinates of Response in Bipolar Depression

William G. Frankle, M.D., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, Suite 580, Boston, MA 02114*; Stephen M. Gray, B.A., Louisa D. Grandin, B.A., Roy H. Perlis, M.D., Thilo Deckersbach, Ph.D., Gary S. Sachs, M.D., Andrew A. Nierenberg, M.D.

Summary:

Objective: To exam the duration of depressive episodes in bipolar illness and determine the effect of antidepressant treatment on this duration.

Methods: We reviewed charts of bipolar patients in our clinic. Standardized assessments and charting techniques were used during routine, open treatment of patients between January 1, 1998, and December 15, 2000.

Results: We studied 55 individuals (41.8% male; 42.9 years old; 78.2% bipolar I, 9.1% bipolar II, 7.3% bipolar NOS, 5.4% other) with at least one major depressive episode (MDE) during the study period. Median time to recovery from the first observed MDE was 40.5 days by Kaplan-Meier cumulative survival. Logrank (Mantel-Cox) test indicated no difference in time to recovery between those on antidepressants at some point during the episode (N=20) and those not on antidepressants (N=35), (χ^2=.02, p>.05).

Conclusion: The use of antidepressants in the treatment of bipolar depression is controversial. This is largely due to the potential for these medications to precipitate mania. This is the first report, to the best of our knowledge, on the duration of treated bipolar depression, managed with modern pharmacotherapy. The median duration of episodes was about five weeks. Those patients who took antidepressants appear to recover no sooner than those who took other medications.

NR88 Monday, May 7, 9:00 a.m.-10:30 a.m.

The Relationship of Personality Dimensions to Current Major Depressive Episode Subtypes

Candace N. White, M.Ed., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114*; Timothy J. Petersen, Ph.D., Jordan W. Smoller, M.D., Maurizio Fava, M.D., Jerrold F. Rosenbaum, M.D.

Summary:

Background: The DSM-IV criteria for the atypical subtype of current major depression include interpersonal rejection sensitivity, while the melancholic subtype includes lack of mood reactivity. Both features could reflect personality differences. No studies have examined scores on the NEO-FFI in identifying such differences. Our goal is to further examine the nosology of the atypical and melancholic subtypes using NEO-FFI factor scores.

Methods: A total of 67 currently depressed participants in a genetic study of bipolar and unipolar disorders were included in the analysis. Each participant completed the NEO-FFI, Form S, and met DSM-IV criteria for current MDE (11 atypical unipolar, eight atypical bipolar, 32 melancholic unipolar, and 16 melancholic bipolar) as determined by the Structured Clinical Interview for DSM-IV Axis I Disorders (SCID-P).

Results: Atypical depressed participants scored significantly higher than melancholic participants on the agreeableness factor (p<.05) after adjusting for diagnosis (bipolar vs. unipolar). No significant differences were noted for the other four NEO factors.

Conclusion: These preliminary results suggest a relationship between current atypical depression and agreeableness, an interpersonal style that may be related to rejection sensitivity. Future research will be needed to clarify whether agreeableness predisposes to atypical presentation or whether atypical depressive episodes produce an apparent increase in agreeableness.

NR89 Monday, May 7, 9:00 a.m.-10:30 a.m.

Stability of Rapid-Cycling Bipolar I Disorder in an Outpatient Population

Courtney L. Koslow, B.A., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, 5th floor, Boston, MA 02114*; Caragh J. Reilly, B.A., Roy H. Perlis, M.D., Gary S. Sachs, M.D.

Summary:

Objective: To assess the stability of rapid cycling among a cohort of bipolar I outpatients.

Methods: Twenty-eight patients with a historical diagnosis of rapid cycling bipolar I disorder were systematically followed for up to three years. The first, and, for 19 of these patients, the last year of treatment were analyzed for number of affective episodes and duration of euthymia.

Results: Mean age was 41±10.88, and 82% were female. During the first year, patients experienced a mean of 1.07±0.90 depressive episodes and 0.82±0.82 elevated/mixed episodes; during the final year, patients experienced a mean of 1.00±0.97 depressive episodes and 0.84±0.83 elevated/mixed episodes. In addition, 20/25 (80%) had two or more months of euthymia in the first year, and 14/18 (78%) in the last year. In the first year, 3/28 (10.7%) met criteria for rapid cycling, and in the last year, 3/19 (15.8%). Only one patient met criteria for rapid cycling in both the first and the last year assessed.

Conclusions: The a low rate of rapid cycling on follow up in this population of bipolar I patients suggests either a favorable prognosis, instability of rapid cycling, or poor reliability of rapid cycling assessed retrospectively.

NR90 Monday, May 7, 9:00 a.m.-10:30 a.m.

Predictors of Suicidal Ideation in a College Population

Shamsah B. Sonawalla, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WAC 812, Boston, MA 02114*; Karen E. Kelly, B.A., Nicole B. Neault, B.A., David Mischoulon, M.D., Amy H. Farabaugh, M.A., Joel A. Pava, Ph.D., Albert Yeung, M.D., Maurizio Fava, M.D., Maurizio Fava, M.D.

Summary:

Objective: Suicide is the third leading cause of death in the U.S. college-aged population (1, 2). The purpose of this study was to assess the prevalence of suicidal ideation and possible predictors of suicidal ideation in a college-population.

Methods: We screened 301 college students (mean age: 21±3 years; 56% women; 29% minority) in a college in the greater Boston area. After obtaining written, informed consent, the Beck Depression Inventory (BDI) was distributed to all students. Students who scored ≥ 16 on the BDI and consented to be interviewed were assessed using the MDD module of the Structured Clinical Interview for DSM-IV. The chi square and logistic regression were used for data analysis.

Results: While 16.3% of the students scored ≥ 16 on the BDI, 13.6% had suicidal ideation (BDI item # 9 score ≥ 1). Age and gender did not predict suicidal ideation, although there was a trend for minority status to predict suicidal ideation on the BDI (22% rate in minority vs 15% in nonminority; p=0.1). Severity of depression, as assessed by total BDI scores, was a significant predictor of suicidal ideation (R squared=0.25; p<0.001). When each of the individual items of the BDI was examined with respect to its relationship with suicidal ideation, the items concerning sadness (#1) and disappointment (#7) were the strongest predictors.

Conclusion: Suicidal ideation was noted in 16% of this sample from an urban college population, with severity of depression being a significant predictor of suicidal ideation, and, in particular, degree of sadness and disappointment. Our study emphasizes the importance of screening for depression and suicidal ideation among college students.

NR91 Monday, May 7, 9:00 a.m.-10:30 a.m.

Prevalence of Psychiatric Illness and Neonatal Outcome in a Tertiary Obstetrics Service

Laura Fagioli-Petrillo, M.D., *Department of Psychiatry, Massachusetts General Hospital, Fruit Street, Boston, MA 02114*; Adele C. Viguera, M.D., John Hennen, Ph.D., Lee S. Cohen, M.D.

Summary:

Mood disorders cluster in women during the child-bearing years. The purpose of this study was to investigate potential relationships between psychotropic drug use, maternal psychiatric history, demographic variables, and neonatal outcomes.

Method: We retrospectively reviewed clinical course in 1,128 cases pregnancies (1,140 deliveries) among women seen through the obstetrics service at a tertiary care hospital. Data were obtained from the computerized electronic medical record.

Results: Prevalence of psychotropic drug use was 3.2%. Presence of a psychiatric disorder and use of psychotropic medications during pregnancy each were independently associated with an increased number of non-psychiatric hospitalizations during pregnancy, an increased number of telephone calls to obstetric providers during pregnancy, and an increased number of post-partum telephone calls to providers. Patients who experienced psychiatric symptoms during pregnancy had an increased percentage of infants with NICU admissions, and a higher proportion of adverse outcomes compared with mothers who did not experience such symptoms compared to patients receiving treatment with psychotropics.

Conclusions: These findings demonstrate increased morbidity and greater utilization of healthcare resources by patients who develop psychiatric symptoms during pregnancy. These findings suggest that guidelines are needed regarding the safest use of psychotropic medications during pregnancy.

NR92 Monday, May 7, 9:00 a.m.-10:30 a.m.

Self-Silencing Behaviors in a Depressed Population: Improvement Following Antidepressant Treatment

Christina M. Dording, M.D., *Department of Psychiatry, Massachusetts General Hospital, WACC 812,15 Parkman Street, Boston, MA 02114*; Lindsay M. Dececco, B.A., Robert L. Gresham, Jr., B.A., Joel A. Pava, Ph.D., Jonathan E. Alpert, M.D., Andrew A. Nierenberg, M.D., Maurizio Fava, M.D.

Summary:

Background: The Silencing the Self Scale (STSS), which includes four subscales, externalized self-perception care as self-sacrifice, silencing the self, and divided scale, was developed on the basis of interviews with depressed women and was proposed to account for the greater vulnerability of women to develop depression. A consistent relationship between self-silencing and depression has been found for women. Some studies have duplicated these findings in men.

Objective: To examine whether self-silencing behaviors change in those patients whose depression has responded to fluoxetine.

Method: We recruited 101 acutely depressed outpatients [51 women (50%); mean age: 38 years ±10 years] with major depressive disorder (diagnosed with the SCID-P and having HAM-D-17 scores ≥16). Patients were administered the STSS at baseline and at the end of eight weeks of acute treatment with fluoxetine 20 mg/day.

Results: Overall, there was a significant reduction in total STSS scores following antidepressant treatment ($p<0.0001$ by paired t-test). There was also a significant difference in the change of total STSS scores ($p<0.01$) as well as three of four subscales including externalized self-perception ($p<0.05$), silencing the self ($p<0.0007$), and divided self ($p<0.02$) between responders vs. nonresponders to antidepressant treatment.

Discussion: These findings suggest that self-silencing behavior, which is significantly related to depression, improves significantly following antidepressant treatment, with a greater degree of change in behavior among responders compared to non-responders.

NR93 Monday, May 7, 9:00 a.m.-10:30 a.m.

The Effects of Combined Pharmacologic and Cognitive Therapy on Subthreshold Symptoms and Well-Being in Continuation Treatment of MDD

Roy H. Perlis, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC-812, Boston, MA 02114*; Karen E. Kelly, B.A., Andrea H. Sickinger, B.A., Joel A. Para, Ph.D., Jonathan E. Alpert, M.D., Maurizio Fava, M.D., Andrew A. Nierenberg, M.D.

Summary:

Introduction: Patients with major depressive disorder (MDD) who remit with antidepressant treatment may continue to experience subthreshold symptoms. These symptoms might improve with added cognitive therapy but few studies have examined the actual effect.

Methods: Patients who remitted (HAM-D ≤7 for at least three weeks) with open treatment with fluoxetine 20mg/day all had fluoxetine increased to 40 mg and were then randomized to have cognitive therapy or clinical management for a six-month continuation phase. Depressive symptoms were assessed using the Symptom Questionnaire (SQ) before and after the continuation phase.

Results: A total of 133 patients entered continuation phase (mean age 39.9+/–10.2, 54% female). Of those who entered, 64.7% completed the continuation phase; the dropouts included eight patients who relapsed. In an intent-to-treat analysis, the two treatment groups did not differ significantly in mean changes in SQ measures of hostility, depression, anxiety, or somatization. They also did not differ in mean changes in SQ measures of somatic well-being, friendliness, or relaxation. There was a trend toward increased contentment score among the patients treated with combination therapy (mean change =.49+/–2.53, vs –.5+/–1.50; t=1.808, p=.08).

Conclusion: In our sample of outpatients with remitted MDD, combining cognitive therapy with fluoxetine 40mg failed to yield any significant symptomatic benefit over treatment with fluoxetine 40 mg alone.

NR94 Monday, May 7, 9:00 a.m.-10:30 a.m.

Prevalence of Depression in Women with Polycystic Ovary Syndrome

Rekha C. Rao, M.D., *Department of Psychiatry, UCLA-NPI, 760 Westwood Plaza, Los Angeles, CA 90024*; Natalie L. Rasgon, M.D., Sun Hwang, M.P.H., Lori L. Altshuler, M.D., Joni Zuckerbrow-Miller, Stanley Korenman, M.D.

Summary:

Objective: To make a preliminary assessment of the prevalence of depression in polycystic ovary syndrome (PCOS).

Method: women with a self-reported diagnosis of PCOS were recruited from three populations: (1) anonymous visitors to the National PCOS Association Website, (2) local PCOS association meeting attendees, and (3) international PCOS society meeting attendees. Subjects completed the self-administered Center for Epidemiological Studies-Depression Scale (CES-D). We scored each questionnaire, first considering the standard cut-off score of ≥16 to indicate depression. To reduce the rate of false positives, we re-analyzed the questionnaires using the more stringent cut-off score of ≥27.

Results: Of 180 anonymous responders from the website, 161 (89%) scored ≥16, and 126 (70%) scored ≥27. Of 13 women recruited at the local PCOS Association meeting, nine (69%) scored ≥16, and five (39%) scored ≥27. Of 41 participants from the international PCOS society meeting, 26 (63%) scored ≥16, and 11 (27%) scored ≥27.

Conclusions: These results suggest that the prevalence of depression in women with PCOS exceeds that in the general population. This warrants further investigation into the relationship between depression and dysfunction of the hypothalamic-pituitary-gonadal axis.

NR95 Monday, May 7, 9:00 a.m.-10:30 a.m.

Behavioral Characteristics of Children and Adults with Early-Onset Versus Late-Onset MDD

Timothy J. Petersen, Ph.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114*; Robert L. Gresham, Jr., B.A., Megan M. Smith, B.A., Joseph Biederman, M.D., Andrew A. Nierenberg, M.D., Maurizio Fava, M.D., Jonathan E. Alpert, M.D.

Summary:

Background and Significance: Children of parents with a history of unipolar depression are at higher risk for the development of depression and behavioral problems when compared with children of nondepressed parents. However, little research has been conducted to examine this risk transmission with consideration to the age of onset of parental depression. The objective of this study was to compare behavioral and emotional characteristics between offspring of parents with early-onset depression (<18 years old) and offspring of parents with late-onset depression (greater than or equal to 18 years old).

Method: Forty-three parents (mean age = 40.8 years), entering clinical drug trials, completed the Child Behavior Checklist (CBCL) at their initial study visit for each of their biological offspring. Children ranged in age from six to 17 years (a total of 57 children). Each parent met DSM III-R or IV criteria for a current major depressive episode as determined by the Structured Clinical Interview, patient edition (SCID). Exclusion criteria for adult participants included <18 or >65 years of age, drug or alcohol abuse during the last six months, psychotherapy initiated within the last two months, bipolar disorder, psychosis, significant suicidal risk, unstable medical conditions, pregnancy, breastfeeding, and concurrent treatment with other psychotropic medications.

Results: For all the CBCL clinical scales, children of early-onset parents obtained higher scores (more severe psychopathology) than children of late-onset parents (all comparisons $p<.01$). This indicates that children of early-onset parents were reported to experience more frequent delinquent and aggressive behavior, attention and other cognitive problems, social difficulties, somatic complaints, and symptoms of anxiety and depression. For all the CBCL competency scales, children of early-onset parents obtained lower scores (less competent) than children of late-onset parents (all comparisons $p<.01$). This indicates that children of early-onset parents were reported to be less competent in extracurricular and social activities as well as school performance.

Conclusions: In this sample, offspring of depressed adults with early-onset unipolar depression experience greater psychiatric disturbance and less competency than offspring of adults with late-onset unipolar depression. Further research is needed to ex-

amine the role of parental comorbid psychiatric conditions and reporting biases in explaining the above results.

NR96 Monday, May 7, 9:00 a.m.-10:30 a.m.

Safety and Tolerability of Rapid-Loading Extended-Release Divalproex Sodium

Brian P. Miller, M.D., *Department of Psychiatry, U C at San Diego, 200 West Arbor Drive, San Diego, CA 92103*; William Perry, Ph.D., Christine Moutier, M.D., Shannon K. Robinson, M.D., David Feifel, M.D.

Summary:

Divalproex sodium has been well accepted as effective treatment for bipolar disorder. Rapid-loading strategies for divalproex sodium have been shown to be safe and effective in treating acutely manic patients. An extended release formulation of divalproex sodium has recently been approved for once-a-day dosing in the treatment of migraine headaches. To date, there is no existing literature on the use of extended release divalproex sodium in bipolar patients. We present data from a small number of acutely manic inpatients treated openly with extended release divalproex sodium. Patients were started on a single dose of 30 mg/kg given once a day. Serial blood levels of valproic acid and scores for the Young Mania Rating Scale (YMRS) were obtained. A retrospective chart review was performed to evaluate side effects and to rate patients' improvement based on the Clinical Global Impression (CGI) Scale. There were no serious adverse events, and no patients had to stop treatment due to side effects. Also, improvement in the YMRS and CGI was consistently shown. These very preliminary results show that extended release divalproex sodium is well tolerated and effective when given as a once-a-day dose of 30 mg/kg in the inpatient setting to stabilize acutely manic patients.

NR97 Monday, May 7, 9:00 a.m.-10:30 a.m.

The Validity of Atypical Depression

Michael A. Posternak, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Providence, RI 02905*; Mark Zimmerman, M.D.

Summary:

Introduction: Studies aimed at validating the atypical features subtype have yielded conflicting results. The present study sought to reevaluate the validity of atypical depression by examining the demographic and clinical features of a large cohort of depressed psychiatric outpatients who met DSM-IV criteria for atypical features.

Method: Eleven hundred and thirty psychiatric outpatients were evaluated as part of the Rhode Island Methods to Improve Diagnostic and Assessment Services (MIDAS) project. All axis I disorder diagnoses were made using the Structured Clinical Interview for DSM-IV. Axis II diagnoses were obtained for 530 patients using the Structured Interview for DSM-IV, Personality Disorders. Based on the available literature, we made a series of *a priori* hypotheses regarding how depressed patients with atypical features would differ from those without atypical features.

Results: While many of the predicted hypotheses were borne out an equal number were not. Correlation analyses revealed that the associations between the atypical symptoms tended to be modest; mood reactivity was not found to be associated with any of the other atypical symptoms.

Conclusion: Our results provide only modest support for the validity of the atypical features subtype.

NR98 Monday, May 7, 9:00 a.m.-10:30 a.m.

The Prevalence of Anger in Psychiatric Outpatients

Michael A. Posternak, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Providence, RI 02905*; Mark Zimmerman, M.D.

Summary:

Introduction: It is unknown how common anger is in psychiatric outpatients. The present study sought to evaluate the prevalence of both subjective anger and angry outbursts in a large sample of psychiatric outpatients.

Method: Thirteen hundred psychiatric outpatients were evaluated for the presence of anger as part of the Rhode Island Methods to Improve Diagnostic and Assessment Services (MIDAS) project. Anger was assessed using items drawn from the Schedule for Affective Disorders and Schizophrenia (SADS). Subjective anger was rated as present when patients reported feeling angry most or all of the time during the past week. Overt expression of anger was rated as present when patients acknowledged throwing things, breaking things, or assaulting somebody in the week prior to evaluation.

Results: According to these criteria, 26.1% of our sample reported feeling angry, and 23.3% reported overtly expressing their anger in the past week. Intermittent explosive disorder, posttraumatic stress disorder, and major depression were the three axis I disorders most likely to be associated with both subjective anger and overt expression of anger. Anger was also associated with personality pathology, particularly cluster B disorders.

Conclusions: Anger is quite common in psychiatric outpatients. Anger and the overt expression of anger appear to be especially common in intermittent explosive disorder, major depression, posttraumatic stress disorder, and cluster B personality disorders.

NR99 Monday, May 7, 9:00 a.m.-10:30 a.m.

Birth Outcomes Following Prenatal Exposure to Antidepressants

Kimberly H. Pearson, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, ACC812, Boston, MA 02114*; Lee S. Cohen, M.D., Vicki L. Heller, M.D., Jennifer R. Poitras, B.A.

Summary:

Background: The prevalence of psychotropic medication use during pregnancy is high. There is a growing literature regarding reproductive safety of certain commonly used antidepressants. Less is known regarding perinatal complications associated with the use of these agents. This study examined perinatal outcomes associated with antidepressant use during pregnancy.

Methods: Obstetrical and neonatal records were reviewed for 70 infants whose mothers were exposed to SSRI's or TCA's during pregnancy and/or labor and delivery including fluoxetine, paroxetine, sertraline, nortriptyline, imipramine, desipramine, amitriptyline, and clomipramine as well as buproprion and venlafaxine. The records were blindly scored by two different raters with respect to the presence of obstetrical complications and other perinatal outcome variables including APGAR scores, birth weight, gestational age, and admission to Special Care Nursery. Particular attention was given to whether complications noted (if any) were clinically relevant, and whether infants were discharged home with their mothers. The relationship between time of exposure (early trimester versus late trimester) and perinatal outcome was also examined.

Results: Readily apparent treatment-emergent adverse events were not seen in infants whose mothers took SSRI's or TCA's across pregnancy and across labor and delivery. Further analyses evaluating the relationship between medication dose, the timing

of exposure, and potential perinatal adverse effects were also performed.

Conclusions: The use of SSRI's and TCA's during labor and delivery does not appear to be associated with clinically significant readily apparent treatment-emergent effects. Long-term neurobehavioral effects of fetal exposure to these medications remain unknown. However, clinicians may be best advised to continue antidepressant medication across labor and delivery given the potential risk for postpartum depression associated with antidepressant discontinuation as women enter a period of increased vulnerability to mood disturbance.

NR100 Monday, May 7, 9:00 a.m.-10:30 a.m.

The Naturalistic Course of Untreated Major Depression

Michael Postenak, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Providence, RI 02905*; David A. Solomon, M.D., Timothy I. Mueller, M.D., Andrew Leon, Ph.D.

Summary:

Objective: This study sought to describe the naturalistic course of major depression in those individuals who do not receive somatic therapy for their depressive illness.

Method: Affectively ill individuals were recruited into the Collaborative Depression Study and followed prospectively for up to 15 years. One hundred and thirty subjects who recovered from their intake episode subsequently experienced a depressive recurrence that went untreated for at least 4 weeks following the onset of the recurrence. Forty-six of the 130 subjects eventually obtained somatic therapy without having experienced a remission of symptoms; the durations of these episodes were censored at the time treatment was obtained. Duration of illness was examined using survival analysis.

Results: The median time to recovery in this sample was 23 weeks. Recovery was most likely to occur in the first 3 months following the onset of a depressive episode. Of the 84 subjects whose depressive illness went untreated from its inception through its resolution, the median time to recovery was 13 weeks.

Conclusions: There is a high rate of recovery in individuals not receiving somatic treatment for their depressive illness, particularly in the first 3 months of an episode. We found that the median duration of illness in individuals not receiving somatic therapy for major depression was 23 weeks. Because treatment-seeking behavior is known to be associated with a worse prognosis, this figure probably represents a lower-limit approximation of the untreated course of major depression.

NR101 Monday, May 7, 9:00 a.m.-10:30 a.m.

Differences in Heart-Rate Pattern in Depressed Versus Healthy Outpatients

Michael Gaetz, Ph.D., *Department of Psychiatry, University of British Columbia, 2255 Wesbrook Mall, Vancouver, BC V6T 2A1, Canada*; Edward J. Rzempoluck, Ph.D., Grant L. Iverson, Ph.D.

Summary:

Objective: To investigate the usefulness of non-linear analytical methods for the detection of disturbed circadian physiology often reported in major depression.

Method: Twenty-two non-depressed medical outpatients and 30 outpatients with depression wore a cardiac and movement monitor for 24 hours. Minute averaged heart rate and horizontal (walking) movements were recorded (1,440 data points). A generalized regression neural network (GRNN) and Approximate Entropy (ApEn), a statistic used to estimate the regularity of time-series data, were used to quantify differences in cardiac physiology between groups.

Results: The GRNN analysis of the cardiac data resulted in a best overall classification rate of 69.2% [16/30 (53.3%) for the depressed cases, 20/22 (90.9%) for control cases]. Mean ApEn, averaged over the 24-hour period, was greater for patients with depression compared to medical control subjects; this finding approached significance despite the small sample sizes ($t = 1.6$; $p = 0.057$).

Conclusions: These results suggest that a subset of depressed individuals have altered cardiac physiology that may reflect disturbed circadian sleep/wake patterns. Although there was only a trend toward significance in ApEn, the differences observed with this algorithm and the GRNN generally replicate a previous study that used healthy community volunteers and outpatients with depression.

NR102 Monday, May 7, 9:00 a.m.-10:30 a.m.

Serum-Free T4 and Shorter Hospital Length of Stay in Depressed Male Patients

Natasha S. Sane, M.D., *Department of Psychiatry, UCLA NPI, 760 Westwood Plaza, Los Angeles, CA 90024*; Mark A. Frye, M.D., Lindsay R. Kiriakos, M.D., Anthony Cossolino, M.D., Lori L. Altshuler, M.D., Vishaal Mehra, M.D., Jim Mintz, Ph.D.

Summary:

Many but not all studies of patients with depression have reported a relative increase (i.e., within the normal range) in serum free T4 (FT4). Subsequent FT4 decreases have been greater in responders (versus nonresponders) to a number of treatments including ECT, antidepressants, and psychotherapy. This retrospective review was conducted to evaluate thyroid function and its predictive potential for treatment response as represented by hospital length of stay (HLOS).

Medical records of 83 patients (27M/56F) hospitalized between 1988–1992 for a depressive disorder were reviewed. Blind to diagnosis and HLOS, admission thyroid function data were harvested and log transformed. Accelerated failure time regression (SAS LifeReg) was utilized with time to discharge (HLOS) as the dependent variable. Separate analyses were used with TSH, free T4, and T3 as independent variables.

Admission TSH, free T4, and T3 were obtained in 76, 50, and 45 patients, respectively. There was no significance difference in age, log TSH, T4, or T3 by gender. Controlling for age and date of hospital discharge within the 5-year study period, survival regression modeling including gender and each thyroid function revealed a significant interaction between gender and free T4 (χ^2=8.30, df=1, p=0.004). Separate gender analyses revealed an inverse relationship between FT4 and HLOS in men (Beta = −1.86, SD=0.44; χ^2=17.78, df=1, p=0.0001), but not women (Beta = −0.06, SD=0.25, χ^2=0.06, p=0.81). There was no significant relationship between HLOS and TSH or T3 in either men or women.

These data suggest that men who have relatively elevated FT4 are more likely to have a faster treatment response as represented by hospital length of stay. Prospective study is encouraged to clarify the significance of thyroid axis "overdrive," potential gender differences, and its treatment implications for depression.

NR103 Monday, May 7, 9:00 a.m.-10:30 a.m.

Validation of an Abbreviated Hamilton Depression Rating Scale: Hamilton Rating Scale for Depression, Six Item

Roger S. McIntyre, M.D., *Department of Mood and Anxiety, CAMH-Clarke Site, 250 College Street, Toronto, ON M5T 1R8, Canada*; Sidney H. Kennedy, M.D., Robert M. Bagby, Ph.D., David Bakish, M.D.

Summary:

The Hamilton Rating Scale for Depression (HRSD) (Hamilton 1960) has been used for four decades as the "gold standard" instrument to assess severity of depression and outcome in pharmacotherapy research. Frank et al (1991) defined remission, the goal of antidepressant therapy, as an HRSD (17-item) score of less than 8. The clinical utility of the HRSD scale is hampered by the length of time to administer and by the lack of inter-rater reliability. Bakish and Hooper (2000) described the utility of a six-item version of the HRSD, which correlated well with the 17-item version as a measure of response. As several lines of research evidence have highlighted the importance of achieving full remission as one modifiable avenue to minimize risk of relapse and recurrence, it would be helpful to develop cut-off scores for this shorter version, allowing clinicians to practically implement a tool which distinguishes between remission and response.

Based on a sample of 248 patients with major depression who received standard clinical treatment at CAMH, we derived our own short version, which attempts to identify those items which have the best correlation with the 17-item. We then derived cut scores for the Bakish and Hooper six-item scale and for our own scale to assess response and remission as identified by the full 17-item. We will present data comparing the predictive validity of these two short-version scales as measures of full and partial remission.

NR104 Monday, May 7, 9:00 a.m.-10:30 a.m.

Randomized, Single-Blind Comparison of Topiramate and Bupropion Sustained Release as Add-On Therapy in Bipolar Depression

Roger S. McIntyre, M.D., *Department of Mood and Anxiety, CAMH-Clarke Site, 250 College Street, Toronto, ON M5T 1R8, Canada*; Deborah A. Mancini, M.A., Sonia M. McCann, B.S.C., Janaki Srinivasan, M.D., Doron Sagman, M.D., Sidney H. Kennedy, M.D.

Summary:

Objective: To compare the efficacy and tolerability of topiramate and bupropion SR when added to mood stabilizer therapy in patients with bipolar I/II depression (DSM-IV).

Methods: A total of 36 outpatients with Hamilton Depression Rating Scale (HDRS-17) scores ≥16 were randomly assigned to receive escalating doses of either topiramate (50–300 mg/day) or bupropion (100–400 mg/day) for 8 weeks. Data were analyzed on an intent-to-treat basis using the last observation carried forward method.

Results: Baseline demographic and clinical parameters were comparable between the two treatment groups. The mean doses of study medication were 176 mg/day for topiramate and 250 mg/day for bupropion. A significant and comparable reduction in depressive symptoms was observed from baseline to endpoint following topiramate and bupropion treatment, according to ≥50% reduction in HDRS-17 and the Clinical Global Improvement Scale (CGI-I) score. Both topiramate and bupropion were generally well tolerated. Thirteen patients discontinued: two because of lack of efficacy, one due to withdrawal of consent, and 10 following side effects (six in the topiramate and four in the bupropion group). There were no cases of affective switch in either treatment arm. Weight loss was experienced by patients in both groups (mean weight loss after 8 weeks was 1.2 kg following bupropion treatment and 5.8 kg following topiramate treatment).

Conclusions: These preliminary data suggest that topiramate may possess comparable antidepressant activity to bupropion in acute bipolar depression and warrant further investigation in double-blind, placebo-controlled trials.

NR105 Monday, May 7, 9:00 a.m.-10:30 a.m.

Reproductive and Metabolic Risks of Divalproex in Bipolar Females

Roger S. McIntyre, M.D., *Department of Mood and Anxiety, CAMH-Clarke Site, 250 College Street, Toronto, ON M5T 1R8, Canada*; Deborah A. Mancini, M.A., Sonia M. McCann, B.S.C., Janaki Srinivasan, M.D., Sidney H. Kennedy, M.D.

Summary:

Purpose: To describe the effects of divalproex sodium on menstrual function and endocrine and metabolic milieu in women with bipolar disorder.

Methods: Thirty-eight female subjects, aged 18 to 50, meeting DSM-IV criteria for bipolar I or II disorder in any phase of illness were enrolled. Subjects with primary hormonal abnormalities or receiving exogenous hormones such as oral contraceptive pills were excluded. Subjects receiving divalproex sodium for acute and/or maintenance treatment were compared to subjects receiving either lithium or carbamazepine using chi-square and analysis of variance. Parameters included measures of androgenization, sex hormones, and glucose homeostatic network. Current and prior histories of menstrual and endocrine functioning were collected.

Results: Baseline demographic characteristics were comparable between the two groups. Overall, 50% of the divalproex-treated women reported menstrual irregularities compared to 15% of the women receiving lithium. Fifty-eight percent of the women with menstrual abnormalities exhibited laboratory evidence of elevated androstenedione concentrations, while 15% of women with normal menstrual cycles showed high concentrations of androstenedione. Additional metabolic and hormonal parameters will be presented.

NR106 Monday, May 7, 9:00 a.m.-10:30 a.m.

Screening for Depression: Observer Versus Self-Ratings

Mark Schor, M.D., *Department of Psychiatry, New York University Medical School, 325 East 21st Street, #1, New York, NY 10010*; Eric D. Peselow, M.D., Waguih W. Ishak, M.D.

Summary:

Objective: The purpose of this presentation is twofold: 1) to evaluate the utility of the Online Depression Screening Test (ODST), a 10-item (0–4 point) self-report depression rating scale developed as a user friendly screening for depression that enables users to be screened for depression in the privacy of their own home, and 2) to compare the utility of this self-report scale with the Beck scale (another self rating scale) and to correlate both of these self-report scales with the observer rating scales such as the Hamilton Depression Scale, Montgomery-Asberg Depression Scale, and CGI to see if there is a relationship between how observers see the patient's depression and how the individual rates his or her depressive symptoms

Method: To date, 40 patients with depression, 48 patients with panic disorder, 45 patients with both depression and panic disorder, and 26 normal control subject, have been rated with the above two self-report scales (Beck and ODST) and the three observer rating scales (Hamilton, Montgomery-Asberg, and CGI). We then attempted to correlate differences between diagnoses as well as Pearson correlations between all scales.

Results: Overall there were consistent differences on all scales with respect to diagnoses (e.g., ODST mean scores of 13 for depressed alone group versus 14 for depression + panic patients versus mean scores of 4 for panic disorder alone and 3 for normal control subjects). It did appear that the ODST had better correlations with the observer rating scales (average r=0.90) than with the Beck (r=0.082). ODST scores of 8 or above correlated with a diagnosis of major depression in 98% of cases.

Conclusion: This report will highlight differences between observer versus self-report scales in addition to discussing the crucial role of screening for depression in outpatient populations

NR107 Monday, May 7, 9:00 a.m.-10:30 a.m.

Ondansetron Attenuates CCK-Induced Satiety by Blocking Vagal Activity

Eric M. Brown, M.D., *Department of Psychiatry, University of Minn., 2450 Riverside Avenue, Minneapolis, MN 55454-1495*; Randall S. Daughters, B.S., Randall D. Hofbauer, M.D., Aaron W. Grossman, B.S., Anne-Marie Marshall, B.S., Boyd K. Hartman, M.D., Patricia L. Faris, Ph.D.

Summary:

Bulimia nervosa is a psychiatric disorder characterized by altered gastrointestinal (GI) functions including binge eating, altered satiety, and purging behavior. Serotonin-3 (5-HT_3) receptor antagonists have been shown to be helpful in the treatment of several disorders involving altered GI function, including bulimia nervosa. CCK is a polypeptide that has well-documented effects on food intake, including, significantly, the production of satiety at lower doses, and nausea at higher doses. To evaluate potential interactions between CCK and 5-HT_3 receptors, the effect of a 5-HT_3 antagonist, ondansetron, on exogenous CCK-induced satiety and c-fos activation was determined. Ondansetron attenuated both CCK-induced satiety and c-fos activation by approximately 50%. The reduction in c-fos was localized to a specific subregion of the dorsal medulla, suggesting that a distinct subpopulation of CCK receptive fibers is modulated by 5-HT_3 ligands. These results suggest that 5-HT_3 antagonists may affect endogenous CCK functions.

NR108 Monday, May 7, 9:00 a.m.-10:30 a.m.

Analysis of Vitamin D Receptor, Estrogen Receptor, and Collagen Ial Gene Polymorphisms in Patients with Anorexia Nervosa

Azucena Diez, M.D., *Department of Pediatrics, University of Navarra, PIO XII SN, Pamplona 31080, Spain*; Ana Patino, Ph.D., Christina Azcona, M.D., Cesar A. Soutullo, M.D., Juan Jimeno, M.D., Ignacio Landecho, M.D., Elena Sotillo, M.B.

Summary:

Objective: Osteopenia is a medical complication in patients with anorexia nervosa (AN). Several genetic polymorphisms of vitamin D receptor (VDR), estrogen receptor (ER), and collagen Iα (collαI) genes are thought to contribute to bone mineralization (BM). Our objective is to identify the polymorphisms of the VDR, ER, and CollαI genes and its association with AN.

Methods: A total of 28 patients with a DSM-IV diagnosis of AN, and 109 healthy controls were included in the study. BM was determined by osteosonography. We asessed the following markers of the alleles: VDR gene: FokI I, Apa I, TaqI; ER gene: PvuII, XbaI; CollαI gene: MscI.

Results: We found a statistically different distribution of genotypes for the ER gen markers *pvuII* (p=0.082) and *XbaI* (p=0.031). The analysis of the controls' genotypes showed a linkage disequilibrium between markers of the VDR and ER genes. The AN heterocyguos (Ff) patients for the *FokI* marker of the VDR gene tended to have higher BM values (p=0.086). Mean BM was −1.87 SDS.

Conclusion: Bone mineralization assessed by osteosonography is reduced in patients with anorexia nervosa. The AN heterozygous (Ff) patients for the *FokI* marker of the VDR tended to have higher Ad-SOS values.

Supported by a grant of PIUNA (University of Navarra Research Projects)

NR109 Monday, May 7, 9:00 a.m.-10:30 a.m.

The Association Between Dissociation, Alexithymia, Depression, and Suicidality in the General Population

Paivi Maaranen, M.D., *Department of Psychiatry, University of Kuopio, P O Box 1777, Kuopio 70211, Finland*; Antti Tanskanen, M.D., Kaisa Haatainen, M.H.S.C., Kirsi Honkalampi, Ph.D., Heimo Viinamaki, M.D.

Summary:

Objective: Most people experience occasional dissociation, but only a minority suffer from frequently occurring dissociative symptoms. Several previous studies have examined dissociation in the general population, but the relationships between dissociative experiences, alexithymia, depression, and suicidality are largely unknown at the population level.

Method: A large cross-sectional survey of psychosocial risk factors among Finnish adults was carried out in 1998. A total of 2,020 men and women aged 25–64 years responded. The level of dissociation was estimated with the Dissociative Experiences Scale. A cutoff score of 20 (or more) was used to define high level of dissociation (N=147, i.e. 7.3%). Alexithymia was assessed using the 20-item version of the Toronto Alexithymia Scale, depressive symptoms with the 21-item Beck Depression Inventory, and suicidality with one of the BDI-items.

Results: After adjustment for gender, age, marital status, education, place of residence, work ability, financial situation, subjective health, alcohol intake, and smoking, the risk of high level of dissociation was 5.41 (95% CI's: 3.53–8.31, p<0.0001), 4.88 (3.16–7.55, p<0.0001), and 3.13 (2.04–4.82, p<0.0001) in alexithymic, depressed, and suicidal subjects, respectively.

Conclusions: This is the first study to demonstrate the positive relationships between dissociation, alexithymia, depression, and suicidality in the general population.

NR110 Monday, May 7, 9:00 a.m.-10:30 a.m.

Depression Does Not Distinguish Alzheimer's from Lewy Body Dementia

Jeremy A. Burd, M.D., *Department of Psychiatry, Mt. Sinai, One Gustave L Levy Place, Box 1230, New York, NY 10029*; Adam M. Brickman, B.A., Steven C. Samuels, M.D., Vahram Haroutunian, Ph.D., Dushyant P. Purohit, M.D., Michael J. Serby, M.D.

Summary:

Although not considered a pathognomonic feature, previous studies have indicated an increased incidence of depression in patients with dementia with Lewy bodies (DLB) compared to those with Alzhemier's disease (AD).

Purpose: The purpose of this study was to examine depressive symptomatology in cases of DLB and AD confirmed by autopsy.

Methods: The cases came from a consecutive series of demented, nursing home subjects (N=56, CDR ≥ 0.5) who received CERAD neuropathological assessment and assessment of Lewy body (LB) count in five cortical areas. Cases were divided into DLB and AD groups. DLB cases (N=17) had a total cortical LB count of 1 or greater. AD cases (N=39) met CERAD neuropathological diagnostic criteria for definite AD. Formal postmortem chart reviews were conducted. Clinical data describing depressive symptomatology included the presence of lifetime depression as well as a DSM-IV depressive symptom checklist.

Results: Chi-squared analysis revealed no differences between frequency of lifetime depression diagnosis in AD (13%) and DLB (18%) (p=n.s.). An exploratory correlation between total depressive symptoms and cortical LB count showed no significant relationship (r = 0.09; p = 0.74).

Conclusion: This study suggests that presence or absence of depression does not distinguish between AD and DLB. Further-

more, there does not appear to be a relationship between depressive symptoms and LB density.

NR111 Monday, May 7, 9:00 a.m.-10:30 a.m.

Palliative and Aggressive Care of Dementia Patients at End of Life

Martin M. Evers, B.S., *Department of Psychiatry, Mount Sinai, One Gustave Levy Place, Box 1230, New York, NY 10029*; Vahram Haroutunian, Ph.D., Lucia Capitelli, R.N., Margaret C. Sewell, Ph.D., Hillel T. Grossman, M.D., Khalid M. Khan, M.D., Deborah B. Marin, M.D.

Summary:

Introduction: End-stage dementia patients are treated aggressively for medical complications despite the relative futility of and discomfort associated with these measures. In contrast, palliative measures are often not offered to this population. We determined whether this holds true in a sample of well-characterized dementia patients who came to autopsy.

Methods: Palliative care (nasal oxygen and pain medications) and aggressive interventions (antibiotics) were reviewed for 42 Alzheimer's disease patients within the last 6 months of life. The patients were divided into "mild-to-moderate" (N=10) and "severe" (N=32) dementia cohorts.

Results: Fifty-eight percent of severely demented and 44% of mild-to-moderately demented patients received oxygen. Seventy-eight percent of severely demented and 80% of the less demented were given pain medications. Sixty-three percent of severely demented and 40% of mild-to-moderately demented patients were given antibiotics. Differences across groups were not significant for any intervention.

Conclusion: Despite the higher mortality associated with severe dementia, palliative interventions were provided to both cohorts with similar frequency. The finding that over 63% of severely demented patients were administered antibiotics is of concern. Physician education and care plans may reduce such interventions, thereby increasing the quality of life of terminally ill dementia patients.

NR112 Monday, May 7, 9:00 a.m.-10:30 a.m.

Quitting Strategies Used by Nontreatment-Seeking Marijuana Smokers

Susan J. Boyd, M.D., *IRP, NIDA, 5500 Nathan Shock Drive, Baltimore, MD 21224*; David A. Gorelick, M.D., Marilyn A. Huestis, Ph.D., Stephan J. Heishman, Ph.D., John C. Dermand, Michael S. Simmons, Donald P. Tashkin, M.D.

Summary:

Marijuana is a widely used illicit substance, yet little published literature exists on coping strategies employed by marijuana smokers trying to quit. This study examines self-reported quitting strategies employed by a convenience sample of 83 non-treatment-seeking marijuana smokers: 49 participating in a UCLA lung health study and 34 in nontreatment studies at the NIDA IRP. Subjects were largely unmarried (77%), employed (72%), white (73%) males (87%), average age 39.3 years (SD = 10.2). Most were currently using marijuana (79%), averaging 2.6 (SD=3.6) joints per day. Subjects had used marijuana for 19.3 (SD=8.4) years and made 3.5 (SD=11.4) "serious attempts" to quit. Forty-six percent had quit for more than 6 months. Subjects reported using an average of 1.9 (SD=2.4) quitting strategies. A Categorical Principal Components Analysis (CatPCA) identified two factors: environmental changes (e.g., avoiding people or places where marijuana was used, used by 42% of subjects) and social support (e.g., using self-help groups, encouragement from others, used by 31.3%). Using a General Linear Model, no significant association was found between any quitting factor or strategy and duration of quit episode. The absence of any significant association suggests that, in this population, success in quitting is determined by factors other than quitting strategies employed.

Acknowledgment: Supported by NIDA intramural funds and NIH grants DA03018 and DA04268.

NR113 Monday, May 7, 9:00 a.m.-10:30 a.m.

Microecology of Crime in Proximity to Fixed-Site Methadone Clinics

Susan J. Boyd, M.D., *IRP, NIDA, 5500 Nathan Shock Drive, Baltimore, MD 21224*;

Summary:

Although methadone treatment programs have been shown effective in reducing crime among their patients, their impact on neighborhood crime rates has been debated. No previous studies exist on the impact of crime in the immediate vicinity (approximately one city block) of fixed-site methadone maintenance programs. The present study is an ecological analysis of different types of crime in the vicinity of 11 urban methadone maintenance clinics. Arrest data from January 1994 to February 1997 were geocoded to determine the location of each arrest. Concentric circular "buffers" were drawn at 25, 50, 75, 100, 200, and 300-meter radii around each methadone program site (MPS) to define non-overlapping geographic areas for comparison. Counts per unit area within each buffer for six categories of arrests were obtained: all, drug-related, heroin-related, cocaine-related, violent, and financial. All six categories of arrests reached an apparent low point at 75 meters from the MPS's. Total arrests and cocaine-related and drug-related arrests appeared to peak at 50 meters and again at 200 meters. Financial-, violent-, and heroin-related arrests displayed no clear relationship to distance from MPS's. This study found no linear relationship between geographic proximity to a methadone program and arrests.

NR114 Monday, May 7, 9:00 a.m.-10:30 a.m.

The Use of Paroxetine for Methamphetamine Craving

Geraldine M. Steinagel, M.D., *Department of Psychiatry, University of Nevada School of Medicine, Mail Stop 354, Reno, NV 89557-0046*; Melissa P. Piasecki, M.D., Ole J. Thienhaus, M.D.

Summary:

Introduction: Methamphetamine abuse and dependence are growing problems nationally and worldwide. There are currently no effective pharmacologic treatments. Animal studies with SSRI's suggest that serotonergic agents alter methamphetamine's subjective effects and decrease self-administration.

Objective: This exploratory study is a trial of the effects of the SSRI paroxetine versus placebo (in a double-blind design) on craving and use in a population of methamphetamine users.

Method: Volunteer outpatient subjects received either paroxetine 20 mg/day or inactive placebo. Subjects were assessed weekly with urine drug tests and the Obsessive Compulsive Drug Scale to measure self-reported craving.

Results: Many subjects dropped out of the study, but those in active treatment who completed the 8-week trial had a decrease in methamphetamine craving compared to the placebo treatment. Only one subject maintained drug abstinence.

Conclusion: The preliminary data suggest a role for serotonergic agents in the treatment of methamphetamine abuse and dependence and recommend further trials of paroxetine in a larger sample. A context of behavioral interventions previously shown to engage and retain individuals in treatment for stimulant dependence would increase subject retention in such trials.

NR115 Monday, May 7, 9:00 a.m.-10:30 a.m.

Dual Diagnosis and Outcome of Adolescents in Substance Abuse Treatment

Brian K. Wise, M.D., *Department of Psychiatry, University of Colorado, 4200 East 9th Avenue, Box C249-51, Denver, CO 80262*; Steven P. Cuffe, M.D.

Summary:

Objective: Examine the prevalence of comorbid psychiatric disorders and factors associated with successful participation of adolescents in a residential substance abuse treatment program.

Method: Retrospective record review of all admissions for a year to a residential adolescent substance abuse treatment program (N = 91). Psychiatric and substance use disorders were diagnosed by DSM-IV criteria.

Results: Successful participation was based on multiple factors assessed by the treatment team. There was considerable comorbidity (63.7%) with both disruptive (ADHD, 11%; conduct disorder, 24%) and other disorders (depression, 24%; adjustment disorder, 7.7%; bipolar disorder, 3.3%). Male gender was negatively associated (OR = 0.23, p=0.019) with successful participation in univariate analyses, as was attention deficit/hyperactivity disorder (ADHD) (OR=0.18, p = 0.007). Conduct disorder (CD) (OR=0.37, p=0.053) approached significance. In the multivariate analysis, having ADHD was significant while having CD and being male approached significance. Psychotropic medication use and other diagnoses were not associated with successful participation.

Conclusion: Consistent with prior studies, a high rate of psychiatric comorbidity with substance use disorders was found. Being male and having ADHD is associated with poor treatment outcome.

NR116 Monday, May 7, 9:00 a.m.-10:30 a.m.

Does Abstinence Improve Hepatitis C?

Denise C. Bridgeford, M.D., *Department of Psychiatry, Denver VAMC, 1055 Clermont Street, 116, Denver, CO 80220*; Diana Bialkowski, R.N., Thomas P. Beresford, M.D.

Summary:

Objective: Recent studies have observed an increased prevalence of HCV infection in chronic alcoholics varying from 15% to over 50%. Evidence suggests that individuals who abuse alcohol have higher titers of HCV RNA. The role of abstinence in improving HCV related liver dysfunction is unclear. We hypothesized that abstinence occasioned by disulfiram use would reduce HCV hepatic injury as measured by ALT.

Methods: We conducted a chart review of 12 HCV+ alcoholic patients who began disulfiram therapy. All patients were middle aged and treated in a substance abuse outpatient program. Baseline ALT levels were compared with the average ALT levels taken on two subsequent assessments during a six-month period after disulfiram initiation.

Results: Analysis revealed that ALT levels following disulfiram initiation decreased significantly (p<0.001) compared with baseline. In most cases, ALT levels dropped into the normal range.

Conclusion: These results suggest disulfiram-aided abstinence lowers ALT in HCV infected patients. If true, disulfiram-aided abstinence may be an indicated treatment in alcoholics infected with HCV.

NR117 Monday, May 7, 9:00 a.m.-10:30 a.m.

Coping Styles and Ethnicity in Substance Abusers

Denise C. Bridgeford, M.D., *Department of Psychiatry, Denver VAMC, 1055 Clermont Street, 116, Denver, CO 80220*; Levester Lyons, M.S.W., Brandon K. Martin, B.A., Thomas P. Beresford, M.D.

Summary:

Objective: Few studies have examined coping mechanisms used by Caucasian alcohol and drug abusers and no studies of defense mechanisms used by racial/ethnic minorities with substance use disorders exist. We hypothesized that types of defenses endorsed on a previously validated scale of defense mechanisms would separate the groups by culture and socialization.

Method: The Defense Style Questionnaire (DSQ) was administered to 23 Caucasian, 29 African-American, and 12 Hispanic substance abuse patients enrolled in a VA treatment program. Subjects included 63 males and one female with an average age of 46.8.

Results: Contrary to our expectation African Americans and Caucasians did not differ on any of the defense subscales. Hispanics endorsed isolation more frequently than A.A. subjects (p<0.02). As compared with Caucasians, Hispanics were more likely to endorse splitting (p<0.03) and passive aggression (p<0.03); they were less likely to endorse anticipation (p<0.03). Length of sobriety did not appear to play a role in the defense mechanism used.

Conclusion: These preliminary pilot data suggest the possibility that culture and socialization may play a role in how individuals cope with stress. Individuals with substance use disorders may benefit from therapeutic programs designed to address their coping style and train them in the use of problem focused coping-strategies.

NR118 Monday, May 7, 9:00 a.m.-10:30 a.m.

Abstinent Chronic Alcoholic Men Are Characterized by Normal Hormonal Measures

Sonia P. Yovtcheva, M.D., *Department of Psychiatry, University of VA/Roanoke-Salem Psych. Program, 1970 Roanoke Boulevard, VAMC, Salem, VA 24153*; Quasir Raza, M.D., Grigor Varlakov, M.D., David B. Trinkle, M.D., Ali Iranmanesh, M.D.

Summary:

Discrepant reports of endocrine and metabolic abnormalities in chronic alcoholism are possibly due to the heterogeneous nature of this disorder, as well as sporadic rather than combined functional evaluation of various endocrine systems in a single study population. To this end, we studied 10 alcoholic men (mean age= 45 years, SD=3) by measuring the height, weight, BP, heart rate (HR), waist (W) and hip (H) circumferences, and skin fold (triceps, scapula) thickness, as well as circulating concentrations of lipids, glucose, insulin, testosterone, E2, FSH, LH, TT4, TSH, leptin, and IL-6. The protocol was conducted in a fasting state and after 4–6 weeks of abstinence from alcohol. The results were compared to 49 age-matched healthy men (mean age=44 years, SD=1.2). Regression analysis revealed a positive correlation between insulin and leptin in healthy subjects (r=0.48; p=0.0005) but not in alcoholic men (r= –0.19; p=0.60). Alcoholic men did not reveal significant differences in the measures of systolic and diastolic blood pressure, lipids, peripheral insulin resistance (HOMA), thyroid and gonadal function tests, or circulating concentrations of DHEAS, E2, and IL-6. All cardiovascular, anthropometric, metabolic, and hormonal values were comparable in a subgroup of eight alcoholic and eight healthy men matched for age and BMI, except for significantly increased serum LH concentrations in alcoholic men (5.8 [SD=0.8] versus 3.6 mIU/ml [SD=0.03]; p=0.03), as well as a trend toward increases in HR (80 [SD=2.6] versus 71 bpm [SD=4]; p=0.08) and decreases in serum concentrations of leptin (4.1 [SD=0.5] versus 6.2 ng/ml [SD=0.9]; p=0.08). We conclude that healthy chronic alcoholics are spared from a number of cardiovascular, metabolic, and hormonal consequences re-

ported in this patient population and that such abnormalities are probably due to concomitant presence of malnutrition and/or alcohol-induced damage to various organ systems, such as the liver. The lower BMI could well be due to a hypermetabolic state, induced by chronic hyperactivity of the adrenergic system, which could in turn explain the relative increases in heart rate as well as the decreased circulating concentrations of leptin and its dissociation with insulin.

NR119 Monday, May 7, 1:00 p.m.-2:30 p.m.

Effects of Supraphysiological Thyroxin on Cerebral Glucose Metabolism in Bipolar Depression: A PET Study

Michael Bauer, M.D., *Department of Psychiatry, UCLA, 300 UCLA Medical Plaza, Suite 2330, Los Angeles, CA 90024*; Edythe London, Ph.D., Steven Berman, Ph.D., Natalie L. Rasgon, M.D., Mark Mandelkern, M.D., Mark A. Frye, M.D., Lori L. Altshuler, M.D.

Educational Objectives:

At the conclusion of this presentation the participant should be able to recognize the use of thyroid hormones as an adjunctive treatment in mood disorders.

Summary:

Objective: Thyroid hormone supplementation as an adjunctive treatment in mood disorders is widely accepted as an effective therapeutic option. In the present open-label study we determined the effects of adjunctive supraphysiological levothyroxine (T_4) on regional cerebral glucose metabolism in six euthyroid women with bipolar depression using positron emission tomography (PET) with [^{18}F]fluorodeoxyglucose (FDG).

Method: Each patient received one PET scan prior to T_4 administration and another after a 7-week course of therapy (mean T_4 dose=333.3, SD=51.6 μg/day). Relative glucose metabolism in individual brain regions selected on the basis of a *priori* hypotheses was calculated from decay-corrected raw counts of radioactivity in 10 bilateral regions using a volume of interest (VOI) approach. A voxel-by-voxel method (Statistical Parametric Mapping, SPM99) was also used.

Results: Hormonal effects of treatment (increase in serum total T_4 and suppression of basal TSH; $p<0.01$) accompanied behavioral and cerebral metabolic effects. The treatment significantly improved mood, as indicated by decreases in mean scores on the HAMD-21 (from 23.0 ± 3.7 to 6.3 ± 2.8) and Beck Depression Inventory (from 39.6 ± 8.9 to 15.5 ± 8.4) ($p<0.001$ for both). In parallel, VOI analysis indicated a relative increase in metabolism in the left middle frontal gyrus and a decrease in the hippocampus ($p<0.05$). SPM99 analysis revealed that the T_4-induced reduction in hippocampal activity was part of a widespread deactivation of limbic and subcortical structures, including the amygdala. Using a $p<0.005$ voxel cutoff, this deactivation was maximal in parahippocampal gyri and thalamus/brainstem.

Conclusion: The findings suggest that T_4 produces improvement in mood by actions on specific limbic/cortical and subcortical circuits that have been implicated in the pathophysiology of mood disorders. Additional studies to elucidate the relationship between changes in the pattern of brain metabolism and response to T_4 are warranted.

References:

1. Bauer M, Hellweg R, Gräf KJ, Baumgartner A: Treatment of refractory depression with high-dose thyroxine. Neuropsychopharmacology 1998; 18:444–455

NR120 Monday, May 7, 1:00 p.m.-2:30 p.m.

Repetitive Transcranial Magnetic Stimulation in Major Depression: Efficacy Depends on Stimulation Intensity

Frank Padberg, M.D., *Department of Psychiatry, University of Munich, Nussbaumstrasse 7, Munich 80336, Germany*; Peter Zwanzger, M.D., Martin E. Keck, M.D., Nicola Toschi, Ph.D., Patrick Mikhaiel, M.D., Heike Thoma, M.D., Rainer Rupprecht, M.D.

Educational Objectives:

To recognize the impact of stimulation intensity on the efficacy of rTMS in major depression.

Summary:

Objective: Repetitive transcranial magnetic stimulation (rTMS) of the prefrontal cortex (PFC) exerts modest to substantial antidepressant effects compared to sham rTMS. Controversy, however, persists concerning effective stimulation parameters (Padberg et al. 1999). In the present controlled study, we asked the question whether therapeutic efficacy may depend on stimulation intensity.

Method: Thirty-one patients suffering from a pharmacotherapy-refractory major depressive episode were randomly assigned to three groups: 1) rTMS at 100% of motor threshold (MT) intensity, 2) rTMS at 90% MT intensity, and 3) rTMS with the coil angled by 90° at 100% MT intensity (usual sham condition). To further characterize stimulation conditions, the respective induced current densities were calculated applying a previously established physical model (Keck et al. 2000). In a double-blind design, patients were rated using the Clinical Global Impression (CGI), the Hamilton Rating Scale for Depression (HRSD), and the Montgomery-Asberg Depression Rating Scale (MADRS).

Results: The antidepressant efficacy linearly increased over all groups with the best response (30% reduction in HRSD score) at 100% MT rTMS. Clinical improvement was correlated with the induced peak current density calculated using the physical model.

Conclusion: The present study provides evidence that the antidepressant efficacy of rTMS is linked to the applied stimulation intensity and supports the notion of a specific rTMS-mediated antidepressant effect.

References:

1. Padberg F, Zwanzger P, Thoma H: Repetitive transcranial magnetic stimulation (rTMS) in pharmacotherapy-refractory major depression: comparative study of fast, slow and sham rTMS. Psychiatry Res 1999; 88:163–171
2. Keck ME, Sillaber I, Ebner K: Acute transcranial magnetic stimulation of frontal brain regions selectively modulates the release of vasopressin, biogenic amines and amino acids in the rat brain. Eur J Neurosci 2000; 12:3713–3720

NR121 Monday, May 7, 1:00 p.m.-2:30 p.m.

Neuroendocrine Effects of Repetitive Transcranial Magnetic Stimulation in Major Depression

Robin Ella, M.D., *Department of Psychiatry, University of Munich, Nussbaumstrasse 7, Munich 80336, Germany*; Frank Padberg, M.D., Peter Zwanzger, M.D., Thomas C. Baghai, M.D., Christo Minov, M.D., Patrick Mikhaiel, M.D., Rainer Rupprecht, M.D.

Educational Objectives:

To recognize the neuroendocrine effects of single and repetitive rTMS.

Summary:

Objective: To evaluate neuroendocrine effects of single and repeated rTMS in depression, the Dex-CRH test and measure-

ments of cortisol, TSH, GH, and prolactin kinetics were carried out in antidepressant-free patients.

Method: Patients suffering from a major depressive episode received rTMS (10 minutes, 10 Hz, left dorsolateral prefrontal cortex, 100 % of motor threshold intensity) and were rated by standard depression scales (HRSD, MADRS). 27 patients underwent Dex-CRH tests before and after rTMS treatment. On day 1 and day 10 cortisol, TSH, GH, and prolactin hormone kinetics were examined in 15 patients during rTMS treatment.

Results: Dex-CRH Test: 11 out of 27 patients responded with a 50 % HRSD reduction. There were no statistically significant changes in the areas under the curves (AUC) either in responders or in nonresponders after rTMS. Kinetics: 10 out of 15 patients responded with a 50 % HRSD reduction. Cortisol levels (AUC) were lower at day 10 compared with day 1. GH levels (AUC) were higher at day 10 than at day 1. Prolactin and TSH concentrations were unchanged. An increase in TSH at day 1 as previously reported (George et al. 1996, Szuba et al. 2000) did not occur.

Conclusion: rTMS exerts effects on GH and cortisol kinetics. However, the Dex-CRH test as the most sensitive parameter for HPA axis activity was unchanged. This underlines the importance of subsequent antidepressant therapy for relapse prevention also in rTMS responders.

References:

1. George MS, Wassermann EM, Williams W: Changes in mood and hormone levels after rapid-rate transcranial magnetic stimulation (rTMS) of the prefrontal cortex. J Neuropsychiatry Clin Neurosci 1996; 8:172–180
2. Szuba MP, O'Reardon JP, Evans DL: Physiological effects of electroconvulsive therapy and transcranial magnetic stimulation in major depression. Depress Anxiety 2000; 12:170–177

NR122 Monday, May 7, 1:00 p.m.-2:30 p.m.

Modulation of Infant Salivary Cortisol by Maternal Depression

Kelley A. Calhoun, B.S., *Department of Psychiatry, Emory University, 1639 Pierce Drive, WMB, Suite 4003, Atlanta, GA 30322*; Patricia Brennan, Ph.D., Elaine F. Walker, Ph.D., Angela D. Fisher, B.S., Zachary N. Stowe, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant will have a better understanding of the impact of maternal depression on infant salivary cortisol.

Summary:

This study assessed the impact of maternal depression in pregnancy and postpartum on infant salivary cortisol changes in response to laboratory stress induction tasks. Participants in this study were 19 6-month-old infants of mothers with a history of major depressive disorder and 11 infants of mothers with no history of axis I disorders. Mothers with a history of major depression were referred from the Emory University Pregnancy and Postpartum Mood Disorders Program. These mothers were followed prospectively on monthly basis using four self-rated scales and two clinician-rated scales. For the current study, mothers were administered the BDI, SCID, FH-RDC, and a stressful life events questionnaire. Infants participated in the following sequence of laboratory tasks: baseline rest period, habituation task, sound burst exposure, arm restraint task, videotaped mother-child interaction task, and neurological screen. Infant saliva was collected six times throughout the tasks. There was no difference in baseline cortisol between the two groups. Infants of mothers with a history of depression demonstrated hyperresponsivity to stress as demonstrated by infant salivary cortisol (p=0.002). Remarkably, these data parallel laboratory findings on maternal separation. The reactivity of the infant HPA axis may be predetermined by prenatal maternal stress.

References:

1. Plotsky PM, Meaney MJ: Early postnatal experience alters hypothalamic corticotrophin-releasing factor (CRF) MRNA, median eminence CRF content and stress-induced release in adult rats. Molecular Brain Research 1993; 18:195–200
2. Taylor A, Littlewood J, Adams D, Dore C, Glover V: Serum cortisol levels are released to moods of elation and dysphoria in new mothers. Psychiatry Research 1994; 54:241–274

NR123 Monday, May 7, 1:00 p.m.-2:30 p.m.

Brain MRI White Matter Hyperintensities and Treatment Outcome in Depression

Dan V. Iosifescu, M.D., *Department of Psychiatry, Massachussetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114*; Nicole B. Neault, B.A., Joyce R. Tedlow, M.D., Lindsay M. Dececco, B.A., Maurizio Fava, M.D., Amy H. Farabaugh, M.A., Perry F. Renshaw, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should understand the prevalence and the significance of brain MRI T2 white matter hyperintensities (correlated by many authors with brain vascular pathology) in subjects with major depression.

Summary:

Objective: We investigated the relationship between brain MRI T2 white matter hyperintensities (WMH) in subjects with depression and the outcome of antidepressant treatment.

Method: A total of 76 outpatients (40.8% women) meeting DSM-IV criteria for major depression were administered brain magnetic resonance images (MRI) scans to detect T2 WMH. The mean age was 40.5, SD=10.4. We measured brain WMH in all subjects with the Fazekas classification system. Fifty-eight depressed subjects completed an eight-week open treatment with fluoxetine 20 mg/day. The 17-item Hamilton Rating Scale for Depression (HamD-17) was administered at baseline and every two weeks for the remaining eight weeks during the study to assess the clinical response to antidepressant treatment.

Results: The presence of WMH in the brain MRIs of depressed subjects did not correlate significantly with the degree of clinical improvement following antidepressant treatment and did not differ between responders and non responders, even after adjusting for age and gender.

Conclusion: The presence of brain MRI T2 white matter hyperintensities (WMH) does not appear to have an impact on the patients' chance of responding to antidepressant treatment. Our findings challenge the concept of "vascular depression," defined by increased brain WMH, as a separate clinical entity with a different clinical course and raise questions about the significance of WMH in depressed subjects.

References:

1. Hickie I, Scott E, Mitchell P, Wilhelm K, et al: Subcortical hyperintensities on magnetic resonance imaging: clinical correlates and prognostic significance in patients with severe depression. Biol Psychiatry 1995; 37(3):151–60
2. Krishnan KR, Hays JC, Blazer DG: MRI-defined vascular depression. Am J Psychiatry 1997; 154(4):497–501

NR124 Monday, May 7, 1:00 p.m.-2:30 p.m.

Prevalence of BDD in Psychiatric Inpatients

Jon E. Grant, M.D., *Department of Psychiatry, University of Minnesota, 2450 Riverside Avenue, Minneapolis, MN 55454-1495*; Suck Won Kim, M.D., Scott J. Crow, M.D.

Educational Objectives:

Recognize the need to screen for body dysmorphic disorder in psychiatric inpatients and to understand that recognition of the disorder may have treatment implications.

Summary:

Objective: Body dysmorphic disorder (BDD), a distressing and impairing preoccupation with an imagined or slight defect in appearance, is a relatively common yet underrecognized psychiatric disorder. BDD is associated with high rates of functional impairment and suicide attempts. The prevalence of BDD and its associated clinical features have received little investigation.

Method: 101 consecutive adult patients and 21 consecutive adolescent patients presenting for psychiatric inpatient admission to a university teaching hospital participated in the study. Subjects completed the Body Dysmorphic Disorder Questionnaire (BDDQ), a brief self-report measure that screens for BDD. For patients who screened positive for BDD on the BDDQ, a follow-up interview was conducted using a reliable clinical-administered semistructured diagnostic instrument for DSM-IV BDD.

Results: Sixteen (13.1%) of the 122 subjects who consented to the study were diagnosed with BDD (14.3% of adolescents; 12.9% of adults). None of the subjects with BDD had been diagnosed by their treating physician during hospitalization. All 16 subjects reported that they would not raise the issue with their physician unless specifically asked because of feelings of shame.

Conclusion: BDD appears to be a relatively common but underdiagnosed comorbid psychiatric disorder. As we had anticipated, no patients were screened for or diagnosed with BDD during inpatient hospitalization.

References:

1. Phillips KA: Body dysmorphic disorder: the distress of imagined ugliness. Am J Psychiatry 1991; 148:1138–1149
2. Phillips KA, Nierberg AA, Brendel G, et al: Prevalence and clinical features of body dysmorphic disorder in atypical major depression. J Nerv Ment Dis 1996; 184:125–129

NR125 Monday, May 7, 1:00 p.m.-2:30 p.m.

Quality of Medical Care and Excess Mortality in Patients with Mental Disorders

Benjamin G. Druss, M.D., *Department of Psychiatry, Yale University, 950 Campbell Avenue, 182, West Haven, CT 06516*; David Bradford, Ph.D., Martha J. Radford, M.D., Robert A. Rosenheck, M.D., Harlan M. Krumholz, M.D.

Educational Objectives:

Understand the potential impact of poor medical care on excess mortality in patients with mental disorders.

Summary:

Background: This study investigated whether differences in quality of medical care might explain a portion of the excess mortality associated with mental disorders in the year after myocardial infarction.

Methods: The authors examined a national cohort of 88,241 Medicare patients aged 65 years and older who were hospitalized for clinically confirmed acute myocardial infarction. Proportional hazard models compared the association between mental disorders and mortality before and after adjusting five established quality indicators-reperfusion, aspirin, beta blockers, ACE Inhibitors, and smoking cessation counseling. All models adjusted for eligibility for each procedure, demographic characteristics, cardiac risk factors and history, admission characteristics, left ventricular function, hospital characteristics, and regional factors.

Results: After adjusting for the potential confounders, presence of any mental disorder was associated with a 19% increase in 1-year risk of mortality (Hazard Ratio=1.19 [95% CI=1.04–1.36]). After adding the five quality measures to the model, the association was no longer significant (Hazard Ratio=1.10, (95% CI=0.96–1.26]).

Conclusions: Deficits in quality of medical care appeared to explain a substantial portion of the excess mortality experienced by patients with mental disorders after myocardial infarction. The study suggests the potential importance of improving these patients' medical care as a step towards reducing their excess mortality.

References:

1. Frasure-Smith N, Lesperance F, Talajic M: Depression following myocardial infarction: impact on 6-month survival. JAMA 1993; 270(15):1819–1825
2. Druss BG, Bradford DW, Rosenheck RA, Radford M, Krumholz H: Mental disorders and use of cardiovascular procedures after myocardial infarction. JAMA 2000; 283(4):506–511

NR126 Monday, May 7, 1:00 p.m.-2:30 p.m.

fMRI Correlates of Gambling Urges

Marc N. Potenza, M.D., *Department of Psychiatry, Yale University, CMHC, 34 Park Street, New Haven, CT 06519*; Marvin A. Steinberg, Ph.D., Cheryl M. Lacadie, B.S., Robert K. Fulbright, M.D., Bruce J. Rounsaville, M.D., John C. Gore, Ph.D., Bruce E. Wexler, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should recognize that pathological gambling and cocaine dependence likely involve similar neurobiologies. This information will help guide research and treatment strategies for individuals with pathological gambling.

Summary:

Background: Previously we identified regional brain activities in response to cocaine-related videotapes in subjects with and without cocaine dependence (CD). We hypothesized gambling urges in pathological gambling (PG) represent an intense emotional/motivational state similar to cocaine cravings in CD and thus involve similar neural pathways.

Methods: We used fMRI to examine regional brain activities in healthy and PG subjects viewing videotaped scenarios designed to elicit extreme motivational (gambling urges) or emotional (happy, sad) states.

Results: Initial findings indicate that in response to the gambling scenarios, healthy subjects rarely report an urge to gamble, generally describe emotional responses (pity, disgust), and display neural activation patterns similar to those displayed by healthy subjects viewing cocaine-related scenarios. In contrast, PG subjects generally report a robust response, most often an urge to gamble, and show brain activations in regions implicated in drug craving responses; e.g., anterior cingulate (AC). AC activation was found to be specific to PG subjects viewing the gambling scenarios and CD subjects viewing the cocaine scenarios.

Conclusions: These findings suggest that gambling urges in PG and cocaine cravings in CD share similar neural contributions.

Support: APA, NARSAD, NIMH, NIDA, & VA MIRECC.

References:

1. Potenza MN. The neurobiology of pathological gambling. Sem Clin Neuropsychiatry, in press
2. Wexler BE, Gottschalk CH, Fulbright RF, Prohovnik I, et al: fMRI of cocaine craving. Am J Psychiatry, in press

NR127 Monday, May 7, 1:00 p.m.-2:30 p.m.

Cognitive-Behavior Therapy for Tinnitus

Shannon K. Robinson, M.D., *Department of Psychiatry, University of California at San Diego, 200 West Arbor, Mail Code 8620, San Diego, CA 92103-8620*; John R. McQuaid, Ph.D., Philippe R. Goldin, M.S.

Educational Objectives:

To describe a cognitive behavioral intervention for the treatment of tinnitus and report on the efficacy of a brief group intervention.

Summary:

Objective: There is evidence that the level of distress and disability caused by tinnitus stems from attention focused on the perceived noise. This project tested whether training in specific skills of distraction, activity planning, and changing unhelpful thinking leads to decreases in distress and impairment.

Methods: Participants were randomly assigned to receive 8 weeks of manualized cognitive behavior therapy either immediately or after an 8-week waiting period. The current report describes the analysis of pre- to posttreatment improvement of all 33 participants who completed treatment, regardless of initial assignment. Participants were assessed on measures of tinnitus-related distress, depression, and internal focus. All measures were assessed pre- and posttreatment.

Results: Repeated measures ANOVA revealed that participants significantly improved on one measure of tinnitus-related distress (the Tinnitus Handicap Inventory: $F=7.8$, $p<0.05$), two measures of depression (Hamilton Rating Scale for Depression: $F=4.8$, $p<0.05$; Beck Depression Inventory: $F=8.3$, $p<0.01$), and one measure of internal focus ($F=7.3$, $p<0.05$). In addition, there were trends toward improvement on several other measures of tinnitus-related distress.

Conclusion: These findings suggest that CBT may reduce the negative impact of tinnitus on functioning and distress. We would like to thank the American Tinnitus Association for their support of this study.

References:

1. Newman CW, Wharton JA, Jacobson GB: Self focused and somatic attention in patients with tinnitus. Journal of American Academy of Audiology 1997; 8:143–149
2. Wilson PH, Henry JL: Psychological approaches in the management of tinnitus. Australian Journal of Otolaryngology 1993; 1:296–302

NR128 Monday, May 7, 1:00 p.m.-2:30 p.m.

Newly Admitted Psychiatric Patient Prescriptions and Pharmaceutical Sales Visits

Daniel J. Kuhles II, M.D., *Department of Psychiatry, SUNY UMU, 99 Wall Street, #1 South, Huntington, NY 11743*; Thomas L. Schwartz, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the relationship between pharmaceutical sales visits and prescription changes in psychiatric residency outpatient sector.

Summary:

There is much literature regarding the interaction of pharmaceutical sales representatives with physicians. However, there is little information available regarding their interactions with psychiatric residents. This paper attempts to quantify the impact of pharmaceutical sales visits upon prescriptions written for newly admitted patients in a psychiatric residency training clinic. A retrospective chart review of 47 consecutive patients was conducted. At the time of review all patients had been admitted to the clinic for less than 3 months. Their psychiatric medication regimens were followed for 3 months. Initiation of new psychotropic medications was recorded. Data were also collected regarding the number of sales visits for resident luncheons during the review's time period. Statistical analyses compared the number of new medication starts to the number of sales visits. Twelve pharmaceutical companies made sales visits. Eleven out of 12 company visits were statistically associated with an increase in new medication starts ($p<0.05$). As the number of sales visits increased, a greater statistical significance ($p<0.001$) was noted for seven out of 11 companies. This study is one of the first to quantify pharmaceutical industry's impact on psychiatric residents' prescribing practices. It appears that psychiatric residents start prescribing companies medications shortly after sales visits. Furthermore, as sales visits increase in frequency, more of their medications may be started in newly admitted psychiatric outpatients.

References:

1. Springarn RW, Berlin JA, Strom BL: When pharmaceutical manufacturers' employees present grand rounds, what do residents remember? Academic Medicine 1996; 71(1):86–88
2. Lurie N, Rich EC, Meyer J, Schiedermayer DL, Goodman JL, McKinney WP: Pharmaceutical representatives in academic medical centers: interaction with faculty and housestaff. JI of Gen Int Med 1990; 5:240–243

NR129 Monday, May 7, 1:00 p.m.-2:30 p.m.

Executive Function in Remitted Bipolar and Schizophrenic Patients and Its Relationship to Functional Outcome

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Educational Objectives:

At the conclusion of this presentation, the participant should be able to understand the neuropsychological differences between bipolar and schizophrenic patients and the weight of clinical and neuropsychological variables with respect to psychosocial functioning in these groups.

Summary:

Objective: Recent studies have reported that differences in cognitive performance between schizophrenic and bipolar patients seem to be narrower than expected. Patients with schizophrenia have consistently shown frontal executive dysfunctions, but studies regarding executive abilities in bipolar patients are scarce and discrepant. As executive function has been associated with psychosocial functioning in schizophrenia, we wanted to investigate if such a relationship is also present in bipolar disorder and the differences between the two groups.

Method: Executive function was assessed in 49 euthymic (at least 6 months in remission, HDRS≤8, and YMRS≤6) bipolar and in 49 schizophrenic, residual type (with at least 1 year without acute exacerbation and predominant negative symptomatology) patients, through WCST, FAS (COWAT), and Trail Making Test. Baseline clinical and psychosocial variables were controlled and psychopathology evaluated by means of the PANSS.

Results: The two groups showed a similar pattern of cognitive deficits in tests of executive function, except for the number of categories achieved in the WCST, which was significantly lower in the schizophrenic group ($F=7.26$; $p=0.009$). Functional outcome was predicted by the negative syndrome (PANSSN) and perseverative errors (WCST) in schizophrenic patients, and general psy-

chopathology (PANSSG) was the best predictor of functional outcome in bipolar group.

Conclusions: Executive function was a good predictor of functional outcome in the schizophrenic group, whereas clinical variables were more predictive for the bipolar one. Patterns of cognitive disturbances in tasks of executive function are similar in both groups but quantitatively more marked in schizophrenia.

References:

1. Zihl J, Grön G, Brunnauer A: Cognitive deficits in schizophrenia and affective disorders: evidence for a final common pathway disorder. Acta Psychiatr Scand 1998; 97:351–357
2. Martínez-Arán A, Vieta E, Colom F, Reinares M, Benabarre A, Gastó C, Salamero M.: Cognitive dysfunctions in bipolar disorder: evidence of neuropsychological disturbances. Psychother Psychosom 2000; 69:2–18

NR130 Monday, May 7, 1:00 p.m.-2:30 p.m.

Exposure to Antidepressant Medications in Pregnancy and Obstetric Outcome

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Educational Objectives:

At the conclusion of this presentation, the participant will have a better understanding of the impact of exposure to antidepressants during pregnancy on obstetric outcomes. The participant will also be able to implement this knowledge in devising a risk/benefit assessment in treating depressed pregnant women.

Summary:

Background: Psychotropic treatment poses a serious challenge in treating depressed pregnant women. Previous reports on the impact of antidepressant exposure on the fetus have failed to control for all potential confounders.

Objective: To examine the impact of various antidepressants on obstetric outcome after controlling for multiple confounders.

Design: A retrospective database review of 254 pregnant women referred to the Emory University Pregnancy and Postpartum Mood Disorders Program. Inclusion criteria included: 1) primary diagnosis of unipolar depression; 2) confirmed compliance with the treatment plan; 3) no history of substance abuse in the past year; and 4) complete obstetric data. Subjects were divided into two groups, exposed and non-exposed. Outcome variables included birth weights, APGAR scores, gestational age at delivery, and obstetric complications.

Results: A sociodemographically homogenous group of 95 subjects was included in this analysis. A multivariate analysis studied the effects of exposure to antidepressants during each trimester on outcome variables. We accounted for such potential confounders as exposure to nonpsychotropic (including over-the-counter) medications, herbal remedies, alcohol, tobacco, and severity of depression. There were no significant differences in obstetric outcomes between non-medicated and medicated groups in each trimester ($p>0.10$). Also, there were no significant differences among the various types of antidepressants utilized with respect to obstetric outcomes ($p>0.10$).

Conclusions: In a very homogenous sample, our study failed to document any adverse impact of exposure to antidepressants, at any time during pregnancy, on obstetric outcome. Further studies are needed to delineate the impact, if any, of intra-uterine exposure to antidepressants on the development of the fetal central nervous system.

References:

1. Pastuszak A, Schick-Baschetto B, Zuber C, Feldkamp M, Pinelli M, Sihn S, Donnenfeld A, McCormack M, Leen-Mitchell M, Woodland C, Gardner A, Hom M, Gideon K: Pregnancy outcome following first-trimester exposure to fluoxetine (prozac). JAMA 1993; 269:2246–2248
2. Chambers CD, Johnson KA, Dick LM, Felix RJ, Jones KL: Birth outcomes in pregnant women taking fluoxetine. N Engl J Med 1996; 335:1010–1015

NR131 Monday, May 7, 1:00 p.m.-2:30 p.m.

H-MRS Imaging of the Caudate Nucleus in the Treatment of Naive Pediatric MDD

Tiffany R. Farchione, *Department of Psychiatry, Wayne State University, 4201 St. Antoine Boulevard, 9B-UHC, Detroit, MI 48201*; Gregory J. Moore, Ph.D., Rachel Madden, B.A., Marla Bartoi, Ph.D., Elisa R. Lorch, M.A., Carol M. Stewart, R.N.C., David R. Rosenberg, M.D.

Educational Objectives:

At the conclusion of this presentation, the participant should be able to demonstrate an understanding of the role of the caudate nucleus in pediatric major depressive disorder, and recognize the potential role of N-acetyl aspartate in the pathogenesis of MDD.

Summary:

Introduction: Neurobiological abnormalities in the caudate nucleus are believed to be involved in the pathophysiology of major depressive disorder (MDD). Although MDD commonly arises during childhood and adolescence, no prior study has examined the caudate nucleus in pediatric MDD.

Methods: In this study, N-acetyl-aspartate (NAA), a putative marker of neuronal viability was measured in the left and right caudate nuclei using a multislice proton magnetic resonance spectroscopic imaging sequence in 13 treatment-naive MDD patients, 9–17 years of age, and 13 case-matched, healthy control subjects. Right and left caudate volumes were also measured.

Results: A significant reduction in NAA was observed in both the right (21%) and left (18%) caudate nucleus in MDD patients compared with control subjects. Right and left caudate volumes did not differ significantly between MDD patients and controls.

Discussion: These preliminary findings suggest decreased neuronal density within the caudate nucleus in pediatric MDD that may not be readily detected with the use of conventional imaging techniques (e.g., structural/volumetric magnetic resonance imaging studies).

References:

1. Steffens DC, Krishnan KRR: Structural neuroimaging and mood disorders: recent findings, implications for classification, and future directions. Biol Psychiatry 1998; 43:705–712
2. Soares JC, Mann JJ: The anatomy of mood disorders—review of structural neuroimaging studies. Biol Psychiatry 1997; 41:86–106

NR132 Monday, May 7, 1:00 p.m.-2:30 p.m.

Mitochondrial Enzymes in Schizophrenia

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Educational Objectives:

These results suggest that in schizophrenia, unlike several other neurodegenerative diseases, reductions in the activities of the key mitochondrial enzymes KGDHC and PDHC are not frequent.

Summary:

Brain metabolism and blood flow are altered in the dorsolateral prefrontal cortex (DLPFC) of patients with schizophrenia. Mitochondria are central in the regulation of brain metabolism and blood flow. Two key mitochondrial enzymes [the α-ketoglutarate dehydrogenase complex (KGDHC) and the pyruvate dehydrogenase complex (PDHC)] are reduced in several neurodegenerative diseases including Alzheimer disease. Thus, we tested whether reductions in these enzymes could underlie the changes in schizophrenia. Assays were performed on DLPFC from patients with schizophrenia (N=27) and normal non-psychiatric control subjects (N=12). KGDHC activities (mU/mg protein; mean ± SEM) in the control (3.03±0.41) and in the schizophrenic group (3.28±0.39) were similar. PDHC activity in the control (23.11±3.47) and the schizophrenic group (24.19±319) did not differ. Separate analyses of the patients matched for age (10:10) or postmortem interval (10:10) gave similar conclusions. A cognitive dementia rating was poorly correlated with activities of KGDHC (r=0.02, p=0.90) or PDHC (r=–0.27, p=0.10). These results suggest that in schizophrenia, unlike several other neurodegenerative diseases, reductions in the activities of the key mitochondrial enzymes KGDHC and PDHC are not frequent.

Supported by grants NIA-AG14930 (JPB, GEG), NIA-AG19589 (GEG), by Merit Review and MIRECC (VH) (Department Veterans Affairs) and NIMH-MH45212 (KLD).

References:

1. Holcomb HH, Lahti AC, Medoff DR, Weiler M, Dannals RF, Tamminga CA: Brain activation patterns in schizophrenic and comparison volunteers during a matched-performance auditory recognition task. Am J Psychiatry 2000; 157:1634–1645
2. Gibson GE, Park LCH, Sheu KR, Blass JP, Calingasan NY: The α-ketoglutarate dehydrogenase complex in neurodegeneration: Neurochemistry International 2000; 36:97–112

NR133 Monday, May 7, 1:00 p.m.-2:30 p.m.

Increased Plasma Interleukin-12 Concentrations in Schizophrenia and Major Depression But Not in Mania

Yong-Ku Kim, M.D., *Department of Psychiatry, Korea University-Ansan Hospital, 516, Go-Jan Dong, Ansan 425-020, Korea*

Summary:

Objectives: It has been postulated that cytokine dysregulation may be involved in the pathogenesis of psychiatric diseases. IL-12 is known to play a key role in promoting T helper 1 responses and subsequent cell-mediated immunity. We investigated the plasma IL-12 levels among patients with schizophrenia, major depression, and mania.

Methods: Thirty-five schizophrenia, 26 major depression, and 18 bipolar manic patients who fulfilled DSM-IV criteria and the same number of age-, sex-, and body mass index-matched normal control subjects were recruited. The severity of symptoms were measured with the BPRS, HDRS, and YMRS, respectively. The plasma concentrations of IL-12 were measured by a quantitative sandwich ELISA technique using available kits (Quantikine; R&D systems). The IL-12 and psychopathology were measured during acute states of illness and after 8 weeks of treatment with antipsychotics or antidepressants.

Results: The plasma IL-12 levels were elevated in the patients with schizophrenia (p=0.01) and major depression (p=0.04) but not in the patients with mania. After treatment, the IL-12 levels were significantly decreased in schizophrenia (p=0.03) and major depression (p=0.05). Furthermore, the changes of IL-12 levels were significantly correlated to those of each psychopathology in each illness. No significant correlations between IL-2 level and age, duration of illness, and subtypes were found.

Conclusions: The findings support the hypothesis that the immune activation may be associated with the pathophysiology in some groups of schizophrenic and major depression patients.

References:

1. Kim YK, Lee MS, Suh KY: Decreased interleukin-2 production in Korean schizophrenic patients. Biol Psychiatry 1998; 43:701–704
2. Kim YK, Kim L, Lee MS: Relationship between interleukins, neurotransmitters and psychopathology in drug-free male schizophrenics. Schizophr Res 2000; 44:165–175

NR134 Monday, May 7, 3:00 p.m.-5:00 p.m.

Enhanced Informed Consent for Research in Older Patients with Psychotic Disorders

Laura B. Dunn, M.D., *Department of Psychiatry, University of California at San Diego, 9500 Gilman Drive, 0603-R, La Jolla, CA 92093-0603*; Laurie A. Lindamer, Ph.D., Lawrence J. Schneiderman, M.D., Dilip V. Jeste, M.D.

Summary:

Objective: Ensuring that participants provide valid informed consent is a prerequisite for ethical research; understanding of relevant information is one fundamental component of informed consent. We examined whether an educationally enhanced presentation improved understanding of research consent in middle-aged and older patients with chronic psychotic disorders.

Method: Subjects included 78 patients over 40 years old, a majority of whom met DSM-IV criteria for schizophrenia or schizoaffective disorder and who were enrolling in an Intervention Research Center, and 19 normal comparison subjects (NCs). Participants were randomly assigned to receive routine or enhanced (PowerPoint® slideshow incorporating reviews and summaries) versions of consent procedures. A 20-item post-test assessed understanding of key elements of consent.

Results: Patients receiving enhanced consent presentations scored significantly higher on Trial 1 of the post-test compared to patients who received a routine consent presentation. On both Trials 1 and 2, patients who received enhanced consent presentations scored as well as NCs who received a routine consent presentation. A greater proportion of patients who received enhanced consent presentations scored 100% on Trials 1 and 2, compared to those receiving the routine version (Trial 1: 36% versus 13%, p=0.017; Trial 2: 82% versus 60%, p=0.039).

Conclusions: In this randomized study comparing routine and enhanced consent presentations in psychiatric patients as well as NCs, patients' understanding of the research protocol was improved with the enhanced version of the informed consent procedures.

NR135 Monday, May 7, 3:00 p.m.-5:00 p.m.

Does Maternal Depression Alter the Neurohormonal Environment of Pregnancy?

Claudia L. Baugh, B.A., *Department of Psychiatry, Emory University, 1639 Pierce Drive, Suite 4003, Atlanta, GA 30322*; Kelley A. Calhoun, B.S., Donald J. Newport, M.D., Kevan Sternberg, B.S., Zachary N. Stowe, M.D.

Summary:

The neuroendocrinological alterations associated with major depression have undergone considerable scrutiny. The impact of major depression and such neuroendocrine alterations on the neurohormonal environment of pregnancy have not been studied. Pregnant women with a history of major depression (n=124) were

followed prospectively throughout pregnancy at monthly intervals. The population was specifically selected for demographic homogeneity (e.g. Caucasian, 100% married, >12 years education, standard prenatal care, all with histories of major depression, no substance abuse within 12 months) thereby limiting psychosocial confounds. Serum was collected cross-sectionally at the initial nonmedicated visit for FSH, LH, progesterone, estradiol, cortisol, TSH, and thyroxine. No significant differences in the mean values of these measures were found between the symptomatic and euthymic group. In women with moderate to severe major depression (BDI>18), analysis by trimester demonstrated nonsignificant increases in the mean serum cortisol in first trimester (+28.5 ng/ml) and second trimester (+33.5 ng/ml), with a decreased cortisol (−24.3 ng/ml) in trimester 3. Additional alterations were found in serum prolactin, estradiol, and progesterone. A consistent pattern of alterations across all three trimesters was not found. In a subset of women (n=19), who declined treatment with antidepressants and underwent serum monitoring monthly from 12 weeks gestation through delivery, serum prolactin was nonsignificantly elevated in symptomatic women (BDI>9) compared with euthymic women in each trimester. The remaining hormonal analyses are pending. These data suggest that untreated depression may alter the neurohormonal profile of pregnancy, and potentially the biochemical environment for the developing fetus.

NR136 Monday, May 7, 3:00 p.m.-5:00 p.m.

SSRI Augmentation with Raloxifene for Treatment-Resistant Depression

Sophie Grigoriadis, M.D., *Department of Psychiatry, CAMH Clarke Division, 250 College Street, Toronto, ON M5T 1R8, Canada*; Sidney H. Kennedy, M.D., Janaki Srinivasan, M.D., Kari Fulton, B.A.

Summary:

Objective: Estrogen may augment SSRI clinical response in postmenopausal women with treatment-resistant major depression (TRMD). Raloxifene, a selective estrogen receptor modulator (SERM) with both estrogen agonist and antagonist activity, has postulated CNS activity although data on its effects in depression do not exist. Can raloxifene augment antidepressant effect in TRMD?

Method: As part of an exploratory pilot project, 20 postmenopausal women will be recruited from the depression clinic at CAMH with TRMD. Subjects will be randomly assigned to receive raloxifene (eight weeks) or placebo for four weeks, then raloxifene for four weeks, and will continue with concurrent use of their SSRI. Measures of baseline and weekly HAM-D scores, antidepressant, and raloxifene side effects scores will be collected.

Results: Preliminary analyses of three women showed they improved and two showed statistically significant change from baseline with HAM-D scores below 15 by the end of the trial. There were no significant treatment-emergent side effects with the combination of raloxifene and SSRI.

Conclusions: Raloxifene may be an effective adjunct for treatment-resistant major depression in combination with a SSRI. Raloxifene provides an opportunity to explore the beneficial effects of estrogen without the potential side effects. A larger trial is warranted.

NR137 Monday, May 7, 3:00 p.m.-5:00 p.m.

Fetal CNS Exposure After Maternal SSRI: A Rodent Model

Angela D. Fisher, B.S., *Department of Psychiatry, Emory University, 1639 Pierce Drive, Suite 4003, Atlanta, GA 30322*; Jessica S. Brown, B.A., Donald J. Newport, M.D., Michael J. Owens, Ph.D., James C. Ritchie, Ph.D., Zachary N. Stowe, M.D.

Summary:

The risk/benefit assessment remains central to the clinical treatment of women during pregnancy and lactation. This study aims to quantify the fetal central nervous system exposure, neonatal clearance following delivery, and the amount of medication in the neonatal CNS associated with breast feeding. Using osmotic minipumps, pregnant rodents were treated with antidepressants. Rodents underwent either cesarean section or natural delivery. Pup blood, brain, umbilical cord blood, and amniotic fluid were collected for analysis of medication concentration during cesarean section. Naturally delivered pups were sacrificed at seven, 14, and 21 days old. To assess breast feeding exposure, a minipump was implanted after delivery and the nursing pups were then sacrificed at seven, 14, and 21 days of life.

Results: Pregnancy phase - six dams (60 pups); Neonatal Clearance phase - three dams (30 pups); Breast Feeding phase - one dam (six pups). The average pup brain concentrations were: 790.1±237.6 ng/mg (fluoxetine, 71.1±27.8% of maternal brain), 3669.6±1006.0 ng/mg (norfluoxetine), 621.4±376.9 ng/mg (sertraline, 45±26.9% of maternal brain), and 2713.7±896.5 ng/mg (desmethylsertraline), which were much higher than expected. The remaining analyses are pending. These preliminary data suggest that use during pregnancy results in fetal exposure that is essentially a therapeutic dose, which is a factor that should be considered in the clinical decision about antidepressant use during pregnancy.

NR138 Monday, May 7, 3:00 p.m.-5:00 p.m.

Medication Use in Pregnant Women with Major Depression

Angela F. Arnold, M.D., *Department of Psychiatry, Emory University, 1639 Pierce Drive, Suite 4003, Atlanta, GA 30322*; Angela D. Fisher, B.S., Jessica S. Brown, B.A., Claudia L. Baugh, B.A., Kelley A. Calhoun, B.S., Zachary N. Stowe, M.D.

Summary:

Do women take both prescription and over-the-counter medications during pregnancy? An international study of 14,778 pregnant women found that 86% of women took medications during pregnancy, averaging 2.9 prescriptions each. Studies suggest that the use of both prescription and non-prescription medication during pregnancy is mediated by factors such as race, age, marital status, and level of education. We hypothesize that a contributing factor may be psychiatric symptoms. A group of 156 women with a history of major depression was prospectively followed throughout pregnancy. Beck Depression Inventory (BDI) scores and medication use were documented at monthly visits. Medication exposure included all over-the-counter (OTC) preparations and prescriptions medications. Women in our study took an average of 2.7 medications over the course of pregnancy. Preliminary analyses indicate that pregnant women with a history of depression who were symptomatic continued to use tobacco and alcohol during pregnancy compared with euthymic patients (p=0.023). In contrast, no significant differences were found for OTC remedies and nonpsychiatric prescription medications. These data extend previous work documenting increased drug, alcohol, and tobacco use associated with depressive symptoms by controlling for a history of depression. The rate of OTC and prescription medication use is comparable with larger epidemiological studies.

NR139 Monday, May 7, 3:00 p.m.-5:00 p.m.

Antidepressants in Amniotic Fluid: Another Route of Fetal Exposure

Jessica S. Brown, B.A., *Department of Psychiatry, Emory University, 1639 Pierce Drive, Suite 4003, Atlanta, GA 30322*; Angela D. Fisher, B.S., James C. Ritchie, Ph.D., Amy L. Hostetter, B.A., Zachary N. Stowe, M.D.

Summary:

The use of antidepressants during pregnancy has undergone considerable scrutiny in the past 5 years. Despite the increased data, the various pathways by which the fetus may be exposed to antidepressants has not been clearly delineated. In early pregnancy, amniotic fluid is predominantly an ultrafiltrate of maternal serum. However, in later pregnancy the major source is from fetal urine. The fetus is bathed continuously in amniotic fluid, therefore any substance in the fluid will be swallowed, inhaled, and potentially absorbed throughout pregnancy. The present study is a naturalistic study of amniotic fluid concentrations of antidepressants in women undergoing amniocentesis for obstetrical reasons (uniformly advanced maternal age in the present sample). A total of seven samples were obtained from women on a stable dose of an antidepressant for greater than 4 weeks. Maternal serum was collected at the same time or within 1 week of amniocentesis for five of these subjects. All analysis was conducted using HPLC with UV detection. The following samples have been collected: fluoxetine (N=3), fluvoxamine (N=1), paroxetine (N=2), sertraline (N=1), and venlafaxine (N=1). Thus far all antidepressants and their metabolites were detectable in amniotic fluid. Samples run to date showed the following concentrations in amniotic fluid: fluoxetine 48 ng/ml (and norfluoxetine 16 ng/ml), fluvoxamine 4 ng/ml, and sertraline 2 ng/ml (and desmethylsertraline 19 ng/ml). These preliminary data confirm our assumption that the fetus remains exposed through several pathways potentially resulting in greater CNS exposure.

NR140 Monday, May 7, 3:00 p.m.-5:00 p.m.

Depression in Primary Care: Effects of Stigma Concerns

Carol A. Roeloffs, M.D., *Department of Psychiatry, UCLA-NPI, 10920 Wilshire Boulevard, Suite 300, Los Angeles, CA 90024*; Cathy S. Sherbourne, Ph.D., Jurgen Unutzer, M.D., Kenneth B. Wells, M.D.

Summary:

Objectives: (1) To examine expectations of depressed patients about the effect of disclosing a history of depression. (2) To compare these to concerns about medical conditions. (3) To characterize individuals with stigma concerns. (4) To determine if stigma concerns were associated with outcomes, use of or unmet need for mental health care.

Methods: Cross-sectional survey of 1,187 depressed patients from managed, primary care clinics throughout the country.

Results: 77% anticipated negative consequences of disclosing depression for gaining employment, 72% for obtaining health insurance, and 30% for maintaining friendships. Stigma concerns associated with depression were higher than for hypertension or diabetes, but less for HIV. Individuals with concerns about stigma affecting employment or friendships were more likely to report unmet need for mental health services than those without concerns. Stigma concerns were not related to decreased service use or poor depressive outcomes.

Conclusions: Depressed primary care patients have substantial stigma concerns related to disclosing a history of depression. Patients with such concerns perceived more unmet need for mental health care but were not different in mental health service use or depression outcomes. Further research is needed to understand the effects of stigma in primary care and other patient populations.

NR141 Monday, May 7, 3:00 p.m.-5:00 p.m.

Gender in Differential Housing: Stress, Immunity, and Behavior in Psychosocial Context

Gretchen L. Hermes, *Institute for Mind and Biology, University of Chicago, 940 East 57th Street, Chicago, IL 60637*; Martha K. McClintock, Ph.D.

Summary:

Over a period of years, several findings in our lab indicated pathological effects associated with long-term individual housing of female Sprague-Dawley rats. Susceptibility to airborne disease, non-normal ovarian cycling, and blunted affect substantiated hypotheses that individual housing created unique pathological risk for females while non-crowded, group-housed females lived substantially longer, healthier lives. Recently, we broadened the scope of our protocols to include the biobehavioral impact of differential housing on males of the species. These experiments represent an attempt to pinpoint how and to what degree differential housing affects biological function, specifically the HPA axis, humoral and cell-mediated immunity, ovarian cyclicity, and the behavior of male and female subjects. Preliminary results in the humoral immune studies show significant gender and housing differences in the magnitude and kinetics of antibody response to antigenic challenge. These findings, we believe, emerge out of architectural differences in local germinal center response to antigen. Corticosterone does not appear to mediate this response; based on further findings, we now speculate that sex hormones may play a significant role in modulating these immunological differences.

Audience members need not have any special preparation or background. An interest in psychoneuroimmunology and/or gender-based biology are the only requirements.

NR142 Monday, May 7, 3:00 p.m.-5:00 p.m.

International Medical Student Exchange Program (IMSEP): The Challenge of the New Millennium

Victor J.A. Buwalda, M.D., *Department of Psychiatry, Free University, Parnasusweg 28-III, Amsterdam 1076-AR, Netherlands*; Keeshn Veenhof, M.D.

Summary:

Objective: We investigated the experiences of Dutch medical students who studied in the United States for a minimum of 6 months.

Methods: We sent more than 50 IMSEP participants to the US (National Institutes of Health, Georgetown University School of Medicine, and Harvard Medical School). We then collected evaluation forms and interviews from American supervisors and the students after their return to the Netherlands.

Results: The IMSEP participants wrote more than 17 abstracts and 23 times were the co-author of an publication. The total dropout of the students who participated in the program was 3%. Five IMSEP participants immediately got a job in medical biology after return to the Netherlands, and two went back to the United States with grants following an invitation from their US supervisors.

Conclusion: IMSEP is a successful program for international medical students and has the potential to become a high-quality program. The supervisors all wanted to continue cooperation with the IMSEP because of the good selection criteria of IMSEP and the quality of the IMSEP participants. The dropout rate of the IMSEP-students during their research period was very low. Some of the supervisors were interested in a continuous turnaround of IMSEP participants.

NR143 Monday, May 7, 3:00 p.m.-5:00 p.m.

The Use of Psychotropic Medications Among Medical Resident Physicians at Rhode Island Hospital

Jody A. Underwood, M.D., *Department of Pschiatry, Rhode Island Hospital, 593 Eddy Street, Providence, RI 02903*; Joseph A. Diaz, M.D., Kelly A. McGarry, M.D.

Summary:

Background: Although the practice of self-prescribing medications is common among resident physicians, the incidence of self-prescribing specifically for psychiatric disorders has not been reported in the literature.

Purpose: To investigate the self-administration of psychotropic medications among resident physicians for the symptoms of depression, anxiety, and sleep disorders.

Methods: A survey was distributed to all internal medicine residents at Rhode Island Hospital. The survey had three sections, one each for depression, anxiety, and sleep disorders. The residents were asked about self-prescribing for the above diagnoses.

Results: Sixty-three percent (79/125) of medical residents responded. Residents self-treated for the symptoms of a sleep disorder most often. Twenty-five residents (32%) used at least one medication for the symptoms of a sleep disorder. Thirteen residents (16%) used at least one medication for the symptoms of depression. Only two residents (2.5%) were under the care of a clinician. Five residents (6%) used at least one medication for the symptoms of anxiety. Only one resident (1%) was under the care of a clinician.

Conclusions: This study suggests that medical residents often self-prescribe for sleep disorders, depression, and anxiety with sleep disorders being most common.

NR144 Monday, May 7, 3:00 p.m.-5:00 p.m.

Psychological and Neuroendocrine Responses in Male Residents After an Overnight Call

Ritu Chahil, M.D., *Department of Psychiatry, University of Virginia at Roanoke/Salem, 1940 Roanoke Boulevard, Building 11, 116A7, Salem, VA 24153*; Ali Iranamanesh, M.D., Jasdeep S. Miglani, M.D.

Summary:

Objective/Hypothesis: Exposure to excessive or cumulative stress can result in damaging physiological and psychological changes that may occur singly or in combination. The neuroendocrine system is vulnerable to stress at a rate highly correlated with type, intensity, and duration of the stressful condition.

Method: To assess the neuroendocrine impact of a night-call, we studied eight healthy male residents (mean age=33 years SEM=2) by measuring salivary cortisol concentration as well as circulating concentrations of total testosterone, FSH, LH, T4, T3U, TSH, prolactin, and proinflammatory cytokines such as C-reactive protein, ICAM-1, and VCAM-1. Validated psychologic instruments—the STAI-S and STAI-T—were used to measure state anxiety and subjective stress and arousal. Studies were conducted in the morning and on 3 separate days (pre-call, on call, and post-call). Each subject functioned as his own control, and ANOVA was used for statistical analysis.

Results: Results are reported as mean ± SEM. Salivary concentration of cortisol was significantly increased after a night call (0.423 ± 0.06 μg/dl), and on call (0.236 ± 0.03 μg/dl). This was associated with significantly lower post-call serum concentrations of total testosterone, when assessed in relation to pre-call and on call values (419 ± 59 versus 495 ± 50 versus 464 ± 54 ng/dl; p=0.04). The lower circulating concentrations of total testosterone after a night on call were accompanied by lower serum concentrations of FSH (4.1 ± 0.6 versus 4.8 ± 0.8 versus 4.7 ± 0.8 mIU/ml; p=0.02) and LH (2.9 ± 0.3 versus 3.9 ± 0.3 versus 3.6 ± 0.4 mIU/ml; p=0.055). Night call did not appear to have a significant effect on the function of thyroid gland, proinflammatory cytokines, lipid profiles, and psychological stress response.

Summary: In summary, stress of a night call is of significant intensity to stimulate the hypothalamic-pituitary-adrenal axis and to centrally suppress the male gonadal function. The dissociated activity of the two axes is presumed to be due to inhibition of the gonadotropin pulsatility by endogenous opiates (beta-endorphin), which are known to be concomitantly released with ACTH, both at baseline and in response to stress.

NR145 Monday, May 7, 3:00 p.m.-5:00 p.m.

Emotional Stress Among Resident Physicians

Carolyn M. Young, M.D., *Department of Psychiatry, SUNY at Buffalo, 462 Grider, Erie County Medical Center, Buffalo, NY 14215*; Rajesh Narendran, M.D., Cynthia A. Pristach, M.D., Antoinette M. Valenti, B.A., Maribel Abbate, M.D.

Summary:

Background: Emotional stress has long been recognized as a nearly inevitable component of residency. The severity of such stress among today's residents and the methods residents use to seek assistance with emotional problems unknown. To address these issues, we conducted a survey of residents within the consortium at SUNY Buffalo.

Methods: 300 residents were surveyed regarding history of significant emotional stress while a resident, contact with mental health professionals, methods of dealing with emotional problems, and reasons for not seeking treatment.

Results: 52% of residents responded; half were international medical graduates (IMG's). Nearly half stated that they had experienced a period of significant stress during residency, but only 12% stated they had ever seen a psychiatrist or therapist. Most residents stated that if they needed help they would approach a family or friend. If a fellow resident needed help, 73% said they would approach that resident, followed by the chief resident (21%), an attending (13%), or the training director (12%). 39% stated they had been prevented from seeking treatment during residency, primarily due to time constraints (28%), confidentiality concerns (22%), lack of awareness of resources (21%), or stigma (14%). IMG's were less likely to have sought treatment in the past and saw more obstacles to treatment during residency.

Conclusions: Rates of psychological stress are high among residents. Seeking professional treatment would appear to be a path fraught with obstacles. However, residents do talk with colleagues and family/friends. These groups would benefit from increased education regarding signs and symptoms of psychiatric illness and resources for referral. It may be predicted that the risk for emotional stress is particularly high for IMG's, thus they are a group that may need special targeting to improve their access to treatment.

NR146 Monday, May 7, 3:00 p.m.-5:00 p.m.

Rating Psychiatry Residency Applicants: Increasing Interrater Reliability Using the Application Evaluation Scale (AES)

Daniel Stewart, M.D., *Department of Psychiatry, Mount Sinai, One Gustave L. Levy Place, Box 1230, New York, NY 10029*; Judith Neugroschel, M.D., James P. Wolberg, M.D., Jorge R. Petit, Jr., M.D., Jack Hirschowitz, M.D., Andrew Aronson, M.D., Deborah B. Marin, M.D.

Summary:

Introduction: Selection of residents for psychiatry programs relies on evaluation of previously identified predictors of competency and success in subsequent training and practice. To date, there

is a relative paucity of literature on reliable scales that meet these aims. To address this, we developed the Application Evaluation Scale (AES). We hypothesized that this instrument would enhance interrater reliability amongst interviewers and provide a ranking system for applicants.

Methods: A committee of senior faculty and residents developed a scale that reflected the qualities we were seeking in our residents. Specifically, applicants were rated for grades, recommendation letters, dean's letter, extracurricular activities, research experience, and strength of their interviews. Each domain had anchor points and descriptors. For example, in the "research" domain, zero reflected no research experience and three reflected multiple publications. For this study, each domain was rated independently by two faculty interviewers. Intraclass correlation coefficients (ICC) were used to determine interrater reliability for each domain and for the total AES score.

Results: ICCs ranged from .26 (extracurricular activities) to .76 (research experience). ICC for the total AES score was 72.

Conclusion: The AES provides a reliable and standardized method for rating resident applicants. The range of ICCs in part reflects the relative variability of applicant accomplishment in certain domains. Nonetheless, the scale provides an excellent opportunity to standardize resident applicants. In addition, the ability of the AES to predict subsequent performance and competence of residents will be evaluated in future studies.

NR147 Monday, May 7, 3:00 p.m.-5:00 p.m.

Church Attendance and Mortality in Older Mexican and European Americans

Norma J. Anderson, D.O., *Department of Psychiatry, University of Texas Health Science Center, 7703 Floyd Curl Drive, MC 7792, San Antonio, TX 78229-3900*; Stephen L. Stern, M.D., Rahul Dhanda, Ph.D., Michael J. Lichtenstein, M.D., Helen P. Hazuda, Ph.D.

Summary:

Objective: To examine whether church function attendance predicts all-cause mortality in a random bi-ethnic sample of community-dwelling older adults.

Methods: Upon entering an epidemiologic survey during 1992–1996, 759 persons aged 64–79—53% Mexican-American—answered questions in English or Spanish about attendance at church and club functions, contacts with family and friends, depression (the Geriatric Depression Scale), physical health, and lifestyle. Stepwise Cox proportional hazards models were used to explore the association of church and non-church social contacts and demographic, health, and lifestyle factors with mortality.

Results: A total of 118 participants had died as of 11/00. In the total sample, church contacts (risk ratio 0.75, 95% confidence interval 0.62–0.90, $p<0.01$), but not other social contacts, predicted decreased mortality in a final Cox model that included baseline medical comorbidity, age, sex, ethnicity, current smoking, depression, and hopelessness. Separate analyses for Mexican Americans and men yielded similar results. In European Americans, however, the effects of church contacts on mortality were explained by smoking, while in women other social contacts but not church contacts predicted longevity.

Conclusion: These findings suggest that contacts with church predict longevity in many, but not all, older adults. Assessing spirituality may be important in the evaluation of older patients.

NR148 Monday, May 7, 3:00 p.m.-5:00 p.m.

Self-Treatment in Depression

Sajida Mathew, M.D., *Department of Psychiatry, UPC Jefferson, 2751 East Jefferson, # 400, Detroit, MI 48207-4100*; Richard Balon, M.D., John R. Sarcar, M.D., Ravi K. Singareddy, M.D.

Summary:

We studied psychiatrists' attitudes toward self-treatment of depression. A brief 11-item questionnaire was sent to 830 psychiatrists in Michigan, and 567 responses were received. Demographic characteristics of responders were as follows: 70% male and 30% female; mean age was 52; 21% were biologically-oriented psychiatrists, 12% were psychodynamically-oriented, and 67% were eclectic. Twenty-eight percent reported that they would consider self-medication for mild/moderate nonsuicidal depression and 29% reported that they would seek treatment from an unknown psychiatrists, while 61% reported that they would seek treatment from an unknown psychiatrist for severe depression with suicidal ideation. Thirty-two percent reported that they would treat both friends and relatives for mild/moderate depression and 54% would treat neither, although 82% reported that they would treat neither group for severe depression. Seventy-four percent reported that stigma would not affect their decision to self-treat and 40% reported that a permanent insurance record would affect the decision. Sixteen percent of psychiatrists had treated themselves and 78% felt that one should not self-treat. Contrary to ethical and practical concerns, a number of psychiatrists would consider treating themselves and/or friends/relatives for depression. The concerns about confidentiality/insurance record seem to play a bigger role in psychiatrists' decision to treat themselves than the stigma of mental illness.

NR149 Monday, May 7, 3:00 p.m.-5:00 p.m.

Court-Ordered Evaluations in Maricopa County, Arizona: A Financial Perspective

Eric E. Goldberg, D.O., *Department of Psychiatry, Maricopa Medical Center, 4132 East Pinchot Avenue, Phoenix, AZ 85018*; Ali Kazim, M.D., Curt Bay, Ph.D.

Summary:

Objective: Funding for the care of seriously mentally ill patients is limited. The authors sought to identify the financial cost of involuntary court-ordered evaluations and potential strategies to reduce the cost.

Method: Medical charges from the time of admission to the time of court hearing were calculated for patients (N=998) who obtained involuntary court-ordered evaluations at Maricopa Medical Center Psychiatric Annex during the year 1999 to determine an average cost of involuntary court-ordered evaluation. The average daily cost of conducting mental health hearings was calculated.

Results: The average medical cost of an involuntary court-ordered evaluation was determined to be $8,236 (SD=2201), and the average cost per day was $686 (SD=86). The average daily cost of conducting mental health hearings was $1,925.00.

Conclusions: Medical charges account for most of the expense of involuntary court-ordered evaluations. These are directly related to the length of hospitalization, which is influenced by the limited availability of mental health hearings. Several options that would reduce patient stay and save millions of dollars are explored, including: expedited evaluations, weekend/holiday hearings, outpatient evaluations, and housing patients in a less acute setting while evaluations are performed.

NR150 Monday, May 7, 3:00 p.m.-5:00 p.m.

Factors Associated with Missed First Appointments to a Psychiatry Clinic

Xiaoyan Wu, M.D., *Department of Neuropsychiatry, Texas Technical University, 3601 4th Street, Lubbock, TX 79430*;

Barbara M. Rohland, M.D., Gina Kruse, B.S., Alan L. Podawiltz, M.D.

Summary:

Objective: To identify characteristics of patients who fail versus keep their scheduled intake assessment at a psychiatric clinic following referral by a state agency.

Methods: The charts of 314 patients consecutively referred for initial appointments at a university department of psychiatry outpatient clinic were reviewed. Failure to attend the initial appointment occurred at a rate of 36.3%. Patients' demographic characteristics, DSM-IV diagnoses, as well as psychopharmacological therapy were compared between patients who missed versus those who did not miss appointments.

Results: Statistical analysis revealed that three factors were significantly associated with missed appointments: poor primary support system, not being treated with psychotropic medications, and presence of health insurance.

Conclusions: The findings from this study suggest that persons who are at increased risk to miss their scheduled intake assessment can be prospectively identified. Measure to increase compliance with first visit appointment could be targeted toward those persons who are at greatest risk to miss their scheduled appointments.

NR151 Monday, May 7, 3:00 p.m.-5:00 p.m.

Impact of Social-History Interviewing on Patient Satisfaction

Geoffrey M. Hopkins, M.D., *Department of Psychiatry, SUNY UNU, 750 East Adams Street, Syracuse, NY 13210*; Thomas L. Schwartz, M.D., Al Hartel, M.D., Chris Wasyliw, B.S.

Summary:

Patient satisfaction has been a subject of medical research since the 1960's. In the last decade, research regarding patient satisfaction has increased in an attempt to delineate those variables that are strongly related to patient satisfaction with health care. While there is a vast literature describing research into patient satisfaction, literature specifically relating to resident physicians, their behaviors, and how they relate to patient satisfaction is relatively limited. The authors surveyed hospital inpatients and asked them to rate satisfaction levels for the admissions process, meals, room, nursing service, tests and procedures, their physician, and other items. These ratings were then correlated via chart review to the amount of social history facts recorded. The results indicate that social history interviewing by resident physicians is strongly correlated with patient satisfaction. In conclusion, it appears that resident physicians may increase patients' satisfaction by increasing the amount of social history discussion in their initial interview.

NR152 Monday, May 7, 3:00 p.m.-5:00 p.m.

Computerized Log Systems in Residency Training: The University of Virginia: Roanoke-Salem Experience

Jasdeep S. Miglani, M.D., *Department of Psychiatry, VA Medical Center, 1970 Roanoke Boulevard, Salem, VA 24153*; James K. Moles, M.D., Roger O'Dell, B.S.

Summary:

Hypothesis/Context: The ability to document detailed information pertaining to the clinical experiences of residents in training has become crucial to quality of postgraduate medical residency training programs. Insuring a diverse patient care experience, documenting this experience for residency review committees (RRC's) and providing details of this experience for credentialing and privileging processes following graduation all require the storage of resident patient encounters in well organized information management systems. Computerized resident log systems, developed from relational database software, offer multiple advantages over the traditional and often cumbersome handwritten log systems in this regard.

Objective: To describe the development, implementation, and impact of a computerized resident log system entitled ResiLog in the University of Virginia Roanoke-Salem Psychiatric Residency Training Program.

Results: ResiLog is specific to the field of psychiatry residency training and overcomes many of the disadvantages of non-psychiatry related commercial systems. This system is currently utilized to help govern the resident case distribution in our ambulatory clinics and has provided important information regarding the clinical diversity of our residency program at a recent RRC site visit. Currently ResiLog has been operational since June 1999 with 15,280 patient encounters representing 6,745 individual patients entered into this system as of August 2000. Major depression and alcohol dependence are the most common adult psychiatric disorders encountered by our resident physicians, while ADHD and conduct disorder are the most common childhood disorders. Patient care of resident physicians can be analyzed in variety of additional configurations.

Conclusion: Computerized residency log systems can enhance the management of information pertaining to the patient care experiences of psychiatry residents in training. Such systems save time, collect more reliable and complete data, and enable complex statistical tabulations with relative ease.

NR153 Monday, May 7, 3:00 p.m.-5:00 p.m.

Assessing Clinical Trial Outcome with Computer-Administered Patient Diaries: A Pilot Study in Irritable Bowel Syndrome

Thomas L. Schwartz, M.D., *Department of Psychiatry, SUNY Health Sciences Center, 750 East Adams Street, Syracuse, NY 13210*; Prakash S. Masand, M.D., Sanjay Gupta, M.D., David E. Kaplan, M.D., Subhdeep Virk, M.D., Kenneth A. Kobak, Ph.D., James W. Jefferson, M.D.

Summary:

Background: The use of patient experience measures is becoming a major focus of pharmacological research. Patient daily diaries collect comprehensive real-time data that avoid these biases. Paper diaried retrospective reports, however, are limited by noncompliance or faked compliance, confounds due to timing of diary entries and review of previous entries, and slow and costly data processing. We utilized a computer-administered patient daily diary administered over the telephone using Interactive Voice Response (IVR).

Methods: Twenty patients participating in an open-label trial of paroxetine for irritable bowel syndrome completed daily diaries of GI symptoms for 13 weeks. Patients accessed the computerized diary by phoning a toll-free number and entering a password and ID number.

Results: A total of 1,382 calls were made during the study. Patients completed 86% of all required daily calls. Most (79%) were made within a consistent two-hour range each night. Out of 15 patients surveyed, all found the system very easy or easy to use, and 12 (80%) found the system convenient. Four (27%) preferred giving the information to the computer, two (13%) a person, and nine (60%) had no preference.

Conclusions: This technology provides a method of real-time data collection that is both reliable, valid, and cost-effective.

NR154 Monday, May 7, 3:00 p.m.-5:00 p.m.

Improving Adherence to Antidepressants by Video and Pharmacist Coaching: Study Design

Hein P. Van Hout, Ph.D., *Institute for Research in Extramural Medicine, Vrije University, Van Der Boechorststraat 7, Amsterdam 1081 BT, Netherlands*; Eibert R. Heerdink, Ph.D., Guy M. Goodwin, M.D., Hugo Nieuwenhuyse, Ph.D.

Summary:

Background: Adherence to antidepressants is reported to be limited. As pharmacists have a central position in the distribution of medication, they can play an important role in improving adherence to antidepressants.

Objective: To investigate whether an informative 20-minute take home video and three coaching contacts by pharmacists improves adherence to non-tricyclic antidepressants of primary care patients.

Setting: 19 community pharmacies in the Netherlands.

Method: A randomized controlled trial with a 6-month follow-up was conducted among consecutive depressive primary care patients attending the pharmacy for second-generation antidepressants. The trial consisted of two arms: 1) a control group receiving care as usual, and 2) an intervention group receiving an informative video and three coaching contacts by the pharmacist.

Outcome: Primary outcome was medication adherence, expressed as intake frequency and (dis)continuation rates and measured by electronic drug container monitors. Among the secondary outcomes were self-rated mental health and quality of life.

Sample size: The randomization took place on a patient level and a one-to-one ratio was achieved. With a sample size of 130 subjects a difference of 13% in adherence can be detected at a significance level of 0.05 (two-sided).

Funding: grants from Organon and SmithKline Beecham.

NR155 Monday, May 7, 3:00 p.m.-5:00 p.m.

A Clinical Trial Comparing Endocrine Effects of Risperidone and Clozapine

Norberto M. Zelaschi, M.D., *Department of Psychiatry, PRA-Korn Hospital, 44 No. 325 ly2, LaPlata, BA 1900, Argentina*; Juana L. Rodriguez, M.D., Sergio Gaitan, M.D., Sergio Panizzo, B.A., Angelica Lopez, B.A., Fernando Archuby, B.A., Luis M. Zieher, M.D.

Summary:

Objectives: To test the hypothesis that some atypical antipsychotic drugs with pharmacological D2 -5HTA2 blocking activity can produce a substained increase of prolactin (PRL) serum levels during long-term maintenance antipsychotic treatment.

Method: We have studied serum PRL levels in a group of 22 hospitalized patients (16 males and six females) suffering from schizophrenic disorders, according to the DSM-IV criteria, the complete period of follow-up was 48 weeks. A series of venipunctures were performed every six weeks in fasting and resting conditions (total: eight dosages for each patient); these are described as periods I through VIII for the statistical analysis. PRL was dosed with ELISA method. The figures obtained were compared, with those of the control group (CG) (n = 21, 11 males and 10 females). The range of doses were for risperidone 2–4 mg/day, and for clozapine 150–300 mg/day.

Results: All the data were expressed in mean +/– 1 SD. The patients under risperidone were males (age: 56.64 / 12.16); in the clozapine's group five were males and six females (age: 44.1 / 10.30.; and in the control group (age 52 / 9.07). The Kruskall-Wallis test (no-parametric ANOVA test) and a multiple comparison test of the mean ranks were applied for the comparison of age and PRL values. Statistical test is positive for age (H=7.43, p= 0.02); even though that the risperidone group is older than the clozapine's group, both of them do not differ significantly with the CG. Values of PRL in the CG were 9.05 (4.04)ng/ml. In the group treated with risperidone (during period I through VIII) PRL increased significantly (H= 45.56; p= 0.000); and there is no difference between the periods; the figures in period I and VIII were 45.35 (42.03) ng/ml and 26.55 (14.77) ng/ml, respectively; in the clozapine group no changes were observed.

Conclusions: Risperidone produces a substancial raise in PRL serum levels during extended antipsychotic drug treatment (one year follow-up). It is possible that the strong antagonism of D2 receptors by risperidone is what accounts for the prolactogenic activity; since these male patients are older, we should not discard that it could be possible that the age factor also plays a role.

NR156 Monday, May 7, 3:00 p.m.-5:00 p.m.

Predicting Response to 2.25 Times Threshold Unilateral ECT

Warren D. Taylor, M.D., *Department of Psychiatry, Duke University, DUMC 3903, Durham, NC 27710*; Andrew D. Krystal, M.D., Richard D. Weiner, M.D.

Summary:

Objective: The efficacy of unilateral nondominant (UL) ECT in the treatment of major depression increases as stimulus intensity increases above the seizure threshold. As with bilateral ECT, greater efficacy unfortunately results in greater cognitive deficits. Optimizing ECT requires administering the lowest UL ECT stimulus intensity leading to response. Because it is not possible to identify this intensity, many practitioners administer high intensity UL ECT in order to achieve efficacy, which may then lead to unnecessary side effects. As a result, we investigated whether it was possible to identify subjects early in the treatment course who are likely to respond to a relatively low intensity UL ECT.

Methods: We retrospectively studied 129 subjects with major depression who received 2.25 times threshold index UL ECT. We evaluated how MADRS scores, administered prior to each treatment, predicted post-course therapeutic outcome.

Results: Significant prediction of therapeutic outcome was possible beginning with treatment 3 ($p<0.001$). For each treatment, we established cutoffs for determining when a switch to a potentially more effective form of ECT is needed.

Conclusions: Predicting the response to low-dose UL ECT early in the treatment course may aid in optimizing ECT stimulus dosing.

NR157 Monday, May 7, 3:00 p.m.-5:00 p.m.

Factors Affecting Dosages of Neuroleptic (CPZ) Equivalents in Outpatients

Leonid Vorobyev, M.D., *Department of Psychiatry, RWJ Medical School, 189 New Street, New Brunswick, NJ 08901*; Mona V. Bijlani, M.D., Robert G. Stern, M.D.

Summary:

Objective: The latest APA guideline suggest that the optimal dosages of conventional neuroleptics are much lower that the dosages prescribed in the community. This study explored which factors affect the dosage of neuroleptics (CPZ equivalents) prescribed to psychiatric outpatients, and specifically tested the hypothesis that typical neuroleptics are prescribed in higher dosages than atypical neuroleptics.

Method: The authors reviewed charts of 540 outpatients, of whom 352 were treated with neuroleptics, to study different factors affecting dosages of neuroleptics. 27% of 352 patients were treated with typical antipsychotics and 73% with atypicals. 32% of patients treated with neuroleptics carried a diagnosis of schizoaffective disorder, 18% - schizophrenia, 20% - major depression,

13% with bipolar disorder. Unmatched t-tests were used to compare between the various groups.

Results: The average CPZ equivalent dosage for the entire sample was 331.83 mg/d (SD 261.15). Neither gender, nor age had any influence on dosages. Race, and diagnoses of schizoaffective, schizophrenia, and major depression had a significant impact on neuroleptic dosages. For the sample as a whole the use of typical neuroleptics was associated with significantly higher CPZ equivalent dosages.

Conclusions: In this sample of neuroleptic treated outpatients the choice of typical neuroleptics and minorities status tended to be associated with higher neuroleptic dosages. Further studies and education of professionals are required to address these findings.

NR158 Monday, May 7, 3:00 p.m.-5:00 p.m.

Nutritional Education in Minimizing Weight Gain Associated with Anitpsychotic Therapy

Charles Tuan-Tu S. Nguyen, M.D., *Department of Psychiatry, UCI Neuropsychiatry, 101 The City Drive, Building 3, Orange, CA 92868*; Tony Ortiz, B.S.

Summary:

Antipsychotic medications, both typicals and atypicals, have the common side-effect profile of weight gain. Atypical agents have significant higher weight-gain potential relative to other agents. However, in spite of the far-reaching benefits of the agents, the potential for weight gain may be perceived as a barrier to treatment. Evidence for the increase of weight gain has been associated with an increase in appetite. The purpose of our research is to investigate whether proper behavioral interventions can prevent weight gain associated with olanzapine therapy. Twenty individuals with schizophrenia (ages 18–54) seen in a community clinic were provided nutritional education and techniques in minimizing intake of high caloric food. Our open-labeled retrospective review shows that with proper nutritional counseling, weight gain associated with olanzapine can be minimized.

NR159 Monday, May 7, 3:00 p.m.-5:00 p.m.

Directly Observed, Highly Active Antiretroviral Therapy (HAART) with Methadone Maintenance

Beth K. Boyarsky, M.D., *Department of Psychiatry, Montefiore, 111 East 210th Street, Rosenthal 169, Bronx, NY 10467*; Julia Arnsten, M.D., Julie Sarlo, B.A., Corinne M. Rogers, M.S., Peter F. Cottone, B.A., Petrie M. Rainey, M.D., Elinore F. McCance-Katz, M.D.

Summary:

Objective: This study examines the efficacy of, and adherance to, directly-observed pharmacotherapy, and identifies significant drug interactions in methadone(M)-maintained individuals on highly active antiretroviral therapy(HAART).

Method: Methadone-maintained individuals with HIV disease were coadministered once-daily, directly-observed HAART (efavirenz 600 mg, didanosine 600 mg, and lamivudine 150 mg twice daily) with their daily dose of methadone. Pharmacokinetic (PK) and pharmacodynamic assessments were obtained at baseline, upon opiate withdrawal, and following methadone restabilization[4] or four weeks of HAART[44]. Adherence was quantified weekly; viral load was obtained monthly:

Results:

	*Subject 1**	*Subject 2***
Time to nondetectable virus (weeks)	8	4
M dose(mg/d)(pr/Post HAART)	90/90/130(44%↑)	130/130
M trough(ng/ml)(Pre/Post HAART)	226/94/223	280/65
M $AUC_{0\text{-}24}$ ng.h/ml(Pre/Post HAART)	7055/3715/7573	8912/3335
Objective Opiate Withdrawal Score at M trough	0/7/1	0/1
Missed doses of HAART	1	3

Conclusions: Directly observed therapy for those receiving methadone maintenance is a promising intervention to increase adherence and positive HIV disease outcomes. Efavirenz may reduce methadone plasma concentrations as has been previously reported. Those receiving efavirenz-containing regimens need individual monitoring as responses to reductions in methadone exposure vary and may not always require methadone dose increases. Further results will be presented for a larger sample in this ongoing study.

Supported by NIDA grant RO1 DA 13004

NR160 Monday, May 7, 3:00 p.m.-5:00 p.m.

Differentially Expressed mRNA in Rat Brain Following Repeated Electroconvulsive Stimulations (ECS)

Ida Hageman, M.D., *Department of Psychiatry, Rigs Hospitalet, Blegdamsvej 9, Copenhagen, DK 2100, Denmark*; Maria L. Wrang, M.S.C., Carsten W. Alsbo, M.S.C., Nils H. Diemer, M.D., Martin B. Joergensen, M.D.

Summary:

Electroconvulsive therapy has been used as an efficient treatment for mood disorders, such as depression, for many years. The mechanism of action remains largely unknown, although changes in expression of a variety of proteins and mRNA have been reported. To analyze the effect of electroconvulsive stimulations (ECS) on mRNA expression, we have applied the new restriction fragment differential display PCR tecnique (RFDD-PCR). To follow the changes in mRNA expression after repeated ECS, we analyzed 24 rats that were subjected to 12 ECS or sham treatment over a period of 4 weeks. They were allowed to survive 1, 7, or 28 days. The RFDD-PCR profiles of ECS-treated rats and sham rats were compared to detect significant differences in expression level. The expression of approximately 400 fragments was found to be changed by ECS. The number of upregulated fragments decreased from 39 at day 1 to 30 at day 28. In contrast, the number of downregulated fragments increased from 45 to 199 in this period. This late adaptive downregulation does not correspond to other established changes following convulsive treatment.

Supported by: The Ivan Nielsen foundation

NR161 Monday, May 7, 3:00 p.m.-5:00 p.m.

Chronic Pain and Yoga: A Study

Sonia D. Gaur, M.D., *Department of Psychiatry, Harbor-UCLA Medical Center, 1000 West Carson, Box 498, Torrance, CA 90509*; Lisa Davidson, Suzan Winders-Barrett, Ph.D., Edward C. Covington, Jr., M.D., Michaelle Star

Summary:

Purpose/Objective: To study the effects of yoga on a heterogenous chronic pain population.

Design: Prospective open study.

Sample: 18 chronic pain patients.

Intervention: The 4-week study consisted of thrice weekly 90-minute sessions. Concomitant antidepressant treatment was continued if the dose had been stabilized prior to study entry. Treatment also included any other medication or form of therapy.

Changes during the study were done by the patients' own physician.

Main Outcome Measures: Variables assessed were 1) pain intensity, 2) mood, 3) functional status, 4) domestic, social and occupational productivity and 5) medication usage. These items were assessed using standardized protocols. Diagnoses were obtained from the patients' physician.

Findings: There were significant decreases in ratings on the Total Mood Disorder Scale (p=0.04), Pain Severity Scale (p= 0.008), and the Medication Quantification Scale (p=0.019).

Conclusion: This study demonstrates that yoga improves mood in chronic pain patients and leads to decreased medication usage and a decrease in pain severity. The results were statistically significant. There was a trend for improvement in a variety of functional activities. Yoga may be used for augmenting chronic pain treatment, as it facilitates improved coping and self-management.

NR162 Monday, May 7, 3:00 p.m.-5:00 p.m.

Long-Term Follow-Up of Treatment-Resistant Depression

Paolo Cassano, M.D., *Department of Psychiatry, University of Pisa, Via Roma 56, Pisa I-56100, Italy*; Lorenzo Lattanzi, M.D., Liliana Dell'osso, M.D., Guilia Battistini, M.D., Mariagrazia Arinozzi, M.D., Marianna Abelli, M.D., Giovanni B. Cassano, M.D.

Summary:

Objective: To evaluate the long-term course of drug-resistant depression and its relationship with treatment.

Methods: Twenty-six patients with treatment-resistant major depressive episode (MDE) were naturalistically followed-up after a 16 weeks of pramipexole (a D2-D3-agonist) add-on therapy. The MADRS, CGI, and LIFE-UP were administered at baseline, week 16, 32, and 48. Responder patients (≥50% reduction of MADRS score at week 8) were analyzed for relapse [≥2 weeks of having a score of 4 or 5 on the LIFE-UP within 8 weeks of having a score≤3] and recurrence [≥2 weeks of having a score of 4 or 5 on the LIFE-UP after 8 weeks of having a score≤3] of MDE.

Results: 16/26 patients had bipolar depression (women: 20/26; mean age: 54.1 years). Mean duration of current MDE was 21.7 months. Mean baseline MADRS and CGI-S were 35.0 (SD=7.3) and 4.7 (SD=0.7), respectively. Eighteen patients responded to an association of two or more antidepressants. All patients were followed-up for ≥16 weeks and 12 for ≥32 weeks. After recovery, one patient experienced a relapse (week 6), and five patients experienced a recurrence (mean=17.8 weeks, SD=9.3). For these five patients, recurrence occurred after their antidepressant treatment was partially (N=4) or totally discontinued (N=1). Two patients recovered once multiple antidepressant association was restored.

Conclusion: In our study, course of treatment-resistant depression was more favorable in patients treated with a multiple antidepressant regimen.

NR163 Monday, May 7, 3:00 p.m.-5:00 p.m.

Pharmacological Treatment of Social Phobia: A Meta-Analysis

Carlos Blanco-Jerez, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive, New York, NY 10032*; Franklin R. Schneier, M.D., Andrew Schmidt, M.S.W., Carmen R. Blanco-Jerez, M.D., Michael R. Liebowitz, M.D.

Summary:

Objective: To conduct a meta-analysis of the pharmacological treatment of social phobia.

Method: MEDLINE and Psychlit were used to locate all double-blind studies that included medication for the treatment of social phobia. The Q-statistic was used to assess homogeneity of estimates of effect size in the totality of studies and in several medication subgroups. Random effects models were used to estimate the effect sizes of all studies together and of homogenous medication groups. Effect size was expressed using Cohen's *d*.

Results: Nineteen studies were found. Overall effect size was d=0.52 (95% CI=0.33–0.71). There was significant heterogeneity of effect sizes when all studies were considered together (Q=65.3, df=18, p<0.05). This heterogeneity disappeared when medications were grouped by pharmacological families. Clonazepam, gabapentin, brofaromine, SSRIs, and phenelzine (in that order) had the biggest effect sizes. There were no significant differences among them, but all of them were superior to moclobemide, atenolol, buspirone, and Org 2766. Power to detect other differences was only 41%.

Conclusion: A number of medications are effective for social phobia. Head-to-head comparisons between selected medications and SSRIs are needed to study the potential superiority of those medications in the treatment of social phobia.

NR164 Monday, May 7, 3:00 p.m.-5:00 p.m.

Neuroprotective Effects of Some Atypical Antipsychotics

Zelan Wei, Ph.D., *Department of Psychiatry, University of Saskatoon, 103 Wiggins Road, Saskatoon, SK S7N 5E4, Canada*; Hong Oing, Ph.D., Xin-Min Li, M.D.

Summary:

Our early study has demonstrated atypical antipsychotics such as olanzapine and clozapine have neuro-protective potential. This study is to further determine whether atypical antipsychotics can protect neuronal cells from cell death induced by hydrogen peroxide (H_2O_2), β-amyloid protein, or MPP+. PC12 cells were first treated by different antipsychotics for 24 hours before exposure to H_2O_2 (4 hours), β-amyloid$_{25-35}$ fragment (24 hours), or MPP+ (24 hours). Then cell viability was measured by MTT assay. Statistical comparisons were made using ANOVA followed by paired *t* test.

Cell viability as a percentage of control conditions decreased in dose-dependent manner, to 66.6 (SD=2.4), 50.2 (SD=2.3), and 18.5 (SD=1.2) with concentrations of 100, 200, and 400 μM H_2O_2, respectively. Clozapine (20 μM) increased the cell viability to 96.3 (SD=3.8)^{44}, 90.8 (SD=2.2)^{44}, and 38.1 (SD=3.0)^{4}, while olanzapine (20 μM) increased the cell viability to 88.3 (SD=2.1)^{4}, 74.9 (SD=8.3)^{4}, and 24.5 (SD=0.8)^{44}, in the presence of the above concentrations of H_2O_2 ($^{4}p<0.01$, $^{44}p<0.001$, N=7). In addition, clozapine (100 μM) and olanzapine (100 μM) could protect PC12 cells from cell death induced by different concentrations of β-amyloid$_{25-35}$ (10^{-14} M to 10^{-5} M) or MPP+ (25, 50 μM).

We propose that at least one of the mechanisms of actions for atypical antipsychotics is through their neuroprotective/antioxidative effects in the treatment of schizophrenia and possible other neurodegenerative disease.

NR165 Monday, May 7, 3:00 p.m.-5:00 p.m.

Olanzapine Treatment of Severe PTSD: A Case Series

Robert C. Stone, *Department of Psychiatry, University of Texas at Southwestern, 5323 Harry Hines Boulevard, Dallas, TX 75390-9070*; Frederick Petty, M.D., Lisa Vinuesa, M.S., Ellen Taliaferro, M.D., Andra Teten, B.A., Don Smith, Ph.D.

Summary:

Posttraumatic stress disorder is a common psychiatric disorder with an 8% lifetime population prevalence in the U.S. Continued investigation into pharmacotherapy for PTSD is important, considering that almost half of patients studied in SSRI trials failed to achieve treatment effect.

PTSD is also a common condition experienced by survivors of torture. While torture is fortunately rare in the U.S., the same cannot be said about many nations. Torture is actively used to punish and dissuade political dissenters who oppose issues such as free elections, women's rights, and racial equality. Torture survivors often seek political asylum in the U.S. Those with PTSD often experience debilitating symptoms that require treatment to regain any significant quality of life and to participate effectively in the asylum process.

This presentation will detail the treatment of eight survivors of severe torture from central and western African countries. All patients had severe PTSD symptoms as diagnosed with the MINI and measured with the TOP-8. Patients were treated with olanzapine (2.5 or 5 mg qhs), either as monotherapy or in combination with an SSRI. After eight weeks of treatment, all eight had >50% reduction in TOP-8 scores and two no longer met criteria for PTSD.

NR166 Monday, May 7, 3:00 p.m.-5:00 p.m.

Common Practices in the Outpatient Treatment of Refractory Depression

Rebecca A. Kornbluh, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114*; Timothy J. Petersen, Ph.D., John B. Herman, M.D., Jerrold F. Rosenbaum, M.D., Andrew A. Nierenberg, M.D., Jonathan E. Alpert, M.D., Maurizio Fava, M.D.

Summary:

Background: Little is known about prescribing practices in the treatment of refractory depression. A multitude of treatment options is available to clinicians when faced with such challenging cases. Unfortunately existing depression treatment guidelines (e.g. APA and AHCPR) do not offer an adequate framework for evaluating which treatment options are most efficacious, especially in cases where several previous treatments have proven unsuccessful. The objective of this study was to gather data from a large group of outpatient clinicians on antidepressant prescribing practices in the treatment of refractory depression.

Method: We asked 835 clinicians attending a psychopharmacology review course to respond to a brief questionnaire including questions concerning a specific case vignette. Of those, 304 (36%; mean age: 50.2 years) consented to participate and filled out our questionnaire. Four questions asked clinicians for their preferred interventions during the course of this fictitious patient's 16-month course of treatment. This patient was presenting with a unipolar, nonpsychotic, severe major depressive episode. The patient had no prior psychiatric history.

Results: 260 (86%) of respondents indicated their preference for an initial treatment that combined medication and psychotherapy, as opposed to either modality alone. As a next intervention (given the patient's nonresponse to two adequate SSRI trials and one atypical antidepressant trial over an eight-month period), 38% of respondents indicated venlafaxine monotherapy as their treatment preference. Combining antidepressants and augmentation were the next most preferred treatment choices (20% and 18%, respectively) at this time point. At the 16-month time point, with the patient having not responded to any interventions, 77% of survey respondents indicated ECT as their next treatment preference. We also examined several clinician variables and whether they were associated with differential response patterns. We found age, gender, type of practice, type of degree, location of practice, and number of years since training to all have no significant relationship with response patterns to our questions.

Conclusions: Switching to venlafaxine, using two antidepressants together, and augmenting a current antidepressant accounted for 76% of respondents' indicated preferences when faced with treating a depressed patient who had not responded to two adequate SSRI trials and one adequate atypical antidepressant trial. 77% of respondents indicated ECT as a treatment preference after 16 months of multiple failed medication trials and nonresponse to psychotherapy. Further research is necessary to elucidate clinicians' reasons for selecting one strategy over another.

NR167 Monday, May 7, 3:00 p.m.-5:00 p.m.

Citalopram for Treatment-Refractory OCD

Darin D. Dougherty, M.D., *Department of Psychiatry, Massachusetts General Hospital, 13th Street, Building 149, 9th Floor, Charleston, MA 02129*; Amanda Beals, M.Ed., Melanie Mathews, B.A., Lee Baer, Ph.D., Michael A. Jenike, M.D.

Summary:

We report a case series of treatment-refractory patients with obsessive-compulsive disorder (OCD) treated with citalopram in an inpatient residential facility. Charts of all patients treated at the facility since early 1997 were reviewed and data for patients treated with citalopram at any time during their stay were entered into a database. Patients who received citalopram for at least eight weeks were included in the final analysis. Patients were receiving concurrent behavioral therapy and most were taking concurrent medications for comorbid diagnoses. Twenty-one patients (11 male, 10 female) with an average age of 37.1 years (range 20–51) received citalopram, average maximum dose of 61.4 mg per day (range 20–90), for an average of 16.1 weeks (range 8–25 weeks). Mean (±SD) Yale-Brown Obsessive Compulsive Scale (Y-BOCS) scores decreased significantly ($p < .001$) from 28.5 ± 5.2 t0 19.6 ± 5.8. Fourteen patients were defined as responders (at least 25% decrease in Y-BOCS). Beck Depression Inventory (BDI) scores (available from 15 patients) decreased significantly from 25.6 ± 12.2 to 18.3 ± 12.3. This case series is the first to demonstrate the efficacy of citalopram for treatment-refractory OCD in a long-term inpatient setting. These data support further studies of pharmacotherapy in conjunction with behavioral therapy in treatment-refractory OCD patients.

NR168 Monday, May 7, 3:00 p.m.-5:00 p.m.

Olanzapine Yields Rapid Improvement in Diverse Syndromal and Subsyndromal Exacerbations of Bipolar Disorders

Suttiporn Janenawasin, M.D., *Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford, CA 94305-5723*; Po W. Wang, M.D., Matthew Schumacher, B.A., Bibi Das, Claudia M. Santosa, M.A., Jenny Mongkolcheep, B.S.C., Terence A. Ketter, M.D.

Summary:

Objective: To evaluate efficacy of olanzapine in syndromal and subsyndromal exacerbations of bipolar disorders.

Method: Open olanzapine was added to prior treatment (five on, seven off mood stabilizers) in bipolar disorder (nine BPI, two BPII, one BPNOS) patients (five women, seven men). At entry, seven patients had elevated and five had depressed mood. Two subjects had psychotic symptoms.

Results: With three days of olanzapine (mean 4.2 mg/day), Young Mania Rating Scale (YMRS) decreased 43% (17.5±10.9 to 10.0±9.0, p=0.01), Hamilton Depression Rating Scale (HDRS) decreased 47% (13.5±8.1 to 7.2± .7, p=0.01), and Clinical Global

Impression (CGI) decreased from 4.5±0.8 to 3.2±1.4 (p<0.01). By nine weeks of olanzapine (mean 7.2 mg/day), YMRS and HDRS decreased 75% (4.4±8.2, p<0.01) and 53% (6.3±6.3, p<0.01), respectively. 6/7 patients (86%) with baseline YMRS> 16 responded (≥50% YMRS decrease). 2/3 patients (67%) with baseline HDRS>18 responded (≥50% HDRS decrease). Final CGI was 2.2±1.4 (p<0.01); 9/12 (75%) patients responded (CGI≤2). Dose, age, gender, marital status, bipolar subtype, psychotic features at entry, and history of rapid cycling were not related to response. Olanzapine was generally well tolerated.

Conclusions: Controlled studies are warranted to explore rapid benefit of olanzapine in diverse exacerbations of bipolar disorders.

Supported by Thai Government Grant and Eli Lilly and Company.

NR169 Monday, May 7, 3:00 p.m.-5:00 p.m.

Prevalence of OCD in Irritable Bowel Syndrome

Nancy J. Keuthen, Ph.D., *Department of Psychiatry, Massachusetts General Hospital, Fruit Street, OCD Program, Boston, MA 02114*; Sanjay Gupta, M.D., Barbara A. Yu-Siao, M.D., Nishant Bhatt, B.S.C., Subhdeep Virk, M.D., Prakash S. Masand, M.D.

Summary:

Irritable bowel syndrome (IBS) occurs more frequently in psychiatric patients than in the general population, with highest comorbidity in patients with anxiety and mood disorders. Irritable bowel syndrome (IBS) has been reported in 10% to 22% of the general adult population. Previous studies have investigated the prevalence of IBS among patients with psychiatric disorders including generalized anxiety disorder (37%), major depression (37%), and panic disorder (16.46%).

A semi-structured clinical interview was administered to patients who were seeking treatment for OCD in outpatient and inpatient settings. Questions related to the diagnosis of IBS were included in the interview. Demographic data consisted of age, sex, marital status, and educational level. Other data included onset of the index episode, maximum improvement, response on the clinical global impression scale (CGI), past and family psychiatric history, history of bowel disease, use of laxatives or antacids. Several questions relating to the diagnosis of IBS such as abdominal pain, stool frequency, form were also included. GI symptoms that occurred after administration of TCAs and SSRIs were not considered.

Of the 26 patients in the OCD group, four patients (15.39461%) met criteria for IBS (Yates corrected p=0.1324). Of these, three (75%) had IBS with alternating diarrhea and constipation. The prevalence of IBS in the control group was 2.5% (p=0.0005). In a similar study conducted in India with patients suffering from OCD, prevalence of OCD was 26.23% vs 3.48% in the control group. There is need for more cross-cultural studies to replicate the findings of our study and also learn more about cross-cultural differences.

NR170 Monday, May 7, 3:00 p.m.-5:00 p.m.

Reisperidone Treatment for Chronic, Combat-Related PTSD

Ludmila Defaria, M.D., *Department of Psychiatry, Miami VAMC & UM, 1201 NW 16th Street, 116A, Miami, FL 33125*; Olga Lapeyra, M.D., Thomas A. Mellman, M.D., Daniella David, M.D.

Summary:

Background: Psychotic symptoms have been reported in chronic PTSD, and neuroleptics have been used in this population, yet little is known about their effectiveness. The study objectives are to determine whether risperidone, an atypical neuroleptic, is effective in decreasing symptom severity and psychosis in PTSD, and whether it is well tolerated.

Methods: This was a pilot, open-label, 12-week, flexible dose trial of adjunctive risperidone treatment in male combat veterans with chronic PTSD. Inclusion criteria were: PTSD as the primary diagnosis; no schizophrenia-spectrum disorder or mania as determined by structured assessment; being only partially responsive to current psychotropics and on stable doses for 4 weeks; free of alcohol and drugs and medically stable. Structured interviews for PTSD (CAPS) and psychosis (PANSS), self-report measures of sleep disturbance and hostility, an ECG, and routine blood tests were obtained at baseline, 6, and 12 weeks. Adverse events were assessed at 2-week intervals. Medication efficacy are evaluated by comparing baseline ratings with the ratings at 6 or 12 weeks by paired t-tests.

Results: Eleven patients completed at least 6 weeks of the trial to date. Mean age was 53.5 years (SD=4.6), 46% were white, 18% were black, and 36% were hispanic. Of the PTSD clusters, re-experiencing symptoms improved at a trend level (t=2.16, df= 10, p=0.06). Psychotic symptoms decreased in all domains but did not reach statistical significance. Of the sleep variables, significant improvement was found in the number of awakenings per night (2.8 [SD=0.9] versus 1.8 [SD=0.7]; t=2.8, df=9, p=0.02). No major adverse events occurred. Common side effects were dry mouth, sedation, and headaches.

Conclusion: Preliminary results demonstrate that risperidone as adjunctive treatment in chronic PTSD may have mild to moderate beneficial effects and is well tolerated.

NR171 Monday, May 7, 3:00 p.m.-5:00 p.m.

Gabapentin in Bipolar Disorder: A Retrospective Analysis

John P. Olarte, *Department of Psychiatry, Vanderbilt University, 1500 21st Avenue, South, #2200, Nashville, TN 37212*; Emily Stoneman, Alan J. Lynch, M.D., Earl Q. Parrott, M.D., Mary J. Kujawa, M.D., Richard C. Shelton, M.D.

Summary:

Objective: To evaluate the effectiveness of gabapentin in bipolar disorder.

Methods: A retrospective chart review at three outpatient sites was conducted for patients meeting criteria for bipolar disorder (BD) (N=117) who had been treated with gabapentin (GP) as a mood stabilizer. In addition to demographic and treatment variables, retrospective Clinical Global Impression (CGI), Severity and Improvement Scales were estimated for immediate (first month), early (first 3 months), and maintenance (>3 months) response.

Results: The mean dose of GP was 1583.6 mg/day (SD=835.9). The mean duration of GP treatment was 12.5 months (at evaluation). GP was maintained in 53% by the time of the evaluation. BD subtypes at GP initiation were manic (20%), depressed (30.4%), mixed (38.3%), euthymic (5.2%), and unknown (5.2%). 15.7% were rapid cyclers, and 36.5% were psychotic. The most common concomitant medication was divalproex (20%). CGI excellent or good ratings for response were as follows: immediate=41.7%, acute = 40%, maintenance=18.3%.

Conclusions: These data indicate that GP produced a good initial effect in a sizable proportion of these patients but that there was not a sustained long-term effect.

Funding Source: Abbott Pharmaceuticals.

NR172 Monday, May 7, 3:00 p.m.-5:00 p.m.

Time Course of Antipsychotics and Prescribing Practices in Acute Care

Babak Mirin-Babazadeghan, M.D., *Department of Psychiatry, Suny-Health Science Center at Brooklyn, 450 Clarkson*

Avenue, Box 1203, Brooklyn, NY 11203-2098; Zinat Sobhani, M.D., Erika Mojciuk, M.A., Edward M. Laski, M.D., Manuel Martinez-Bove, M.D., Alia Shivji, M.D., Peter J. Weiden, M.D.

Summary:

Objective: Newer antipsychotics have long-term advantages but are considered by some clinicians to have slower response times than conventional antipsychotics (1, 2). The goal of this study was to investigate predictors of response to antipsychotic medications in "real-world" acute treatment conditions.

Methods: This prospective study included 43 newly admitted patients at two urban medical centers in Brooklyn, NY. Average age was 33.5 (range=17–61). All were acutely psychotic, and 67% had a primary diagnosis of schizophrenia. Three timepoint assessments were performed for each subject over 2 weeks (baseline and 1 and 2 weeks) using Positive and Negative Scale of Symptoms (PANSS) and Clinical Global Impression (CGI). Medication choice was made as per usual physicians' clinical routine, then each patient was categorized in one of three groups: 1) atypical antipsychotics (N=13), 2) typical antipsychotics (N=15), or 3) combination of both (N=15). We tested the interaction between each category of drug treatment and time response by using 2 by 2 factorial ANOVA.

Results: Baseline level of symptoms was the same for each group. We did not find any significant difference in treatment response among the three groups, but there was a significant difference in prescribing patterns among different sites ($p<0.01$). Furthermore, we found an association between baseline insight scores (PANSS insight item) and prescribing practices, namely, more insight was associated with greater likelihood of being treated with atypical antipsychotic medications ($p<0.05$).

Conclusion: Time course of response does not seem to differ with initial medication selection. Baseline factors influencing choice of antipsychotic treatment seem to include 1) the clinician's prescribing practice, and 2) patient's level of insight.

NR173 Monday, May 7, 3:00 p.m.-5:00 p.m.

Effect of Lithium on Inositol Monophosphatase (IMPase) mRNA Levels in Stabilized Bipolar Disorder Patients

Sang-Yoon Kim, B.S., *Department of Psychiatry, Korea University Hospital, 126-1, 5KA, Anam-Dong, Sungbuk-Ku, Seoul 136-705, Korea*; Min-Soo Lee, M.D., Jin-Eun Choi, M.S.

Summary:

Lithium remains the most widely used drug of choice for bipolar affective disorder. One of the hypothesized mechanisms of action for the therapeutic effects of lithium in bipolar disorder is inhibition of IMPase. Inositol monophosphatase (IMPase) catalyzes the dephosphorylation of inositol monophosphates, which are recycled to inositol, a precursor for the synthesis of inositol phospholipids. To examine for possible quick detection of disease and predictor of the therapeutic response, we investigated the expression of IMPase in fresh lymphocytes. We performed the PCR to quantitate expression of IMPase mRNA with internal reference standard (β-actin mRNA) and investigated the IMPase mRNA expression in peripheral blood lymphocytes from 26 drug-treated bipolar disorder patients (19 men, 7 women) and 26 control subjects (19 men, 7 women). There was statistically no difference ($t=0.091$, $p=0.928$) between bipolar patients and normal control subjects in IMPase relative mRNA expression level. Because of focusing on patients reached at steady state after lithium treatment, IMPase expression levels of bipolar patients may be similar to that of normal control subjects. Further investigations in bipolar disorder with larger samples are necessary to conclude IMPase expression is a predictor of bipolar disorder.

NR174 Monday, May 7, 3:00 p.m.-5:00 p.m.

Effects of Psychotherapy for Personality Disorders Alone and in Combination with Psychopharmacological Treatment

Ludwig Teusch, M.D., *Department of Psychiatry, EV University, Grutholzallee 21, Castrop-Rauxel, D 44577, Germany*; Hildegard Boehme, Jobst Finke, M.D., Markus T. Gastpar

Summary:

Background: There is an increasing interest in data about the efficacy of psychotherapeutic strategies and combinations with medication in the treatment of patients with personality disorders.

Methods: The efficacy of an inpatient client-centered treatment program (CCT) was studied prospectively in 142 patients with personality disorders and additional depressive, anxiety, or eating disorders (ICD-10).

Results: Significant changes in depression, self-esteem, social adjustment were achieved up to discharge and remained stable at 1-year follow-up. The efficacy with regard to individual variables or the total result could not be enhanced by a combination with psychopharmacological treatment (CCT+MED; N=46), mainly antidepressants. Within the subgroups of patients with socially deviant (F60.0–2), emotionally unstable/borderline (F60.3), and histrionic/narcissistic personality disorders (F60.4, F60.8), CCT was significantly superior in the reduction of depression (BRMES-ratings), whereas the response was enhanced by medication in the subgroup of patients with socially dependent "Cluster C"-personality disorders (F60.5–7).

Conclusions: The results are discussed with regard to client-centered therapeutic concepts and to the further development of differential combination strategies.

NR175 Monday, May 7, 3:00 p.m.-5:00 p.m.

Patients' Perspective of Collaborative Treatment

Ravi K. Singareddy, M.D., *Department of Psychiatry, Wayne State University, 2751 East Jefferson, Suite 400, Detroit, MI 48207-4100*; Richard Balon, M.D., Sajida Mathew, M.D., Sarabjit Singh, M.D.

Summary:

The practice of collaborative treatment in which more than one mental health professional manages patients with psychiatric illness has been widespread. In this preliminary study, views and understanding of collaborative treatment were examined in 20 patients seen by both a psychiatrist and another therapist at university outpatient clinics. The subjects were asked to complete a 15-item questionnaire about collaborative treatment. Most of the subjects responded that psychiatrist are M.D.s (17 of 20) and have different training from therapists (15 of 20), but they can do therapy (19 of 20) and that only psychiatrists can prescribe medication (19 of 20). Thirteen patients thought they can call either the psychiatrist or therapist during crisis, but 11 said they would prefer to call the therapist in such a situation. Seventeen patients said they would call the psychiatrist and three felt they can call either of them if they have a problem with medication; in case of side effects from medication, 19 thought it is more appropriate to talk to a psychiatrist. Although 17 subjects said that getting treatment from two different persons is more helpful, 15 thought that psychiatrists are more qualified to treat mental illness and 13 felt that the psychiatrist is overall responsible for the treatment. Psychiatric patients seem to understand the roles of various parties in collaborative treatment and feel that psychiatrists are more qualified than other mental health professionals.

NR176 Monday, May 7, 3:00 p.m.-5:00 p.m.

Psychiatric Symptoms of People in Temporal Houses After the Chi-Chi Earthquake

Li-Shiu Chou, M.D., *Kai-Suan Psychiatric Hospital, 130 Kai-Suan 2nd Ling-Ya District, Kaohsiung 802, Taiwan*; Frank H.C. Chou, M.D., Keng-hsin Lin, M.D., Yung-Lung Lin, M.D., Wei-Tsuen Soong, M.D.

Summary:

Objective: To evaluate mental health problems of people in Tung-Shih temporal houses after the Chi-Chi earthquake in Taiwan.

Methods: We used self-report questionnaires to explore the severity and frequency of psychiatric symptoms and basic information of the people older than 16 years old who were living in Tung-Shih temporal houses 3 months after the Chi-Chi earthquake. The collected data was analyzed with SPSS 7.0 version.

Results: A total of 418 subjects were interviewed and assessed with the post-traumatic symptom scale, but only 398 subjects who completed the assessment could be analyzed. High percentages of subjects suffered from moderate to severe residential damage (97.8%), death of family members and close relatives (25%), and mild to moderate personal physical injury (27.2%). 25% of the subjects experienced sleep disturbance and more than three symptoms of PTSD. The four most common symptoms were exaggerated startle response (48.3%), hypervigilence (38.9), difficulty in concentrating (30.5%), and recurrent and intrusive distressing recollections of the event (29.5%).

Conclusion: People living in temporal houses are at high risk for having PTSD.

NR177 Monday, May 7, 3:00 p.m.-5:00 p.m.

The Role of Affective Liability Among the Recurrently Suicidal

Marnin J. Heisel, M.A., *Suicide Chairman, St. Michael's Hospital, 30 Bond Street, Suite 2004 2DS, Toronto, ON M5B 1W8, Canada*; Paul S. Links, M.D.

Summary:

The present study examined the relationship between affective lability, impulsivity, and suicidality in a clinical sample of recurrently suicidal individuals with borderline personality features. Participants included 21 individuals (13 female and eight male, mean age = 37.3 years, *SD*=10.5) taking part in an outpatient psychosocial intervention group for the recurrently suicidal. Participants completed multiple measures of affective lability, impulsivity, clinical symptomatology, and suicidality upon entry to the study. Participants also completed a single-item Visual Analogue Mood Scale (VAMS) twice daily over a two-week period, assessing the variability and intensity of their current mood. VAMS affective intensity ratings correlated significantly with measures of affective lability (r=.71, p<0.01; r=.50, p<0.05), depressive symptomatology r=.65, p<0.01; r=.56, p<0.05), and suicidality r=.66, p<0.01). Conversely, VAMS affective lability ratings, measured with successive differences mean squared, failed to correlate significantly with these measures, indicating that existing measures of affective lability appear more closely linked to emotional intensity than to emotional variability. Finally, the results of a hierarchical multiple regression analysis demonstrated that affective intensity accounted for significant additional variability of suicidality scores (F-change$_{(1, 12)}$=7.1, p<0.05; R^2=.52), above and beyond the contributions of impulsivity and depressive symptomatology, manifesting the key role of emotional variability in suicidal ideation and behavior. These findings have implications for theory building and clinical practice with recurrently suicidal individuals.

NR178 Monday, May 7, 3:00 p.m.-5:00 p.m.

Classification of Suicides Among Active Duty Military Personnel

Joel R. Carr, D.O., *Department of Neuropsychiatry, Walter Reed, WRAIR, 503 Robert Grant Avenue, Silver Spring, MD 20910*; Charles Hoge, M.D., Gregory L. Belenky, M.D., David Niebuhr, M.D., John Gardner, M.D., Robert Potter

Summary:

Objective: Annual fluctuations in suicide rates have been observed in the active duty military. The potential for misclassification as the fluctuation source has not been investigated. This study examines patterns in the classification of deaths on the military Report of Casualty (DD1300), which are comparable to civilian death certificates.

Method: All military deaths in 1998 and 1999 were reviewed using the Department of Defense Medical Mortality Registry. Records with uncertain or limited detail on the DD1300 were explored using additional resources (Investigative Agency and Medical Examiner Reports). Records were then independently reviewed by three investigators and compared for agreement on classification of death ("suicide," "accident," "homicide," or "undetermined"). Percent misclassification for each death class was then calculated.

Results: 1674 military deaths were recorded in 1998 and 1999. Approximately 7% of military deaths were classified as "undetermined"; some may in fact have been suicide. Additional data are being collected on approximately 240 cases.

Conclusions: This study determined whether there were self-inflicted deaths that might have been misclassified into categories such as "undetermined" or "accident" (injury). Suicide prevalence was estimated, risk factor analysis performed, and reasons for uncertain classifications identified by describing the process by which deaths are coded in the military.

Abstract Word count: 199

NR179 Monday, May 7, 3:00 p.m.-5:00 p.m.

Adequacy of Assessment of Adolescent Suicide Attempts

Daniela M. White, M.D., *Department of Psychiatry, Baylor College, 10930 Braes Bayou Drive, Houston, TX 77071*; John Langdoc, B.S., Xiaotong Han, M.S., Jeffrey Starke, M.D., Kathryn J. Kotrla, M.D.

Summary:

Objective: Because suicide is a leading cause of death in adolescents, this study evaluated the adequacy of the assessment and follow-up care plans of adolescents who presented to the emergency room with their first suicide attempt.

Method: This study utilized a retrospective review of 100 charts to compare the assessment by pediatricians and psychiatrists of known suicide risk factors in suicidal patients. Each chart was reviewed using a checklist of risk factors and quality of assessment variables that were checked as present or absent. The differences between the assessment by pediatricians and psychiatrists were tested using McNemar's test.

Results: Biological risk factors were assessed in higher percentages by pediatricians (69.77%–89.66%) than by psychiatrists (37.21%–74.14%). Psychiatric illnesses, psychosocial risk factors, quality of assessment, and follow-up care variables were assessed in higher percentages by psychiatrists (43.10%–94.83%) than by pediatricians (25.86%–86.21%).

Conclusions: These results raise significant concerns about the adequacy of assessment of adolescents with a suicide attempt, suggesting the need for a standardized suicide assessment and educational interventions by both pediatricians and psychiatrists. This would be especially beneficial for clinical settings without available psychiatric consultation.

NR180 Monday, May 7, 3:00 p.m.-5:00 p.m.

Work Stress and Emotional Health in the U.S. Air Force

Steven E. Pflanz, M.D., *Department of Mental Health, FE Warren Air Force Base, 408 West First Avenue, Cheyenne, WY 82001*

Summary:

Objective: One out of every 10 American workers reports exposure to mental stress at work, and 5% believe that their experience of work stress could be deleterious to their mental health. This study examined the incidence of occupational stress and its relationship to work stress in military personnel.

Methods: 472 military personnel answered a 65-item survey that included items on the perception of occupational stress and reported life events. It incorporated the 43-item Schedule of Recent Experiences (SRE). By adding the weighted values assigned to the 43 items, each respondent was given an SRE score, which is a measure of overall stress and has been shown to be predictive of future illnesses.

Results: Significantly more military personnel reported job stress than the general American working population ($p<0.001$). 26% reported suffering from significant work stress. 15% reported that work stress was causing them significant emotional distress. 8% reported suffering from work stress that was so severe that it was believed to be damaging their emotional health. The average SRE score for all respondents was 160, reflecting increased risk for future illnesses. Generic work stressors were reported far more frequently than military specific stressors.

Conclusions: These results support previous research that indicates that work stress may be a significant occupational health hazard in the military. Using this data, interventions can be planned to mitigate the impact of stress caused by the military work environment on the mental health of military personnel.

NR181 Monday, May 7, 3:00 p.m.-5:00 p.m.

Relationship of Demographic Variables on Illness Knowledge and Empowerment in Schizophrenia

Jo A. Hall, M.D., *Department of Psychiatry, University of Maryland, 701 West Pratt Street, 4th Floor, Baltimore, MD 21201*; Elaine Koukoulas, M.D., Janine C. Delahanty, M.A., Alicia Lucksted, Ph.D., Letitia T. Postrado, Ph.D., Lisa B. Dixon, M.D.

Summary:

Introduction: Empowerment and knowledge are thought to be critical components of illness recovery. This study assessed the relationship between demographic factors and self-perceived illness knowledge and empowerment in schizophrenia.

Methods: The Schizophrenia Patient Outcomes Research Team project interviewed and conducted chart reviews of 719 consenting persons receiving treatment for schizophrenia in two states. Participants rated their illness knowledge and completed an empowerment scale. The independent variables of age, gender, educational level, marital status, and race were entered into a multivariate model with empowerment and knowledge as dependent variables. Patients were a mean of 43.19 years of age, 53.6% Caucasian, 63.1% male, 48.8% ever married, and had a mean of 11.83 years of education.

Results: Younger age ($p<.001$), Caucasian race ($p<.001$), and advanced education ($p<.001$) positively predicted illness knowledge. Caucasian race ($p<.05$) was associated with increased empowerment.

Conclusions: The association of age, education, and race with knowledge, and of race with empowerment, suggest that it is important to target subgroups of persons with schizophrenia for mental health literacy programs. These associations also reflect trends found in nonschizophrenic populations on similar measures.

NR182 Monday, May 7, 3:00 p.m.-5:00 p.m.

Prevalence of Hepatitis C Among Institutionalized Psychiatric Patients

Rayan K. AlJurdi, M.D., *Department of Psychiatry, Baylor College of Medicine, 3620 Garrott, # 16H, Houston, TX 77006*; John W. Burruss, M.D.

Summary:

Psychiatrists are seeing an increasing number of hepatitis C seropositive patients, especifically, patients with a history of substance abuse and those undergoing psychological evaluation before starting IFN-alpha treatment. While hepatitis C affects 1% to 2% of the general population, very few reports in the literature attempt to document prevalance of hepatitis C infection among institutionalized psychiatric patients. All patients admitted to a large, urban, charity hospital between October 15 and December 15, 2000, were tested for hepatitis C utilizing Enzyme-Linked Immunosorbent Assay (ELISA). A total of 83 of 96 patients (86.5%) underwent serum testing of which 14 (16.9%) were positive for hepatitis C antibodies. Prevalence of hepatitis C was significantly higher among homeless patients and those with a history of sexual abuse, physical abuse, IV drug abuse, and STDs. A total of 38.5% of patients with cluster B personality disorder were hepatitis C positive compared with 10.0% of patients with no axis II diagnosis ($P=0.48$). A total of 31% of patients with depression were found to be hepatitis C positive, compared with 10.0% with bipolar disorder and 8.8% with psychosis. These findings suggest that institutionalized mentally ill patients form a high-risk population for hepatitis C infection. Notably, patients without a history of substance abuse were also found to be at a significantly higher risk of acquiring hepatitis C.

NR183 Monday, May 7, 3:00 p.m.-5:00 p.m.

Empowerment, Depression, and Burden Among Family Members of Individuals with Severe Mental Illness Enrolled in a Self-Help Program

Sandeep S. Saroch, M.D., *Department of Psychiatry, University of Maryland, 701 West Pratt Street, 4th Floor, Baltimore, MD 21201*; Lisa B. Dixon, M.D., Marcia Hoffman, M.A., Betty Stewart, B.S., Alicia Lucksted, Ph.D., Cherise Wilmore, B.S.W., Colleen McGuire

Summary:

Introduction: Families of persons with severe mental illness (SMI) experience stress and burden. This study assesses the relationship between demographic characteristics of family members and factors of the family experience of severe mental illness among 104 family member enrollees of the NAMI Family-to-Family Education Program (FFEP).

Methods: A total of 104 consenting family members from Maryland agreed to participate in the study of FFEP effectiveness. The waitlist assessments included standardized measures of family burden, mastery, depression, and empowerment. Analyses of variance and correlations were performed on waitlist interviews to assess whether family member age, education, gender, race, relationship to ill family member, and marital and employment status were associated with different family experience.

Results: Women ($N=74$) reported more depression ($p=0.01$) and greater service system empowerment ($p<0.05$) than men ($N=30$). Non-Caucasians ($N=29$) scored higher on overall empowerment ($p<0.001$) and its family ($p<0.001$) and service system subscales than Caucasians ($N=70$). Unmarried family members ($N=41$) also scored higher on family empowerment ($p=0.05$) than

those who were married (N=63). Parents (N=59) reported more worry (p=0.01) than other family members (N=44). Employed family members (N=65) had higher community empowerment (p<0.05) and higher self-esteem (p<0.02) than those not working (N=39).

Conclusion: These preliminary results suggest subgroups of family members who have greater resources or who might need special help in coping with severe mental illness, whether that help is delivered via the traditional service system or through a family self-help program.

NR184 Monday, May 7, 3:00 p.m.-5:00 p.m.

Use and Outcome of Conditional Release in Civilly Committed Patients

David M. Montani, M.D., *Department of Psychiatry and Law, Rush University, 1720 West Polk, Room 022, Chicago, IL 60612; M.A.*

Summary:

Objective: Forced outpatient treatment outside the criminal commitment setting is one tool for reducing hospital recidivism. Outcome studies are rare, and results have been mixed. Since such treatment is a matter of state law, conditions of its use vary widely, limiting generalization of findings. This study examines the use and outcome of conditional release in civilly committed patients in Missouri.

Methods: Chart reviews were performed at Metropolitan St. Louis Psychiatric Center (MPC) on every patient committed in 1997–98 and eligible for conditional release (N=154).

Results: Conditional release was granted in 63 hospitalizations, while the other 91 ended in a regular discharge. Those receiving conditional release were more likely to have longer hospitalizations and commitment times, to have received schizophrenia spectrum diagnoses, and to have been admitted to an academic floor. Those not receiving conditional release were more likely to have been suicidal and have affective disorder and personality disorder diagnoses. Demographic factors and rate of psychosis, assaultiveness, and substance use did not differ between the two groups. Compared with the year prior to incident hospitalization, those receiving conditional release showed a reduction in their MPC use while the others did not.

Conclusions: While individual physician practices varied, conditional release was used on a distinct patient population and was associated with less MPC usage.

NR185 Monday, May 7, 3:00 p.m.-5:00 p.m.

Suppression of Cellular Immunity in Subjects with a History of PTSD

Noriyuki Kawamura, M.D., *Division of Psyhcosom., National Institute of Mental Health, 1-7-3 Kounodai, Ichikawa Chiba 272-0827, Japan*; Yoshiharu Kim, M.D., Nozomu Asukai, M.D., Toshio Ishikawa, M.D., Komaki Gen

Summary:

Objective: Increased rates of medical morbidity and increased visits to the medical office have been reported in posttraumatic stress disorder (PTSD) subjects. This might suggest that some profound biological changes may accompany PTSD. We examined lower immune function in subjects in remission from past PTSD.

Method: Out of 1,550 Japanese male workers, 12 with past PTSD were recruited through the Impact of Event Scale-Revised (IES-R) and Structured Clinical Interview for DSM-IV (SCID). We matched the control subjects by age and smoking habit, which affects immunity, and compared NK cell activity, lymphocyte subset counts, and interferon γ (IFN-γ) and IL-4 production through phytohemaglutinin (PHA) stimulation in vitro.

Results: The numbers of lymphocytes and T cells, NK cell activity, and especially total amounts of IFN-γ and IL-4 were significantly lower in the past PTSD group.

Conclusion: PTSD leaves a long-lasting immunosuppression and has long-term implications for health.

This work was supported by the aid of the grant of PTSD research from Ministry of Health and Welfare of Japan: 10B-4.

NR186 Monday, May 7, 3:00 p.m.-5:00 p.m.

ECT in Canada: A Survey of Senior Residents in Psychiatry

Edward S. Yuzda, M.D., *Department of Psychiatry, CAMH, 250 College Street, Room 814B, Toronto, ON M5T 1R8, Canada*; David S. Goldbloom, M.D., Kathryn Parher, M.A., Vivien Parher, M.D., Justin Geagea, M.D.

Summary:

Objective: A survey of senior psychiatric residents' experience of electroconvulsive therapy (ECT) training was undertaken by one of us approximately 12 years ago. Since then, guidelines have been published in both Canada (1992) and the United States (1990) regarding ECT training in psychiatry residency programs. This study examines whether these guidelines have altered Canadian residents' experience.

Method: Confidential questionnaires assessing the training of and attitudes toward ECT were sent to all 133 psychiatric residents in their final year of training in Canadian medical schools.

Results: A response rate of 68.3% was attained. 88.9% of respondents felt that theoretical and practical training of ECT should be a mandatory component of psychiatric residency programs. No marked improvements have occurred with respect to both didactic and bedside training of ECT when compared with the original study. Only 18% of respondents said that they feel completely competent regarding the administration of ECT. Despite this, 59.3% of them anticipate working in an inpatient setting.

Conclusion: The publication of training guidelines has made little impact on the training in and attitudes toward ECT in senior psychiatric residents in Canada.

NR187 Monday, May 7, 3:00 p.m.-5:00 p.m.

Harnessing the Media: Innovative Methods in Psychiatric Education

Dahlia A. Saad, M.D., *Department of Psychiatry, Mayo Clinic, 200 First Street, SW, Rochester, MN 55901*; Lois E. Krahn, M.D.

Summary:

It is somewhat intuitive that psychiatry of all the medical specialties provides fertile subject matter for the arts. Movies, music and literature, fiction and biographical, depict psychiatric issues. This innovative medical school course was designed with two goals in mind. One was to harness the effective power of various art genres to aid in learning while utilizing the content of these excerpts from popular film, music, and literature to illustrate personality styles, axis I psychopathology, as well as treatment. The other aim was to encourage students to become more astute observers of behavior, necessary for success as physicians in any field.

Faculty and student feedback after these sessions has been that the use of this type of material has generated enthusiastic participation and discussion on the part of the students who took the initiative to bring in material for "dissection." It has also served to demystify psychiatric illness and treatment, starting a discussion, instead, on the stigmatization of the psychiatrically ill.

The details of the structure and content of this lecture series will be presented. Results of a short survey completed by the students, including quotations, will also be presented.

NR188 Monday, May 7, 3:00 p.m.-5:00 p.m.

Audience Preferences for the Programming and Presentation of Grand Rounds

John S. Teshima, M.D., *Department of Psychiatry, SunnyBrook, 2075 Bayview Avenue, Toronto, ON M4N 3M5, Canada*

Summary:

Objective: Grand rounds has been a traditional source of continuing medical education in psychiatry. However, its current format, dominated by discrete didactic lectures, may not be as educationally effective as it could be. Suggestions for improving the educational impact of grand rounds include planning a formal curriculum and using more interactive teaching methods. This study proposed to find out how receptive a grand rounds audience would be to such changes.

Method: An anonymous questionnaire was distributed to all members of a general hospital psychiatry department, asking about their preferences for the programming and presentation of grand rounds.

Results: The return rate was 59%. Respondents favored discrete presentations over an integrated program of presentations. Teaching formats in which the audience plays a more passive role were favored over interactive formats.

Conclusions: These findings suggest that changes to make grand rounds more educationally effective may not be very acceptable to the target audience. Reasons for this lack of acceptance may include a lack of familiarity and comfort with more effective educational formats. Further research is needed to explore why audiences may prefer less effective formats.

NR189 Monday, May 7, 3:00 p.m.-5:00 p.m.

Psychological Effects of Informing Arabic Children with Leukemia About Their Diagnosis

Tarek Sherif, M.R.C., *Department of Psychiatry, King Khalid Ng Hospital, P O Box 9515, Jeddah 21423, Saudi Arabia*; Mona Harthi, B.Psych., Chris Fryer, M.R.C., Mustafa K. Saadani, M.D., Sami Felimban, M.D.

Summary:

Some families in the Middle East region do not wish their children to be told of the diagnosis of leukemia. The aim of this study was to ascertain if there were more behavioral changes, depression, and physical symptoms in the children with leukemia who were not informed about their diagnosis compared to informed children.

Methods: Children who were eligible for this study had been diagnosed with leukemia within 6 months of study entry. There were two such groups. Twenty-one children had been informed about their diagnosis. A second group of 19 children had not been told of their diagnosis at their parents' insistence. Eighteen healthy children with similar sociocultural and demographic data were chosen as control subjects. All children were administered the Arabic Children Depression Inventory and the Brief Scale for the Assessment of Child and Adolescent Behavior.

Results: The mean scores of both scales were significantly higher in the group whose families refused to inform their ill children about their diagnosis (χ^2=–2.08 and –3.87, p=0.001 and 0.37, respectively). The children with leukemia who had been told of their diagnosis had similar scores to the control group.

Conclusion: Informing children with leukemia of their diagnosis reduces the psychological sequelae of the diagnosis. Failure to inform these children resulted in adverse emotional and behavioral changes.

NR190 Monday, May 7, 3:00 p.m.-5:00 p.m.

Event-Related Potential (ERP) Response to Performance Feedback: A Marker for Anhedonia?

Amy R. Noll, B.A., *Department of Psychiatry, Duke University, P O Box 3309 DUMC, Durham, NC 27710*; Andrew D. Krystal, M.D., Jean Hamilton, M.D.

Summary:

Objectives: Anhedonia is a central feature of major depression; however, its neurophysiology is poorly understood. Some evidence suggests that anhedonia in depression is characterized by (1) diminished response to positive feedback, (2) enhanced response to negative feedback, and (3) enhanced expectancy of negative outcomes. Based on preliminary data we plan to study neurophysiologic correlates of these phenomena by assessing the event-related EEG potential (ERP) response to performance feedback. As a first step, we carried out this pilot study of the ERP response to feedback in a simple word task in three normal subjects.

Methods: For each trial subjects were presented with a test word, asked to choose the best synonym from a subsequent pair of words, and given feedback ("correct" or "wrong"). ERPs were derived from time-locked averaging (over hundreds of trials) of the 21-channel EEG response immediately prior to and after feedback.

Results: We found a complex surface-positive potential lasting from 800–400 msec prior to feedback, which had different morphology and topology for positive and negative feedback.

Conclusions: We may be able to study the neurophysiology of the expectation component of anhedonia with this paradigm. Results of analysis, including additional subjects, will be presented.

NR191 Monday, May 7, 3:00 p.m.-5:00 p.m.

Psychosis in Dementia: Further Findings from the Cache County Study of Memory in Aging

Iracema Leroi, M.D., *Department of Psychiatry, Johns Hopkins University, 600 North Wolfe Street, Olser 320, Baltimore, MD 21287-5371*; Argyro Voulgari, Ph.D., Constanine G. Lyketsos, M.D., John C.S. Breitner, M.D.

Summary:

Objective: To examine in a population sample the prevalence, severity, clinical, and demographic associations of individual symptoms of psychosis in Alzheimer is disease (AD) and vascular dementia (VAD).

Method: A total of 260 participants with dementia, derived from the Cache County Study on Memory in Aging (CCSMA), were examined with the Neuropsychiatric Inventory (NPI), a method for ascertainment and classification of dementia-associated mental and behavioral disturbances. Individual symptoms on the NPI subsets of delusions and hallucinations were examined.

Results: Psychosis (hallucinations and/or delusions) was more prevalent, but of comparable severity, in AD (26.9%) as compared with VAD (15.3%). Delusion of theft was the most common form of delusion in both types of dementia. In AD, persecutory delusions were more prevalent than in VAD (16% vs. 6.8%, respectively), whereas, there was no significant difference in the prevalence of misidentification phenomena between the two groups. The risk factors for delusions in AD were older age of onset (over 85), longer duration of illness, and female sex.

Conclusion: This is the first U.S. population-based study of mental/behavioral disturbances in dementia. Although there were

significant differences in prevalence and type of certain psychotic phenomena, AD and VAD could not be distinguished by psychotic symptoms alone.

NR192 Monday, May 7, 3:00 p.m.-5:00 p.m.

Redefining Remission in Late-Life Depression

Jordan F. Karp, M.D., *Department of Psychiatry, Columbia University-NYSPI, 1051 Riverside Drive, Box 94, New York, NY 10032*; Steven P. Roose, M.D., Harold A. Sackeim, Ph.D., Vanessa Pesce, B.A.

Summary:

There have been numerous attempts to characterize the natural course of unipolar depression. Such information provides a framework for a coherent, long-term treatment plan. A schema was proposed by Frank et. al. in their 1991 paper that describes the five "R's" of depression: response, remission relapse, recovery, and recurrence. These investigators stated that a need for operationalization and empiric validation of these terms was necessary for the development of improved treatment guidelines for clinical practice.

While Frank and colleagues offered definitions of full and partial remission, they did not quantify or provide specific empirically proven criteria. Their definitions included statements such as "an improvement of sufficient magnitude . . ." or ". . . continues to evidence more than minimal symptoms." These descriptions will obviously be applied differently by different investigators. Even if the definitions are quantified there is variability. Criteria have ranged from Hamilton scores as low as 7 to as high as 11 (Nierenberg and Wright, 1999). In our own study of late-life patients with unipolar depression, patients are considered to have responded to treatment and to be in remission if they have a final HRSD score ≤ 10 and a reduction ≥ 50% in HRSD score from the end of the placebo period to the end of the 12-week acute phase of treatment.

We report the results of a double-blind, randomized controlled trial of sertraline versus nortriptyline in unipolar depressed patients over 60, whose remission criteria was a priori defined as a final HRSD score ≤ 10. To date 33 patients have met response criteria after 12 weeks of acute treatment. Seventy nine percent of the patients had a final HRSD score ≤ 6. Of these 26 patients, 24 also met response criteria in the previous week. Twenty one percent had HRSD > 6, and all had final HRSD scores of either 9 or 10. Of these seven patients, only one met criteria for remission in the previous week. Perhaps most intriguingly, 18 of the 29 patients (62%) who had final HRSD scores ≤ 6 completed 6 months of continuation treatment, and all but one patient (94%) remained in remission at the end of 6 months. Among patients with final HRSD score > 6, six of the seven patients (86%) completed the continuation phase. Of these, only 50% remained well.

These data suggest that remission criteria should be empirically constructed on the basis of a final HRSD that predicts a sustained and robust response and not be arbitrarily designated. In addition, meeting this criteria for two successive HRSD scores may be a better predictor of improved response.

NR193 Monday, May 7, 3:00 p.m.-5:00 p.m.

Predictors of Psychiatric Consultation in Nursing Home Residents

Joanne Fenton, M.D., *Department of Psychiatry, Baltimore VA, 10 North Greene Street, Baltimore, MD 21201*; Allen Raskin, Ph.D., Ann L. Gruber-Baldini, Ph.D., Srikumar Menon, M.D., Bruce A. Kaup, M.D., David J. Loreck, M.D., Paul E. Ruskin, M.D.

Summary:

Objective: To determine if depression and/or behavioral problems increase the rate of psychiatric consultation in nursing home residents.

Methods: Subjects were recruited from a stratified random sample of 59 nursing homes across Maryland. All new admissions from September 1992 through March 1995, aged 65 years and older who had not been a resident in a nursing home in the previous year, were eligible for the study. A total of 2,015 subjects are included in this analysis. Variables examined were the Cornell Depression Scale, the Psychogeriatric Dependency Rating Scale (Behavioral Subscale), demographic information (age, sex, race), and whether the resident had a psychiatric consultation within 90 days of admission.

Results: Twenty percent (n=404) of the residents had a psychiatric consultation. There was no significant association with demographic variables. Logistic regression revealed that both agitation and depression independently increased the rate of psychiatric consultation ($p<.05$). However, residents with both behavioral problems and depression did not have a significantly higher rate of consultation than those with just one of these problems.

Conclusion: Behavioral problems and depression are common reasons for a psychiatric consultation. It would seem that nursing home staff are sensitive to depressive symptoms as well as behavioral disturbances.

Supported by the National Institute of Aging (Grant R01 AG 08211), the Veterans Affairs Maryland Healthcare System, and the Veterans Affairs Capital Network Mental Illness Research, Education, and Clinical Center (MIRECC)

NR194 Monday, May 7, 3:00 p.m.-5:00 p.m.

Predicting Vulnerability to Depression Following Spousal Bereavement in Older Individuals

Ni A. Khin, M.D., *Department of Geriatric Psychiatry, NIMH-NIH, 10 Center Drive, MSC 1275, Bethesda, MD 20892-1275*; Marilla Geraci, M.S.N., Larry Bauer, M.A., Eleanor Cannon-Spoor, M.A., Robert A. Lasser, M.D., Trey Sunderland, M.D.

Summary:

Loss of a spouse has been ranked as the most stressful life event among varied age groups and backgrounds (Holmes and Rahe, 1967). Among bereaved individuals, it is not known who is at greatest risk for increased morbidity from depression. Previous studies have suggested that high scores, on the Inventory of Complicated Grief (ICG,>25) may identify a vulnerable population (Prigerson 1995). In this study, individuals (n=71) over the age of 50 in stable health, were recruited from the community. Subjects were evaluated within three months of the loss and then followed monthly for the first year of bereavement. Subjects were divided into high ICG, (scores >25, n=27) and low ICG (scores <25, n= 44). A major depressive episode (MDD) was experienced by 9/27 high ICG, versus 4/44 low ICG subjects. Baseline Geriatric Depression Scale (GDS) scores were 11.16+(6.78, SD), and 4.56+(3.96, SD) in high/low ICG groups ($F=23.48$, $p<0.0001$). Twelve-month GDS scores were, 8.00+(4.54, SD), and 2.90+(3.29, SD), for high/low ICG groups ($F=8.61$, $p<0.001$). Additional factors such as anticipation of spousal death and premorbid experience of emotional trauma will be discussed as possible influences on the expression of depression during bereavement. Preliminary results from the study indicate that high ICG individuals are more likely to experience MDD, and longer adjustment difficulties, suggesting high ICG scores early in the bereavement process may select at-risk individuals, who will suffer from depression later.

NR195 Monday, May 7, 3:00 p.m.-5:00 p.m.

Behavioral Disturbances in Alzheimer's Disease: Direct and Indirect Costs

Ceri E. Hadda, M.D., *Department of Psychiatry, Mt. Sinai Medical Center, 1 Gustave Levy Place, Box 1228, New York, NY 10029*; Micheline Dugue, M.D., Deborah B. Marin, M.D., James Schmeidler, Ph.D., Steven C. Samuels, M.D., Judith A. Neugroschl, M.D., Kenneth L. Davis, M.D.

Summary:

Introduction: This study investigated the longitudinal course of behavioral disturbances and the direct and indirect costs in Alzheimer's disease patients.

Methods: A total of 44 patients living with caregivers were evaluated at six-month intervals over one and a half years. Indirect caregiving costs were assessed using the Caregiver Activity Survey (CAS), a five-item instrument measuring the amount of time a caregiver spends in daily tasks. A dollar value was given to each hour of care measured by the CAS. The level of behavioral disturbance was measured with the Alzheimer's Disease Assessment Scale, noncognitive subscale (ADAS-nc). Cognitive status was measured with the Mini Mental Status Exam (MMSE).

Results: The mean age of patients was 73.9 years (sd = 8.6); 34% were female. Mean MMSE was 12.8 (sd = 8.2). ADAS-nc correlates cross sectionally with CAS cost (in four samples, from r=.36, p=.07 to r=.64, p<.001) but not longitudinally (r=.04, p=.75). However, ADAS-nc does correlate longitudinally with the cost of hospitalization (r=0.31; p, .01) and inversely with the cost of medication (r=−.24; p<.05).

Conclusion: This is the first study to our knowledge to longitudinally evaluate the relationships of both cost and behavioral disturbance in Alzheimer's disease. Caregiver costs are cross-sectionally correlated with behavioral disturbance. The direct costs of medication and hospitalization also correlate longitudinally with behavioral disturbance. The negative result with longitudinal course could be due to the waxing and waning nature of behavioral disturbances.

Supported in part by National Institute of Aging grant #AG-02219, and a grant from Novartis.

NR196 Monday, May 7, 3:00 p.m.-5:00 p.m.

ApoE e4 Allele and Anticholinergic Cognitive Toxicity in the Aged

Hla Tun, M.D., *Department of Psychiatry, Cabrini Hospital, 227 East 19th Street, New York, NY 10003*; Raymundo T. Hernando, M.D., Corazon B. De La Pena, M.D., Keith Wesnes, Ph.D., Thomas Cooper, M.A., Nunzio Pomara, M.D.

Summary:

Background: The elderly exhibit considerable intersubject variability in the adverse cognitive effects of anticholinergic drugs, which cannot always be explained by pharmacokinetic factors such as increased serum anticholinergic activity. Several reports suggest that the ApoE ϵ4 allele, which is the major genetic risk factor for sporadic and late-onset familial Alzheimer's disease, could influence the sensitivity to anticholinergic cognitive toxicity. This pilot study examined the relationship between polymorphisms of the APOE gene and the cognitive effects of trihexyphenidyl, a muscarinic anticholinergic agent with documented effects on different cognitive functions including memory.

Methods: Nineteen elderly cognitively intact subjects (mean age=67.6 years ± SD=4.0), who were free of psychiatric and medical illnesses, participated in a double-blind, cross-over, placebo-controlled trial involving three sessions, each one week apart, in which they received single oral doses of Artane 1 mg or 2 mg, or placebo. A cognitive battery was administered at baseline, and at one, 2.5, and five hours following each acute drug challenge. This report will focus on the effects of trihexyphenidyl on the Buschke Selective Reminding Test (Total/Delayed Recall).

Results: Subjects with ApoE ϵ4 allele (n=7) showed a significant decrease in total delayed recall compared with placebo (ANOVA, p<0.01) at 2.5 hours following Artane (2 mg), whereas subjects with other ApoE alleles (n=12) showed no drug effect. Subjects with ApoE ϵ4 allele also exhibited a significantly greater deficit in delayed recall (p<0.05) than individuals without the ApoE ϵ4 allele.

Conclusion: These preliminary findings, if confirmed, suggest that the ApoE ϵ4 allele may be associated with increased sensitivity to anticholinergic drug-induced cognitive toxicity in the elderly.

NR197 Monday, May 7, 3:00 p.m.-5:00 p.m.

Antidepressant and Anxiolytic Use in a Nursing Home Population

Jane M. DeVeau, M.D., *Department of Psychiatry, Baltimore VA, 10 South Greene Street, Baltimore, MD 21201*; Bruce A. Kaup, M.D., David J. Loreck, M.D., Allen Raskin, Ph.D., Ann L. Gruber-Baldini, Ph.D., Srikumar Menon, M.D., Paul E. Ruskin, M.D.

Summary:

Objective: This study examines the longitudinal prescribing patterns over 24 months for antidepressants and anxiolytics in a nursing home admission sample.

Methods: Data from 2,285 persons selected from all patients or proxy providing informed consent admitted to 59 Maryland nursing facilities between 1992–1995 was obtained through family, patient, nursing staff interviews, and medical chart review. For the present analysis, a subset of 336 patients were reviewed for medication usage at baseline and 6-month intervals for 24 months. Chi square and t tests were utilized to examine relationships between anxiolytics and antidepressant use and cognitive, behavioral, and depressive symptoms.

Results: At admission of the 336 patients reviewed, 17.0% (N= 57) were prescribed anxiolytics, and 14.6% (N=49) prescribed antidepressants. Twelve months later the prescribing of antidepressants increased to 30.9% (N=47 of 152) while anxiolytics decreased to 13.2% (N=20 of 152). Twenty-four months later prescriptions for antidepressants were 25.4% (N=30 mof 118) versus 14.4% (N=17 of 118) for anxiolytics. At admission antidepressants were significantly more frequently prescribed to women, patients with mild to moderate cognitive impairment, and with Geriatric Depression scores greater than/equal to 11. Anxiolytics were more frequently prescribed to residents with behavioral disturbances on the Psychogeriatric Dependency Rating Scale at admission.

Conclusion: During the 24 months following admission, antidepressant medications were used more frequently while anxiolytics were prescribed less frequently in this nursing home population. The specific reasons for this trend remain unclear and perhaps reflect closer scrutiny in prescribing in the era after OBRA.

NR198 Monday, May 7, 3:00 p.m.-5:00 p.m.

Treatment of Bipolar Disorders by Outpatient Psychiatrists

Gonzalo E. Laje-Rivademar, M.D., *Department of Psychiatry, New York University Medical School, 75 West End Avenue, #C22F, New York, NY 10023*; Carlos Blanco-Jerez, M.D., Mark Olfson, M.D.

Summary:

Objective: To examine the prescribing patterns for bipolar disorder of office-based psychiatrists.

Method: The authors analyzed physician-reported data from the 1992–1998 National Ambulatory Medical Care Survey, focusing

on physicians specializing in psychiatry. Kendall's tau b was used to examine temporal changes in prescription patterns.

Results: Lithium was the most commonly prescribed mood stabilizer in every surveyed year, followed by valproic acid. However, there was a steady increase throughout the years in the percentage of visits that were prescribed valproic acid, and a similar decrease in the number of visits that were prescribed lithium. In every year, prescription of antidepressants, benzodiazepines, and antipsychotics was common, but about a third of the total visits did not have a mood stabilizer prescribed. There were no significant variations in the prescription patterns of any class of medications.

Conclusion: Despite important advances in the availability of mood stabilizers, pharmacological treatment of bipolar disorder continues to be an area with substantial opportunity for quality improvement.

NR199 Monday, May 7, 3:00 p.m.-5:00 p.m.

Long-Term Efficacy of SSRIs and Tricyclic Antidepressants in Panic Disorder

Gonzalo E. Laje-Rivademar, M.D., *Department of Psychiatry, New York University Medical School, 75 West End Avenue, #C22F, New York, NY 10023*; Eric D. Peselow, M.D., Mary T. Guardino, B.A.

Summary:

Objective: Approximately 10% of the population will have a panic attack at some point in their life. Though pharmacological and cognitive-behavioral treatments are effective in short-term treatment for panic attacks, the efficacy and long-term course of panic disorder remains unstudied.

Method: To date we have followed 192 patients who after 12 weeks of initial pharmacotherapy recovered with a complete cessation of full-blown panic attacks. These patients were then followed over a succeeding 3–60 month period (average 33 months) while taking either an SSRI (N=139) or a TCA (N=53) alone (medication to which they had initially responded) until one of three outcomes: continuously well until the endpoint of this preliminary analysis, dropout, or relapse (defined as having a breakthrough full-blown panic attack). These patients at baseline and at 3-month intervals were rated with the Hamilton Anxiety Scale, Panic Inventory, Montgomery-Asberg Depression Scale, and CGI rating for anticipatory anxiety, phobic avoidance, spontaneous panic attacks, functional impairment, and overall severity of illness.

Results: Over an average 33-month course, approximately 50% of the sample had a recurrence. There was no statistical difference between the SSRI or TCA group. Phobic avoidance and initial degree and severity of anticipatory anxiety negatively correlated with length of time free of a full-blown panic attack. The probability of remaining free of a full-blown panic attack was approximately 70% at 1 year, 55% at 2 years, and 40% at 3 years. Patients who received cognitive-behavioral treatment in addition to pharmacotherapy had better outcomes.

Conclusion: There was a high rate of recurrence of panic disorder despite treatment.

NR200 Monday, May 7, 3:00 p.m.-5:00 p.m.

Marital Rates, Age of Onset, and Gender Among Patients with OCD

Luana M. Miller, *Department of Psychology, SUNY at Buffalo, 266 Highland Parkway, # 6, Buffalo, NY 14223*; Michelle T. Pato, M.D., Joanne Davila, Ph.D.

Summary:

Objective: Investigated romantic relationship dysfunction among OCD patients to further identify aspects of social impairment associated with OCD.

Method: A naturalistic epidemiological study of the marital status of 368 OCD patients seen in an OCD specialty program in a large urban area from 1996–2000. Data included gender, OCD age of onset, and marital status.

Results: Among participants who were 18 years or older at intake (n = 295), 51% were never married, 34% were married/cohabiting, and 15% were divorced/separated. This stands in sharp contrast to marital rates in the general population, which have been estimated at 80% (U.S. Census Bureau, 1996). In addition, female OCD patients were more than twice as likely to be married compared with males, and patients who were never married had a significantly earlier age of onset compared with married/cohabiting patients. Males and females did not differ on age of onset. More data on correlation of these findings with OCD symptom severity and romantic dysfunction will also be presented.

Conclusions: OCD may cause interference with the development of romantic relationships and marriage, particularly among men and people with an early age of onset. These results highlight the need for early identification of and intervention in OCD, especially among men.

NR201 Monday, May 7, 3:00 p.m.-5:00 p.m.

Efficacy of Citalopram Treatment of OCD and Obsessive-Compulsive Spectrum Disorders

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Summary:

Objective: The aim of our investigation was to evaluate the efficacy of citalopram in a naturalistic setting for patients with OCD and OC-spectrum disorders, many of whom had had previous SRI trials.

Method: Patients taking citalopram in a private practice setting (n=81, 34 males, 47 females) were recruited to participate in this study.

Design: Assessment of efficacy was made based on a clinician rated Visual Analog Scale (100 scale). The threshold for response was considered a global improvement of 50. A retrospective chart review was performed to ascertain each patient's history of SRI treatment. In addition to analyzing the sample as a whole, we compared treatment naïve patients with those with previous SRI trials.

Results: The average improvement on citalopram was 62.7% (±31.4sd) with no statistical difference between treatment naïve and treatment experienced patients. Response within treatment naïve patients was 85.7% and treatment experienced patients was 79.1%. Incidence of side effects on citalopram was 40.7% and lower than retrospective reports with other SRI's. In addition, citalopram appeared to be better tolerated than other SRIs. Specific case examples in OC-spectrum and previously treatment-resistant cases will be presented.

Conclusion: These findings continue to support previous recommendations to try another SRI in treatment resistant cases.

NR202 Monday, May 7, 3:00 p.m.-5:00 p.m.

Anxiety Sensitivity and Depression in Anxiety Disorders

Johanna W. Guerrero, M.A., *Department of Psychology, Fairleigh Dickinson University, 1000 River Road, #874, Teaneck, NJ 07666*; Juliana R. Lachenmeyer, Ph.D.

Summary:

Comorbidity of anxiety and depression has been well documented with a significant amount of research focused on distinguishing the components that are uniquely associated with either

disorder (Beck, 1979) and those components that under the rubric of negative affect are found in both disorders (Clark, 1994).

The present study examines the relationship between anxiety sensitivity (ASI, Reiss et al, 1986) and depression (BDI, Beck, 1979). Seventy-seven participants were recruited from the Anxiety and Stress Treatment Program at North Shore University Hospital with 33% meeting DSM-IV criteria for GAD, 40% for OCD, and 27% for PD.

The results indicated that the level of depression reported by the GAD group was significant higher than that of either PD or OCD (p=.01). While comparisons of ASI scores did not indicate significant differences between the GAD and PD groups, both groups were significantly higher than the OCD group (p<.01). Anxiety sensitivity and depression were positively correlated in the GAD and the PD groups but not in the OCD group.

Implications of the relative loading of anxiety and depression in the different disorders will be discussed. Further analysis and discussion of the shared components of anxiety and depression will be undertaken.

NR203 Monday, May 7, 3:00 p.m.-5:00 p.m.

Avoidance and Social Anxiety in PTSD

Peter S. Brodrick, M.D., *Department of Psychiatry, VA Medical Center, 109 Bee Street, Psychiatry-116A, Charleston, SC 29401*; Richard Faldowski, Ph.D., Jeffrey P. Lorberbaum, M.D., Mark B. Hamner, M.D.

Summary:

Background: PTSD is characterized by reexperiencing the trauma, avoidance of trauma stimuli, and increased autonomic arousal. Frequently, patients with PTSD exhibit personal detachment and decreased activity leading to social isolation and substantial impairment. One explanation for these behaviors may be that PTSD patients experience high levels of social anxiety. This study examines the relationship between specific social anxiety symptoms, the PTSD avoidance symptom cluster, and other PTSD phenomenology.

Methods: Combat veterans with chronic PTSD (n=16) undergoing baseline assessments for medication studies were evaluated using the SCID-DSM IV, Clinician-Administered PTSD Scale (CAPS), Leibowitz Social Anxiety Scale (LSAS), and other rating scales. The relationship between CAPS and LSAS scores was assessed using Pearson correlation coefficient analyses.

Results: Preliminary data analysis shows LSAS scores comparable with those seen in social phobia (mean = 64.4±33.3, range = 12–124). LSAS scores correlated positively with CAPS avoidance (r=.703, p<0.002), but not with CAPS total (r = .384, p < .143), arousal (r = .336, p < .204), or reexperiencing scores (r = –.390, p<.135).

Conclusions: Specific social anxiety symptoms are elevated in PTSD patients. These symptoms appear to be strongly and uniquely associated with the PTSD avoidance symptom cluster. Further data from this ongoing study will be discussed.

NR204 Monday, May 7, 3:00 p.m.-5:00 p.m.

Psychodynamic Group Treatment for Generalized Social Phobia

Daniela Z. Knijnik, M.D., *Department of Psychiatry, Federal University of Rio Grande do Sul, Rua Costa 30/506, Porto Alegre, RS 90110–270, Brazil*; Flavio Kapczinski, Ph.D., Eduardo Chachamovich, M.D., Regina Margis, M.D., Betina C. Kruter, M.D., Leslie Sokol, Ph.D., Claudio L. Eizirik, Ph.D.

Summary:

Social phobia is characterized by fear of humiliation and embarrassment while engaged in social interaction or performance in front of others. The aim of this study is to explore the effectiveness of psychodynamic group therapy in patients with generalized social phobia. Thirty patients participated in a randomized, single-blind clinical trial comparing psychodynamic group treatment (PGT) with a credible placebo control group (CPC) for generalized social phobia (DSM-IV). PGT consisted of 12 sessions of psychodynamic-oriented group psychotherapy. Control patients received a treatment package consisting of lecture-discussion and group support that was compared with PGT. At pretest, midtest, and posttest of 12 weeks, patients completed assessments that included Clinical Global Impression Scale (CGI), Hamilton Anxiety Scale (HAS), Hamilton Depression Scale (HDS), and Liebowitz Social Anxiety Scale (LSAS). Both groups improved on most measures. No differences were found between groups at endpoint in the outcome variables assessed in the present study. It is likely that the effect of PGT and CPC on the outcome variables is due to nonspecific factors related to group therapy.

NR205 Monday, May 7, 3:00 p.m.-5:00 p.m.

Pathological Worry in Major Depression and Comorbid Anxiety Disorders

Iwona Chelminski, Ph.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Providence, RI 02905*; Mark Zimmerman, M.D.

Summary:

Objective: Anxious apprehension, defined as a future-oriented mood state in which one is ready to cope with upcoming negative events, is present in all anxiety disorders. High frequency and self-perception of uncontrollability have been hypothesized as the most important features of worry in GAD. At least two studies found that a high level of worry distinguishes reliably patients with GAD from those with other anxiety disorders. Starcevic (1995) found scores on a measure of worry equally elevated in patients with MDD only and those with GAD only, and concluded that worry is not confined to GAD. The aim of the present study was twofold. First, we reexamined whether pathological worry is higher in patients with GAD than other anxiety disorders. Second, patients with MDD, GAD, and MDD with comorbid GAD were compared.

Method: Eight hundred six outpatients were evaluated with the Structured Clinical Interview for DSM-IV (SCID), and completed PSWQ upon presentation for treatment.

Results: The total PSWQ score was higher in the patients with GAD than in patients with each of the other anxiety disorders. The total scores were also significantly higher in those with GAD only as compared with MDD only, as well as in depressed patients with versus without comorbid GAD.

Conclusions: This analysis suggests that the degree of pathological worry, as measured by PSWQ, is specific for the diagnosis of GAD. High levels of worry reliably discriminate individuals with GAD from those with other anxiety disorders, as well as with depression.

NR206 Monday, May 7, 3:00 p.m.-5:00 p.m.

Social Anxiety Disorder and Body Image Disturbances

Jessica I. Yunker, B.A., *Department of Psychiatry, Montefiore Medical, 111 East 210th Street, Bronx, NY 10467*; Gregory M. Asnis, M.D.

Summary:

Social anxiety disorder (SAD) is the most prevalent anxiety disorder, with a lifetime prevalence of about 13%. Onset usually occurs in the teen years and becomes chronic, leading to significant dysfunction. In a recent clinical trial for the treatment of SAD, clinicians detected that several of the subjects in the trial had a

preoccupation with their own body image which, in most cases, preceded the onset of SAD. These subjects did not meet criteria for a somatoform disorder, though six out of 18 patients (approximately one-third) described this association; this may prove even more prevalent if structured rating scales for body dysmorphic symptoms (BDS) are used.

The subjects who described a preoccupation with their own body image felt that others were judging them based on what they perceived as an abnormal physical appearance. For example, one self-described "late bloomer" stated that he never felt comfortable in his now fully-grown body. Another patient developed acne in early adolescence and felt that strangers were talking about her complexion. Other subjects, while they did not identify specific abnormal physical features, indicated on a general questionnaire (SCL-90) that they had vague thoughts that others were commenting on or noticing their physical appearance. The association between SAD and BDS is not surprising since SAD and body dysmorphic disorder share a serotonin dysfunction (Baldwin et al., 1999; Hollander et al, 1999). This poster will present in detail several cases describing the BDS observed in SAD subjects, and describe implications for the treatment of these cases.

NR207 Monday, May 7, 3:00 p.m.-5:00 p.m.

Fluoxetine and Moclobemide: Treatment for Intrusive and Evitative Symptoms in Acute Stress Disorder (ASD)

Cecilia P. Soto, M.D., *Instituto Seguridad de L'tradajo, Alvarez 662, Vina Del Mar, Chile*

Summary:

Objective: Prospectively examine the course of intrusive and evitative symptoms in patients with acute stress disorder (32) treated with fluoxetine or moclobemide during a four-week trial.

Method: All patients diagnoses were based on DSM-IV criteria. Symptoms were assesed using the Impact of Event Scale, a structure clinical interview, and a self-answer questionaire both based on DSM-IV criteria.

Results: In the presence of intrusive symptoms, moclobemide was superior on general evaluation of its treatment. Fluoxetine-treated patients responded better when presenting evitative symptoms. When either drug was used closer to exposure of trauma, no signs of posttraumatic stress disorder was observed.

Conclusion: Despite the shortage of sample, symptoms improved better when using fluoxetine for evitative symptoms; moclobemide for intrusive symptoms.

NR208 Monday, May 7, 3:00 p.m.-5:00 p.m.

Anxiety Disorders: Recognition and Treatment in an Urban Primary Care Practice

Adriana Feder, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive, Unit 24, New York, NY 10032*; Marc Gameroff, M.A., Mark Olfson, M.D., Milton Fuentes, Psy.D., Renee Goodwin, Ph.D., Myrna M. Weissman, Ph.D.

Summary:

Objective: Little is known about the diagnosis and treatment of anxiety disorders in primary care, especially in urban primary care settings.

Methods: This study compares physician recognition and treatment of anxiety disorders, depressive disorders, and comorbid anxiety and depressive disorders in a random sample of 161 patients at a university-affiliated general medicine practice serving a low-income population in Northern Manhattan. Trained interviewers diagnosed current psychiatric disorders with the WHO Composite International Diagnostic Interview (WHO-CIDI), and physicians completed an encounter form including items about recognition and treatment of mental health problems during the index visit.

Results: The overall sample was predominantly female (75.2%) and Hispanic (70.2%). Current anxiety disorders included generalized anxiety disorder (N=7), social phobia (N=7), specific phobia (N=27),panic disorder (N=1), and agoraphobia without panic disorder (N=1). Physicians were more likely to 1) *identify* patients with comorbid anxiety and depression as having "ongoing mental problems" than patients in the other groups (anxiety + depression = 90.9%, anxiety only = 68.8%, depression only = 80.0%, and neither anxiety or depression = 34.7%; $p < 0.001$); 2) *counsel* these patients (anxiety + depression = 72.7%, anxiety only = 37.5%, depression only = 20.0%, neither = 25.4%; $p = 0.010$); 3) *discuss their possible mental diagnosis* with them (anxiety + depression = 63.6%, anxiety only = 25.0%, depression only = 30.0%, neither = 11.0%; $p < 0.001$); 4) *refer them to a mental health specialist* (anxiety + depression = 27.3%, anxiety only = 7.7%, depression only = 10.0%, neither = 2.6%; $p = 0.010$); and 5) *prescribe/monitor a psychotropic medication* for them (anxiety + depression = 45.5%, anxiety only = 17.6%, depression only = 30.0%, neither = 6.6%; $p < 0.001$). Results will be adjusted for various sociodemographic factors.

Conclusion: These results suggest that anxiety disorders are underdiagnosed and undertreated in this urban primary care practice, a particular tendency if patients present without comorbid depression. (supp. investigator-initiated grants: Eli-Lilly & Co./ Pharmacia-Upjohn).

NR209 Monday, May 7, 3:00 p.m.-5:00 p.m.

The Importance of Being Specific: Autobiographical Memory Scoring in PTSD

Dewi S. Abramoff-Moehadjir, M.D., *Centrum 45, Rijnzichtweg 35, Oegstgeest 2342-AX, Netherlands*; Bas J.N. Schreuder, Ph.D.

Summary:

Objective: To compare different tests for the characterization of autobiographical memory (AM) in post-traumatic stress disorder (PTSD) patients, and find suitable tests for AM scoring in fMRI protocols.

Methods: 15 patients were included from our outpatient clinic (Dutch War Victims Center) diagnosed with combat-related PTSD using the Clinician Administered PTSD Scale. AM was characterized using three published scoring methods: Williams AM-Test (AMT), Singer's Classification-System for self-defining Memories (CSM), and Suedfeld Integrative-Complexity-Score (ICS). The scoring protocols were carefully followed during two separate 60-min sessions 1 month apart, 15 min for the AMT, and 25 min for 10 AM descriptions (recorded on tape). The AMT, CSM, and ICS scores were obtained independently by two raters and analyzed using ANOVA.

Results: Patients had low specifity scores (AMT), low single-event scores (CSM), and low differentiation and integration (ICS) scores (partial analysis). Correlation between CSM and ICS was higher than between these and AMT.

Conclusions: ICS and CSM may test a different aspect of AM than AMT, if a single event AM on the CSM corresponds to high complexity on the ICS. Low specificity in remembering the past may influence PTSD outcome. ICS and CSM may be more attractive for fMRI protocols, since they are scored retrospectively.

NR210 Monday, May 7, 3:00 p.m.-5:00 p.m.

Carbon Dioxide-Induced Panic Attacks: A Clinical Phenomenologic Study

Alexandre M. Valenca, M.D., *Department of Psychiatry, University Feder Rio Janeiro, Min Otavio Kelly 467 AP 1204 B,*

Niteroi, RJ 24220-300, Brazil; Antonio E. Nardi, M.D., Isabella Nascimento, M.D., Fabiana L. Lopes, M.D., Marco A. Mezzasalma, M.D., Walter A. Zin, M.D.

Summary:

Objectives: 1. To verify the sensitivity of panic disorder patients to a carbon dioxide challenge test. 2. To verify the intensity, duration, and symptomatology of panic attacks induced by this gas in these patients, comparing these data with those from spontaneous panic attacks.

Methods: 31 patients with panic disorder with or without agoraphobia (DSM-IV) were selected. After a 1-week drug free period, these patients underwent two vital capacity inhalations of a carbonic mixture (35% CO_2 and 65% O_2) and compressed atmospheric air ("placebo"), chosen randomly and separated by a 20-minute interval. These inhalations were repeated after 2 weeks. During this period no patient received any kind of psychotropic drug.

Results: 22 patients (71%) had a panic attack in at least one of the tests where the CO_2 mixture was used. Among these patients, the most frequently reported symptoms were breathing difficulty (N=20, 90.9%), suffocation or asphyxia sensation (N= 18, 81.8%), dizziness (N=18, 81.8%), trembling (N=14, 63.6%), palpitations (N=13, 59.1%) and fear of becoming crazy (N=12, 54.5%). Eleven patients (50.0%) considered the laboratory-induced panic attacks as more intense when compared to spontaneous panic attacks.

Conclusion: Panic disorder patients have a high sensitivity to CO_2. The inhalation of the 35% CO_2 mixture provoked symptoms in these patients similar to those felt during spontaneous panic attacks. This test may be considered a good laboratory model for panic disorder.

NR211 Monday, May 7, 3:00 p.m.-5:00 p.m.

Psychiatry Disorders in Asthmatic Outpatients

Isabella Nascimento, M.D., *Department of Psychiatry, Federal University Rio Janiero, Rua Guimaraes Rosa 203, Apto 305, Rio De Janeiro, RJ 22793-090, Brazil*; Antonio E. Nardi, M.D., Alexandre M. Valenca, M.D., Fabiana L. Lopes, M.D., Marco A. Mezzasalma, M.D., Walter A. Zin, M.D.

Summary:

It has been reported that the lifetime prevalence of panic disorder (PD) in pulmonary patients is higher than the prevalence for PD in the general population. We aim to evaluate the frequency of anxiety disorders in 86 subjects from the Asthmatic Outpatients Clinics. Psychiatric diagnoses were assessed by the Mini International Neuropsychiatric Interview Version 4.4 - M.I.N.I. Forty-five asthmatic patients (52.3%) reported at least one current anxiety disorder. The frequency of PD with/without agoraphobia (Ag) was 13.9% (N=12) and Ag without PD was 26.7% (N=23). Social anxiety and generalized anxiety disorders occurred in 9.3% (N=8) and 24.4% (N=21) of the sample, respectively. Twenty-nine patients (33.7%) reported a major depressive episode. The psychiatric morbidity of the sample was 61.6% (N=53). Our results confirm the high morbidity of anxiety disorders in asthmatic outpatients, especially within the PD/Ag spectrum.

NR212 Monday, May 7, 3:00 p.m.-5:00 p.m.

Impact of Gamma-Aminobutyric Acidergic (GABAergic) Treatment on CCK-4-Induced Anxiety

Peter Zwanzger, M.D., *Department of Psychiatry, University of Munich, Nuss Baumstrasse 7, Munich 80336, Germany*; Frank Padberg, M.D., Cornelius Schule, M.D., Thomas C. Baghai, M.D., Christo Minov, M.D., Hansjurgen Moller, M.D., Rainer Rupprecht, M.D.

Summary:

Objectives: There is increasing evidence that selective enhancement of GABAergic neurotransmission reduces anxiety-related behavior in experimental animals (Sherif et al. 1994). To evaluate the impact of selective GABA enhancement on anxiety in humans we investigated anxiolytic effects of vigabatrin and tiagabine on cholecystokinin-tetrapeptide (CCK-4)-induced panic (Bradwejn et al. 1994).

Methods: A CCK-4 challenge was performed before and after treatment. In a first study, 10 healthy volunteers received vigabatrin for 7 days. In a second still ongoing study healthy volunteers received tiagabine for 7 days. Panic was assessed using the API and PSS scores.

Results: All subjects reported a marked reduction of CCK-4 induced panic symptoms and anxiety after vigabatrin treatment. API and PSS scores showed a significant reduction after treatment. Moreover, we observed a marked and significant blunting of CCK-4-induced stimulation of ACTH and cortisol.

Conclusion: Our data show a marked improvement of CCK-4-induced panic symptoms following GABAergic treatment in healthy volunteers and suggest that GABAergic drugs might be useful in ameliorating panic symptoms also in patients with PD.

NR213 Monday, May 7, 3:00 p.m.-5:00 p.m.

The Influence of Affective Temperaments on Psychometrically Derived Manic Subtypes

Giulio Perugi, M.D., *Department of Psychiatry, University of Pisa, Via Roma 67, Pisa 56100, Italy*; Icro Maremmani, M.D., Cristina Toni, M.D., Giuseppe Ruffolo, M.D., Carlo Torti, M.D., Hagop S. Akiskal, M.D.

Summary:

Objective: The present investigation focuses on symptomatological subtypes of mania and their relationships with affective temperatments and other clinical features of bipolar disorder.

Method: In 153 inpatients with mania according to DSM-III-R, clinical subtypes have been investigated by means of principal component factor analysis of 18 selected items of the Comprehensive Psychopathological Rating Scale (CPRS). We compared other clinical features, depressive and hyperthymic temperamental attributes, and first-degree family history for mood disorders among the various manic subtypes on the basis of the highest z-scores obtained on each CPRS factor (dominant CPRS factor).

Results: Five factors—depressive, irritable-agitated, euphoric-grandiose, accelerated-sleepless, paranoid-anxious—emerged, accounting for 59.8% of the total variance. When the factor-based groups were compared, significant differences emerged in terms of duration of the current episodes, rates of chronicity and incongruent psychotic features—being highest in the "depressive" and "paranoid-anxious" dominant groups. The patients with highest z-scores for the "euphoric-grandiose," "paranoid-anxious," and "accelerated-sleepless" factors were those most likely to belong to the hyperthymic temperament, while the "depressive" dominant group had the highest rate of depressive temperament. Finally, it is noteworthy that the "irritable-agitated" group was high on both temperaments.

Conclusions: The foregoing multidimensional structure of mania—revealing five factors—is generally concordant with the emerging literature. These subtypes are not mere constructs of psychometric analysis, as judged by the fact that contrasting temperamental attributes seem correlated with them. Coupled with several differentiating clinical characteristics, we submit that the foregoing represent genuine phenomenologic subtypes.

NR214 Monday, May 7, 3:00 p.m.-5:00 p.m.

Bipolar II and Unipolar Comorbidity in Social Phobia: Clinical and Therapeutic Issues

Giulio Perugi, M.D., *Department of Psychiatry, University of Pisa, Via Roma 67, Pisa 56100, Italy*; Cristina Toni, M.D., Belen Mata, M.D., Leonardo Moretti, M.D., Franco Frare, M.D., Hagop S. Akiskal, M.D.

Summary:

Objective: We aimed to show whether or not the presence of a lifetime bipolar or unipolar comorbidity could be associated with differences in the clinical features of social phobia (SP).

Method: Clinical characteristics were investigated by a semi-structured interview in 153 outpatients who met DSM-III-R criteria for SP. Social phobic symptoms and the severity of the illness were assessed by the Liebowitz Social Anxiety Scale (LSAS) and the severity scales from the Liebowitz Social Phobic Disorders Rating Scale (LSPDRS).

Results: 9.1% of our patients satisfied DSM-III-R criteria for lifetime bipolar disorder NAS (Bipolar II), while 46.4% had unipolar major depression, and 44.4% had no lifetime history of major mood disorders. Comorbid panic disorder/agoraphobia (PDA), obsessive-compulsive disorder (OCD), and alcohol abuse were reported more frequently in the bipolar group than in the other two subgroups. All the LSPDRS severity scores and the LSAS subscales of social anxiety and social avoidance showed significantly greater values in bipolar patients than in the other two subgroups, even if unipolar patients were recorded more severe than subjects without mood disorders. SP patients with comorbid bipolar disorder also reported a significantly greater number of social situations that they feared than did those subjects without mood disorder.

Conclusions: Severity and generalization of the SP symptoms, multiple comorbidity, and alcohol abuse appeared to be the most relevant consequences of SP-bipolar coexistence. In a significant minority of cases, protracted social anxiety may hypothetically have represented, along with inhibited depression, the dimensional opposite of hypomania.

NR215 Monday, May 7, 3:00 p.m.-5:00 p.m.

Episodic Memory Dysfunction in Bipolar Disorder

Thilo Deckersbach, Ph.D., *Department of Psychiatry, Harvard Medical School, 15 Parkman Street, WACC 815, Boston, MA 02114*; Noreen A. Reilly-Harrington, Ph.D., Gary S. Sachs, M.D.

Summary:

Objective: To determine whether episodic memory impairment previously reported for individuals with bipolar disorder is due to an impairment in structuring verbal information during learning (encoding).

Methods: 20 euthymic subjects with DSM-IV bipolar I disorder and 20 normal control subjects matched for age, gender, handedness, and education completed the California Verbal Learning Test (CVLT). Briefly, the CVLT assesses the learning of a list of 16 words over five successive learning trials as well as short- and long-delayed free recall and recognition. The CVLT also assesses the extent to which subjects cluster (group) words in their semantic categories (e.g., fruits, clothing) during the five learning trials.

Results: Independent t tests indicated that compared to control subjects, bipolar I disorder subjects learned fewer words over the five learning trials (p=0.002). They also clustered words less into their semantic categories than control subjects (p=0.005). Bipolar I subjects also recalled fewer words at the long-delayed free recall (p=0.01). When effects of semantic clustering were partialled out, group differences in learning and long-delayed recall did not remain significant (p=0.18), indicating that impairments in learning and long-delayed free recall in bipolar disorder subjects were mediated by a deficit in structuring verbal information appropriately.

Conclusion: Verbal episodic memory impairment in individuals with bipolar I disorder reflects an impairment in structuring information appropriately during learning. This pattern is consistent with CVLT impairments found in individuals with fronto-striatal dysfunction.

NR216 Monday, May 7, 3:00 p.m.-5:00 p.m.

Cognition and Metacognition in OCD

Thilo Deckersbach, Ph.D., *Department of Psychiatry, Harvard Medical School, 15 Parkman Street, WACC 815, Boston, MA 02114*; Cary R. Savage, Ph.D., Sabine Wilhelm, Ph.D., Antje Bohne, M.S., Scott L. Rauch, M.D., Lee Baer, Ph.D., Michael A. Jenike, M.D.

Summary:

Objective: To explore the relationship between episodic memory, confidence in memory, and subjective prediction of memory performance in individuals with obsessive-compulsive disorder (OCD).

Methods: 24 individuals with DSM-IV OCD and 15 normal control subjects matched for gender, handedness, and education participated in the study. Subjects completed a computerized non-verbal memory task with repeated presentations of the same geometric stimuli (Rey-Osterrieth Complex Figure Test) with recognition memory and confidence ratings assessed after each presentation. Subjects also predicted their recognition accuracy before each presentation.

Results: OCD subjects consistently recognized fewer geometric stimuli than control subjects throughout all learning trials (main effect of group: p=0.04). Both OCD and control subjects improved their recognition performance with repeated presentations (p= 0.001). OCD and control subjects did not differ in prediction of memory performance and in confidence in memory at the first presentation of the stimuli (p=0.90). However, OCD subjects exhibited significantly lower confidence in memory and lower predictions than control subjects at the fifth presentation (p=0.006).

Conclusion: Our results demonstrate the development of a dissociation between objective memory performance (recognition) and subjective aspects of memory (prediction of memory performance and confidence ratings) in patients with OCD. The relationship between these findings and OCD symptoms such as checking/repeating rituals will be discussed.

NR217 Monday, May 7, 3:00 p.m.-5:00 p.m.

Impairment in Motor Inhibition in Tourette's Disorder

Thilo Deckersbach, Ph.D., *Department of Psychiatry, Harvard Medical School, 15 Parkman Street, WACC 815, Boston, MA 02114*; Cary R. Savage, Ph.D., Barbara J. Coffey, M.D., Sabine Wilhelm, Ph.D., Siegfried Gauggel, Ph.D., Michael A. Jenike, M.D., Scott L. Rauch, M.D.

Summary:

Objective: To determine whether individuals with Tourette's disorder exhibit an impairment in response inhibition.

Methods: 10 subjects with DSM-IV Tourette's Disorder (TD) and 10 normal control subjects matched for age, gender, handedness, and education completed the Stop-Signal-Task. The Stop-Signal-Task assesses the speed of response inhibition processes. Briefly, subjects are presented a *go-signal,* after which they are instructed to press a response key as quickly as possible. In some trials a *stop-signal* occurs shortly after the *go-signal* requiring subjects to withhold (inhibit) their reaction. Through systematic variation of the time between the go- and the stop-signals, the time required for inhibition of motor responses can be estimated.

Results: Mann-Whitney U tests indicated no difference in reaction times between TD subjects and control subjects in go-trials where no stop signal was present (p=0.87). However, there was a lower probability of response inhibition for TD patients (p=0.01). Therefore, TD subjects also exhibited a significantly shorter stop-signal reaction time (p=0.03), indicating that TD patients needed more time to inhibit their responses.

Conclusion: Our results suggest that individuals with TD exhibit impairment in inhibition of motor responses possibly related to the occurrence of tics. These results should be considered preliminary due to the small sample size.

NR218 Monday, May 7, 3:00 p.m.-5:00 p.m.

Cognitive Inhibition in Tourette's Disorder

Thilo Deckersbach, Ph.D., *Department of Psychiatry, Harvard Medical School, 15 Parkman Street, WACC 815, Boston, MA 02114*; Cary R. Savage, Ph.D., Barbara J. Coffey, M.D., Sabine Wilhelm, Ph.D., Michael A. Jenike, M.D., Scott L. Rauch, M.D.

Summary:

Objective: To determine whether individuals with Tourette's Disorder (TD) exhibit impairments in visuospatial priming and cognitive inhibition.

Methods: 10 subjects with DSM-IV Tourette's Disorder and 10 normal control subjects matched for age, gender, handedness, and education completed the Visuospatial Priming paradigm (VSP; Swerdlow et al., 1996) and a computerized Stroop task. Briefly, the VSP task assesses facilitatory and inhibitory effects of a visual pre-signal (priming) on the speed of reaction to a target. The Stroop task assesses inhibition of an automatic response in favor of an alternative competing response.

Results: For the VSP task, Mann-Whitney U tests indicated a trend towards decreased reaction times following facilitatory pre-signals in TD subjects but not in control subjects (p=0.06). No such group differences were found for reaction times following inhibitory priming. The Stroop task indicated significantly longer reaction times in interference trials (which require inhibition of automatic responses) in TD subjects when compared to control subjects, indicating reduced cognitive inhibition.

Conclusion: Subjects with Tourette's disorder exhibit abnormal facilitation of visuospatial information processing and reduced cognitive inhibition. These processes may contribute to subjectively reported "sensations" or "urges" that precede tics. These results should be considered preliminary due to the small sample size.

NR219 Monday, May 7, 3:00 p.m.-5:00 p.m.

Anxiety: Personality Traits and Beta Adrenergic Receptor Function

Woo Geum Seok, M.D., *Department of Psychiatry, Samsung Medical, 50 Ilwon-dong Gangnam-Gu, Seoul 135-230, Korea*; Bum-Hee Yu, M.D., Moon-Sun Koo, M.A.

Summary:

Objective: Anxiety is closely related with beta-adrenergic receptor function in patients with anxiety disorder, but it is not well known that various psychological factors are related with beta-adrenergic receptor function in healthy people. This study examined the relationship between beta-adrenergic receptor function and psychological factors such as anxiety, depression, and some personality traits in a normal population.

Methods: Subjects for this study were 19 men and 35 women from 20 to 40 years of age whose body mass index was between 17.5 and 26.1. All of them were healthy subjects who had no previous history of medical or psychiatric illnesses. We administered the Korean versions of the Spielberger State-Trait Anxiety Inventory, Beck Depression Inventory, and Eyesenck Personality Questionnaire. We also measured the chronotropic 25% (CD_{25}) dose of isoproterenol, previously developed to assess in vivo beta-adrenergic receptor sensitivity.

Results: The mean CD_{25} dose was 2.5 (SD=1.2) μg. The correlation between CD_{25} dose and state anxiety levels (r=–0.355, p=0.015) and between CD_{25} dose and trait anxiety level (r=0.346, p=0.019) were statistically significant. CD_{25} dose was also negatively correlated with P scale of the Eyesenck Personality Questionnaire (r=–0.479, p=0.002). CD_{25} dose showed a negative correlation with depression levels (r=–0.289, p=0.052), which just missed achieving statistical significance.

Conclusion: In healthy subjects, the sensitivity of beta-adrenergic receptors increases as anxiety and depression levels become higher. The sensitivity of beta-adrenergic receptors also increases in healthy subjects with high levels of aggression and impulsivity. Thus various psychological factors such as anxiety, depression, and some personality traits could affect beta-adrenergic receptor function in a normal population.

NR220 Monday, May 7, 3:00 p.m.-5:00 p.m.

Time in Seclusion and Restraint: A Function of Policy

Jacob J. Venter, M.D., *Department of Psychiatry, Maricopa Medical, 2601 East Roosevelt, Phoenix, AZ 85008*; Curt Bay, Ph.D.

Summary:

Background: All incidents of seclusion/restraints during a 3-month period at a large community-based psychiatric facility were reviewed in an attempt to identify predictors of release from confinement.

Methods: Data were collected through chart review on 86 patients who had 283 intervals of confinement during 210 separate incidents. Potential predictors of release from confinement included sex, age, length of stay, legal status, diagnosis, reason for seclusion, involvement of other parties in the precipitating incident, proportion of quiet time during confinement, and the effect of medication used.

Results: Length of confinement ranged from 0.5 to 22.5 hours (mean = 3.06 hours, SD=2.5). In 34% of events, patients were released at the end of 3 hours of confinement rather than following 15-minute checks performed by nursing staff. Based on statistical analyses of the first incident of seclusion for each patient, none of the potential predictors of release we studied were significant.

Discussion: Current local practice requires a re-evaluation/order by a physician to continue confinement at the end of each 3-hour interval. These findings suggest that policy, rather than clinical judgement, guides the practice of seclusion and restraint. Recommendations for a more rational approach to seclusion and restraint are discussed.

NR221 Monday, May 7, 3:00 p.m.-5:00 p.m.

Demographic Predictors for Seclusion and Restraint

Jacob J. Venter, M.D., *Department of Psychiatry, Maricopa Medical, 2601 East Roosevelt, Phoenix, AZ 85008*; Curt Bay, Ph.D.

Summary:

Background: The use of the least restrictive alternative is current standard of care. The practice of seclusion and restraint is an emotional and controversial matter. Demographic data of patients admitted in 2000 to a large community hospital were analyzed to help identify a profile of patients at higher risk for confinement.

Methods: Data were collected from the hospital demographic database and the seclusion and restraint register of the psychiatry

department. The total number of patients admitted was 2,171 of whom 254 were secluded. Data collected included age, sex, ethnic origin, length of hospital stay (LOS), number of admissions, and principal diagnosis.

Results: Confined patients were younger and more likely to be male. Ethnic groups were not significantly different. Secluded patients had significantly more admissions during 2000 and a longer average LOS. Interesting and significant differences were noted among diagnostic groups, but the interpretation is unclear.

Discussion: The practice of seclusion and restraint requires a balance between the safety of the patient and the least restrictive alternative. Attempts should be made to identify the patients most likely to be secluded to minimize these events.

NR222 Monday, May 7, 3:00 p.m.-5:00 p.m.

Tics, Inattention, and Obessiveness in Children Versus Adults with Tourette's Disorder

Jacob J. Venter, M.D., *Department of Psychiatry, Maricopa Medical, 2601 East Roosevelt, Phoenix, AZ 85008*; Thomas P. Tarshis, M.D., Drake D. Duane

Summary:

Background: The relationship between tics, inattention, and obsessiveness in a population of Tourette's syndrome subjects was assessed. The difference between adult and pediatric populations were studied.

Methods: Forty-seven patients (37 male, ages 4–52 years) meeting criteria for Tourette's were assessed between 1990 and 2000. Nineteen adults (mean age=32.6 years) and 28 children (mean age=10.4 years) were studied. Instruments included the Yale Tic Rating Scale, Tests of Variables of Attention, Conners Continuous Performance Test, Letter Cancellation Task, Digit Span, Achenbach Child Behavior Checklist, Yale-Brown Obsessive-Compulsive Rating Scale, and the Minnesota Multiphasic Inventory.

Results: Obsessive-compulsive criteria were met in 64% of the children and 68% of the adults (p=N.S.). Inattention criteria were met in 57% of children and 21% of adults (p=0.015). Tics were more prominent in children than adults (p=0.006). There was no correlation between the tic severity score or obsessive and inattentive measures in either group.

Conclusions: These findings support a preponderance of inattention in children versus adults with Tourette's. There was no difference in obsessiveness in these groups. This may suggest that the neuroanatomy involved in Tourette's in children versus adults is different. This evolutionary pattern and its underlying mechanism await confirmatory investigation.

NR223 Monday, May 7, 3:00 p.m.-5:00 p.m.

Treatment Course and Outcome of Post-Stroke Depression in an Inpatient Unit

Jean Y. Liu, M.D., *Department of Psychiatry, Pennsylvania State-Hershey Medical Center, P O Box 850, H073, Hershey, PA 17033-0850*; Paul A. Kettl, M.D., Naina Patil, M.D.

Summary:

Introduction: We sought to examine treatment outcome of patients admitted to a university hospital psychiatry unit with post-stroke depression and with no prior history of depression.

Method: 946 patients were admitted over a 2-year period. A retrospective chart review was done for patients with post-stroke depression (defined as new-onset major depression after age 60 with a stroke preceding admission demonstrated on CT scan) Nine patients fitting the criteria were evaluated by a blind rater using Efficacy Index of Global Impression Scale (EI).

Results: Of the nine patients, three were significantly improved (EI=4), and four patients were much improved (EI=3). Two patients received ECT, and neither improved due to delirium after ECT. All nine patients had stroke on the right side of the brain.

Conclusion: Post-stroke depression is quite treatable. Seven of nine patients improved with antidepressant treatment. Stroke location was on the right side of the brain in all patients.

NR224 Monday, May 7, 3:00 p.m.-5:00 p.m.

Efficacy of ECT in Late-Onset Major Depression

Jean Y. Liu, M.D., *Department of Psychiatry, Pennsylvania State-Hershey Medical Center, P O Box 850, H073, Hershey, PA 17033-0850*; Paul A. Kettl, M.D., Naina Patil, M.D.

Summary:

Introduction: Little data are available on ECT treatment of late-onset (i.e. onset after age 60) depression. We sought to examine our experience of treatment outcomes on a university hospital-based geriatric psychiatry unit.

Method: A retrospective chart review was conducted on all patients with late-onset major depression over a 2-year period. Sixteen patients with late-onset major depression who received ECT were evaluated for treatment success using Efficacy Index of Clinical Global Impression scale. A blind rater assessed these patients.

Results: Eleven of the 16 patients were significantly improved (EI=4), and another patient was much improved compared to baseline (EI=3), representing 75% improvement rate with ECT. Four patients did not improve, and all suffered deliriums from ECT. All patients underwent a CT scan of the brain.

Conclusion: ECT is an effective form of therapy for late-onset major depression. Delirium can complicate treatment course.

NR225 Monday, May 7, 3:00 p.m.-5:00 p.m.

Late-Onset Bipolar Depression Versus Late-Onset Major Depression

Jean Y. Liu, M.D., *Department of Psychiatry, Pennsylvania State-Hershey Medical Center, P O Box 850, H073, Hershey, PA 17033-0850*; Paul A. Kettl, M.D.

Summary:

Introduction: Little data are available for comparison of clinical features and outcome between late-onset bipolar depression (BD) and major depressive disorder (MDD).

Method: A retrospective chart review was conducted for all 946 patients admitted to a geriatric psychiatry unit over a 2-year period. 64 MDD and 10 BD patients met the inclusion criteria (age and age of onset greater than 60, MMSE more than 24). They were analyzed for age, age of onset, MMSE, length of stay, gender, and medications used. Efficacy Index (EI) of Clinical Global Impression was used to gauge improvement. Data were analyzed using chi square and t tests.

Results: Of the 64 MDD patients, 30 patients or 47% were significantly improved (EI=4), and 29 patients or 45% were improved (EI=3). Of the 10 BD patients, seven patients were significantly improved (EI=4), and three were improved (EI=3). Nine out of 64 MDD patients had focal lesions while 0 out of 10 BD patients had focal lesions on brain imaging. SSRIs most significantly correlated with efficacy of treatment (p=0.0002), especially sertraline (p=0.006).

Conclusion: Late-onset BD and MDD are very treatable disorders. Few patients with late-onset MDD (14%) had focal lesions (all on right side of the brain) and none of the BD patients had any focal lesions on brain imaging. SSRIs were most efficacious. Most returned to original living conditions.

NR226 Monday, May 7, 3:00 p.m.-5:00 p.m.

Are There Hormonal Changes in the CSF of OCD Patients?

Mustafa K. Saadani, M.D., *Department of Psychiatry, King Khalid N.G. Hospital, P O Box 9515, Jeddah 21423, Saudi Arabia*; Samir Assaad, M.R.C., Tarek Sherif, M.R.C., Adel Sheashai, M.D., Seham Rashed, M.D.

Summary:

A relatively small number of studies have investigated basal serum hormonal changes in obsessive-compulsive disorder (OCD) patients. A fewer number of studies have investigated hormonal changes in cerebrospinal fluid (CSF) of OCD patients. Aim: We tried to measure hormonal changes in the CSF of severely disturbed OCD patients.

Method: CSF samples from 10 OCD subjects (with Yale-Brown Obsessive Compulsive Scale scores of more than 32) were compared with CSF samples from another 10 psychologically stable control subjects who were comparable with regard to age, sex, and menstrual phase if female. Radio-immuno assay of follicle stimulating hormone (FSH), luteinizing hormone (LH), growth hormone (GH), prolactin (PRL), and thyroid stimulating hormone (TSH) were done for both OCD patients and control subjects.

Results: Hormonal differences between the mean values for OCD patients and control subjects were statistically not significant (t=0.67, 0.44, 0.68, –0.28, and 1.15, respectively, p>0.05). Cortisol was not detected in the CSF of either OCD patients or control subjects.

Conclusion: There were no CSF hormonal differences between OCD patients and control subjects with regard to FSH, LH, GH, PRL, or TSH.

NR227 Monday, May 7, 3:00 p.m.-5:00 p.m.

Pain Control During Intrathecal Chemotherapy: A Randomized Study

Mustafa K. Saadani, M.D., *Department of Psychiatry, King Khalid N.G. Hospital, P O Box 9515, Jeddah 21423, Saudi Arabia*; Adel Abbas, M.R.C., Taha Khattab, M.D., Abdelmoteleb Yousef, M.S., Sami Felimban, M.D., Tarek Sherif, M.R.C., Faris Chedid, M.D., Chris Fryer, M.R.C.

Summary:

Sixty-seven patients with acute lymphoblastic leukemia or non-Hodgkin's lymphoma seen at the King Khalid National Guard Hospital (KKNGH) between January and December 1999 were studied to determine the best method of controlling pain during the intrathecal injection of methotrexate. The age of the patients ranged between 2 and 14 years. They were randomly divided into three groups. The first group consisted of 24 patients (all above the age of 3) who were offered psychotherapy as the sole measure to try and control their pain. A second group of 22 patients were given oral morphine and intranasal midazolam. The third group of 21 children received intravenous morphine and midazolam. Pain was assessed using three standard international pain assessment scales: the CHEOPS, VAS, and the Faces scales. There were no major complications. The group of patients who received intravenous morphine and midazolam scored lowest on the three scales (p<0.05). We conclude that the administration of intravenous morphine and midazolam is a safe and more effective method of reducing pain during the intrathecal injection of methotrexate than psychotherapy alone or oral analgesia.

NR228 Monday, May 7, 3:00 p.m.-5:00 p.m.

Clinical Profile of Dementia with Lewy Bodies (DLB) and Comparison with Possible/Probable Alzheimer's Disease

Ranjan K. Sinha, M.D., *Department of Psychiatry, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213*; Robert A. Sweet, M.D., Bruce G. Pollock, M.D., Kari Kastango, M.S., Jules Rosen, M.D., Benoit H. Mulsant, M.D., Sati Mazumdar, Ph.D.

Summary:

Objective: Initial studies in hospitalized subjects indicated that dementia with Lewy bodies (DLB) was associated with fluctuating cognition, spontaneous parkinsonism, and psychotic symptoms, especially visual hallucinations. Studies that have examined these associations in outpatient settings have less consistently found an association of DLB with psychotic symptoms. This study examined whether the behavioral symptom profile of DLB differed from that of AD in subjects admitted to a psychiatric hospital.

Method: Subjects were identified among geriatric psychiatry inpatients participating in a pharmacotherapy study of behavioral symptoms associated with dementia. Patients were diagnosed according to NINCDS/ADRDA and DLB consensus criteria. Behavioral symptoms were independently rated on the Neurobehavioral Rating Scale.

Results: 53/84 (63%) subjects were diagnosed with possible or probable AD without DLB. Eight (9.5%) subjects were diagnosed with probable DLB. AD and DLB subjects did not differ with respect to age, MMSE, gender, or race. The proportion of AD and DLB subjects experiencing a specific symptom at baseline did not differ with respect to aggression, agitation, hostility, suspicion, or delusions. In contrast, the proportion of patients experiencing hallucinations was significantly higher in the DLB group (50% versus 15%, χ^2=5.4, df=1, p<0.05).

Conclusion: Hallucinations, but not other behavioral symptoms, occurred more frequently in DLB than AD. Further studies are needed to determine which behavioral symptoms are specifically associated with DLB.

NR229 Monday, May 7, 3:00 p.m.-5:00 p.m.

HIV Seroprevalance in a Serial Sample of Patients at the Drug Dependence Treatment Centre (DDTC) at AIIMS, New Delhi, India

Meera Vaswani, Ph.D., *Allindia Institute, Edfmedical Sciences, New Delhi 110029, India*; Nimeshg Desai, M.D.

Summary:

Background: In India, the majority of heroin-dependent patients are non-parenteral users, but gradually a shift to parenteral mode is emerging. The arrival of AIDS in the country in a major way requires that special attention be paid to drug addicts forming a high-risk group for HIV-related risk behavior. In view of increasing number of intravenous drug in users (IDUs) the recent past, there is a need for studying HIV seroprevalence in India.

Objectives: 1) Study the rate of seropositivity in a consecutive sample of patients at DDTC. 2) Study pattern of risk behavior between IDUs and non IDUs. 3) Study the difference (if any) in rates of HIV seropositivity.

Methods: 154 consecutive patients were screened for HIV antibodies and those found positive were confirmed by Western blot test. All patients were explained the nature of the study and relevant information regarding drug use practice and sexual practice were obtained on a structured proforma in a one-to-one setting to ensure confidentiality. High-risk behaviors in drug use practice and sexual practice were studies in a systematic way.

Results: 98.5% of IDU's were poly drug dependent as compared to 83% of non-IDU's, who were heroindependent.

HIV seropositivity in opioid dependents was 5.5%. In IDUs, HIV seropositivity was 8.3% as compared to 1.8% in non-IDUs.

High-risk behavior in drug use practice and sexual practice in IDUs was 65.3% and 36.1% respectively.

High-risk behavior in sexual practice in non-IDUs was 27.7%

Conclusions: These findings may have devastating effects in general population in coming years. Given the fact that India has limited resources, it is imperative to introduce strict HIV prevention strategies at this stage especially for IDUs.

NR230 Tuesday, May 8, 12:00 p.m.–2:00 p.m.

Improving Adherence of Antidepressants by Pharmacies

Hein P. Van Hout, Ph.D., *Institute for Research in Extramural Medicine, Vrije University, Van Der Boechorstsraat 7, Amsterdam 1081 BT, Netherlands;* Eibert R. Heerdink, Ph.D., Guy M. Goodwin, M.D., Bram B. Bakker, Ph.D., Hugo Nieuwenhuyse, Ph.D.

Summary:

Background: As pharmacists have a central position in the distribution of antidepressants, they can play an important role in enhancing the adherence with these drugs.

Objective: To investigate whether coaching by pharmacists together with a take home video, and printed material improves adherence of patients with antidepressants.

Setting: 19 Pharmacies in the Netherlands.

Method: A randomised controlled trial with a six month follow-up will be conducted among consecutive patients attending the pharmacy for second generation antidepressant medication. The trial will consist of two arms: (1) a control group receiving care as usual, (2) an intervention group receiving an informative video and three coaching contacts by the pharmacist.

Outcome: Primary outcome is adherence of medication, expressed as intake frequency and (dis)continuation rate. It will be measured by electronic drug container monitors (eDEM). Among the secondary outcoms are self-rating of psychopathology and quality of life.

Sample size: The randomisation takes place on a patient level and a one on one ration. The sample size needed is 200 subjects. In this sample a difference of 11.3% in adherence can be detected at a significance level of 0.05 (two-sided).

Funding: grants of Organon and SmithKline Beecham. First results in January 2001.

NR231 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

ECT in Treatment-Resistant Schizophrenia: Prediction of Response and Nature of Symptomatic Improvement

Worrawat Chanpattana, M.D., *Department of Psychiatry, Srinakharinwirot University, 681 Samsen Dusit, Bangkok 10300, Thailand*; Harold A. Sackeim, Ph.D.

Summary:

Background: The clinical features of patients with schizophrenia who respond to electroconvulsive therapy (ECT) are uncertain.

Aims: This prospective study examined clinical characteristics and predictive factors associated with therapeutic outcome.

Method: Using a standardized protocol, 293 patients with refractory schizophrenia were treated with combination ECT and flupenthixol. Assessments of outcome included the Brief Psychiatric Rating Scale (BPRS), Global Assessment of Functioning (GAF), and the Mini-Mental State Examination (MMSE).

Results: One hundred-sixty patients (54.6%) met a response criterion. The duration of current episode, followed by the baseline GAF score, duration of illness, baseline MMSE score, duration of the previously failed neuroleptic trials, family history of schizophrenia, and paranoid type could predict the therapeutic outcome. Treatment resulted in marked improvement in positive symptoms but had minimal effect or worsening of negative symptoms.

Conclusions: A number of clinical characteristics could predict the therapeutic outcome to ECT. ECT had no effect on negative symptoms.

NR232 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Cognitive Deficits in Adolescents with a First-Episode Psychosis

John L. Brennan, M.D., *Redbank House, Westmead Hospital, Institute Road, Westmead MSW 2145, Australia*; Dianne J. Fitzgerald, M.A., Sara Lucas, M.A., Antoinette Redoblado, M.A., Anthony Harris, M.D.

Summary:

This study examined whether cognitive deficits in adolescent FEP patients are useful in discriminating between schizophrenia, bipolar affective disorder, and drug-induced psychosis or whether they are more useful in understanding and delineating discrete dimensions of "psychosis."

FEP patients (aged 13–25) (N = 95) and control subjects (N = 29) were administered a comprehensive standard battery of neuropsychological tasks. FEP patients were assigned to one of three diagnostic groups: schizophrenia, bipolar/affective disorder or predominantly drug-induced psychotic disorder. Clinical dimensions were derived from the PANSS in accordance with Liddle's (1987) three-factor model.

Individuals with schizophrenia demonstrated greater cognitive impairment than other psychotic groups, contrasted with control subjects. However, the profiles of cognitive deficits were similar in the three psychotic groups. Examination of clinical dimensions in first-episode schizophrenia patients revealed that the disorganization dimension was associated with several significant cognitive impairments, which was not true of the other clinical dimensions. Thus, cognitive deficits in FEP appear to be independent of diagnosis but are most severe in those with a clear diagnosis of schizophrenia. The implications of these findings for the neurodevelopmental hypothesis of schizophrenia and treatment will be discussed.

NR233 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Factors Affecting the Success of Rechallenge with Neuroleptics After NMS

Michael F. Bristow, M.R.C., *Cheam Resource Centre, 671 London Road, North Cheam SM3 9DL, England*; Dora D. Kohen, M.D.

Summary:

From a series of 38 cases of NMS collected by the authors, extensive details were available about rechallenge with neuroleptics in 22 cases. Eleven of these cases resulted in successful rechallenge and a further four were successfully rechallenge at a later date. Eight out of the 22 challenges were stopped because of a rise in CK or symptoms of NMS (failed challenges). In three of the 22 cases there was marked sensitivity to neuroleptics with two or more failed rechallenges.

The successful and the failed challenges were compared on various indices. There was little difference between the two groups on the time spent neuroleptic free after the onset of the index attack. Neither was there any difference on gender, diagnosis, age, duration of illness, or length of neuroleptic prescribing history. Successful challenges were slightly more likely to involve 'atypical' than typical drugs. The most obvious distinction between the two groups were in factors related to the severity of the index attack.

We would suggest that it is difficult to be prescriptive about when to rechallenge after NMS but that more severe cases will require a longer drug-free period.

This is a submission for a poster session likely to be of interest to General Adult Psychiatrists

NR234 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Comparison of Quetiapine and Haloperidol in Treatment-Resistant Schizophrenia

Peter F. Buckley, M.D., *Department of Psychiatry, Medical College of Georgia, 1515 Pope Avenue, Augusta, GA 30912-3800*; Jeffrey M. Goldstein, Ph.D., Robin A. Emsley, M.D.

Summary:

Objective: To compare the efficacy of quetiapine and haloperidol in patients resistant to fluphenazine.

Methods: Patients with treatment-resistant schizophrenia received fluphenazine (20 mg/day) for 4 weeks. Those with no or partial response to fluphenazine were randomly assigned to quetiapine (600 mg/day) or haloperidol (20 mg/day) for 8 weeks. Efficacy was measured using PANSS total score, BPRS score, CGI Severity of Illness score, and the proportion of patients classified as responders (20% reduction in PANSS score from baseline or CGI score ≤3).

Results: Ninety-five patients had PANSS scores that either stayed the same or increased with fluphenazine (Baseline PANSS scores were 92.8 [N = 54] for quetiapine and 94.0 [N = 41] for haloperidol.) After 8 weeks, changes from baseline for PANSS scores were −14.2 and −9.5 for the quetiapine and haloperidol groups, respectively ($p = 0.28$); for derived BPRS scores, −8.8 and −5.6, respectively ($p = 0.23$); and for CGI scores, −0.67 and −0.24, respectively ($p = 0.072$). Fifty-nine percent of quetiapine-treated patients were classified as responders (PANSS) compared with 38% of haloperidol-treated patients ($p = 0.099$). Using the CGI score, 51% and 25% of quetiapine and haloperidol patients, respectively, were classified as responders ($p = 0.043$).

Conclusions: Quetiapine is more effective than haloperidol in patients with treatment-resistant schizophrenia.

NR235 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Predicting Pre-ECT Mental Status Scores from Post-ECT Mental Status Scores

Julie C. Hathaway, M.S., *Department of Psychiatry, Mayo Foundation, 200 First Street, SW, Rochester, MN 55905*; Karen M. Graszer, M.A., Glenn E. Smith, Ph.D., Teresa A. Rummans, M.D.

Summary:

This study was undertaken to establish the validity of Mini-Mental State Exam scores (MMSE) obtained after first or second ECT treatment as estimators of pre-ECT MMSE. Twenty patients participating in the Consortium of Researchers in ECT (CORE) studies were administered the MMSE prior to initiation of treatment and 12–24 hours after the first and second treatments. Mean Hamilton Rating Scale of Depression (HRSD) score at pre-ECT was 33.4, and HRSD score following the first and second treatments averaged 25.6 and 21.5.

The average pre-ECT MMSE score for this group was 26.35 (SD = 3.5). MMSE scores following the first and second treatments were 26.40 (SD = 3.9) and 27.45 (SD = 3.3). The change from pretreatment to after the second treatment was statistically significant ($p = 0.02$). Correlation between initial MMSE score and MMSE scores obtained after one ECT treatment was significant ($r = 0.79$, $p < 0.05$). Correlation of pretreatment MMSE score and MMSE scores obtained after the second treatment was also significant ($r = 0.84$, $p < 0.05$).

These results suggest that MMSE scores obtained after one or two ECT treatments do provide a good estimate of pre-ECT scores. If MMSE cannot be obtained prior to initiation of treatment, pre-ECT mental status scores can be estimated from scores obtained 12–24 hours after the first or second ECT treatment.

NR236 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Psychometric Qualities of the Edinburgh Postnatal Depression Scale (EPDS) and Depressive Symptomatology Self-Report (IDS-SR) in Postpartum Minority Women

Dana March, B.A., *Department of Psychiatry, Yale Medical School, 142 Temple Street, Suite 301, New Haven, CT 06510*; Ashley Azar, M.S., Kimberly A. Yonkers, M.D., A. John Rush, M.D.

Summary:

Objective: Major depressive disorder (MDD) during the postpartum period remains underdetected and undertreated. Self-report screening questionnaires can increase detection but should be applicable to different populations. We examined performance of Spanish translations of the inventory of Depressive Symptomatology—Self-Report (IDS-SR) and the Edinburgh Postnatal Depression Scale (EPDS) compared with English versions.

Methods: Over 800 postpartum women from primary care obgyn clinics underwent multistage screening for depressive symptoms and SCID-diagnosed MDD. The psychometric performance of the IDS-SR & EPDS in African-American (AA) women (n = 164) and Spanish-only speaking Latina women (n = 604) were evaluated.

Results: The alpha coefficients for the English EPDS and IDS-SR were .83 and .88, respectively, indicating high internal consistency. Similar high internal consistency was found for the Spanish versions (EPDS = .84 and IDS-SR = .84). Using a threshold of 18 on the English version of the IDS-SR, the sensitivity was 1.0, specificity .80, positive predictive value (PPV) .50, negative predictive value (NPV) 1.0. Performance was superior in the Spanish version. Similarly, performance of the Spanish version of the EPDS, using a threshold of 12, was at least as high as the English version (sensitivity = .79, specificity = .90, PPV = .66, NPV = .95).

Conclusion: Performance of self-report depression screening scales among postpartum women was excellent and equivalent in Spanish and English versions.

NR237 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Effect of Long-Term Monotherapy on Weight in Schizophrenia

Martin B. Brecher, M.D., *AstraZeneca, 1800 Concord Pike, Box 15437, Wilmington, DE 19850-5437*; Karen Melvin, B.S.C.

Summary:

Objective: To obtain a clearer interpretation of the direct effects of quetiapine on weight.

Methods: Patients with schizophrenia who received quetiapine monotherapy for antipsychotic treatment were analyzed during open-label extensions of controlled and uncontrolled clinical trials. To assess the long-term effect of quetiapine monotherapy, weight change from baseline to endpoint was examined in a cohort of patients who had received at least six months' treatment (mean 18.6 months). Baseline body mass index (BMI) was calculated and patients were grouped according to NIH National Heart, Lung, and Blood Institute's standard categories for BMI.

Results: Quetiapine had a neutral effect on weight across the BMI spectrum. The 95% confidence intervals of the mean weight change from baseline to endpoint encompassed zero for all BMI categories, except for the severely obese (BMI ≥ 35 kg/m^2) in

whom slight, but statistically significant, weight loss was observed. Additional analysis of the complete cohort suggested no quetiapine dose-related effects on weight change. There was no gender effect on weight change and only one patient withdrew because of weight gain.

Conclusions: Quetiapine's proven efficacy and tolerability combined with its neutral effect on weight suggest that the drug is a first-choice antipsychotic for the long-term treatment of schizophrenia.

NR238 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Safety During Long-Term Exposure to Quetiapine

Jonathan S.E. Hellewell, M.B., *Department of Psychiatry, Trafford General Hospital, Moorside Road, Macclesfield, Cheshire M41 55L, United Kingdom*; Emma Westhead, M.S.C.

Summary:

Objective: To assess long-term safety of quetiapine using data from open-label extension (OLE) phase of clinical trials.

Methods: Patients who completed a trial's randomized treatment phase, or who had completed at least four weeks of randomized treatment and met study withdrawal criteria, were eligible for OLE trial. Open-label treatment with quetiapine consisted of an initial titration period whereby dose was increased according to clinical condition. Thereafter, dosing was flexible, up to a maximum of 800 mg/d, twice daily. Assessment included 478 patients with schizophrenia and schizoaffective disorder. Mean daily doses during OLE treatment averaged between 450–500 mg throughout the three-year observation period. At one year, 160 patients (35%) were receiving quetiapine, and most continued to receive treatment for two additional years. At trial entry, approximately one-quarter of the population were receiving anticholinergic medication; after one year of quetiapine, the proportion taking anticholinergics had dropped to less than one-third that recorded at baseline.

Results: Adverse-event profile during open-label treatment was similar to that observed during randomized periods of individual trials. No new safety concerns were raised.

Conclusions: Quetiapine was well tolerated, with a continuation rate at 12 months similar to those observed in long-term studies with other atypical antipsychotics.

NR239 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Maintenance of Long-Term Efficacy and Safety of Quetiapine in Schizophrenia

Siegfried Kasper, M.D., *Department of General Psychiatry, University of Vienna, Wahringer Gurtel 18-20, Vienna A-1090, Austria*

Summary:

Objective: To demonstrate the maintained efficacy and safety of quetiapine.

Methods: Data were analyzed from four OLE studies in which adults received quetiapine for up to 130 weeks. Patients completing the acute phase were eligible for the OLE, irrespective of trial medication. Efficacy was measured as change from baseline in Brief Psychiatric Rating Scale (BPRS) total, the Clinical Global Impression (CGI) Severity of Illness, and Scale for the Assessment of Negative Symptoms (SANS) total scores. Safety evaluations included Simpson-Angus Scale (SAS), Abnormal Involuntary Movement Scale (AIMS), adverse events, and vital signs. OLE phases included 674 patients. Mean quetiapine OLE dosage was 472.4 ± 175.5 mg/d, with mean total quetiapine exposure of 325.5 days.

Results: The efficacy of quetiapine was maintained throughout the OLE period, with significant ($P < 0.001$ for each) improvements from baseline reported at 13, 26, 52, 78, 104, and 130 weeks for BPRS total, CGI Severity of Illness, and SANS total scores. Quetiapine was well tolerated during long-term therapy with significant ($P < 0.001$ for each) improvements from baseline being observed at 13, 26, 52, 78, 104, and 130 weeks for AIMS and SAS scores.

Conclusions: Quetiapine offers a long-term maintained response for positive and negative symptoms of schizophrenia while being well tolerated.

NR240 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Successful Tamsulosin Treatment of Reboxetine-Induced Urinary Hesitancy

Siegfried Kasper, M.D., *Department of General Psychiatry, University of Vienna, Wahringer Gurtel 18-20, Vienna A-1090, Austria*; R. Wolf, M.D.

Summary:

Objectives: Urinary hesitancy can be an uncomfortable side effect during antidepressant treatment, especially in male patients with prostate enlargement. Urinary hesitancy occurring with prostate enlargement is often treated with the peripheral α_2-blocker, tamsulosin.

Methods: In this study, eight male patients (57–64 years; DSM-IV diagnosis of recurrent depression) treated successfully with reboxetine, but experiencing difficulties urinating, were treated concurrently with tamsulosin (0.4 mg).

Results: All patients experienced relief of urinary hesitancy within 20 minutes, and this relief was sustained. One patient withdrew tamsulosin after two weeks, but continued reboxetine treatment and noticed no further problems from the urinary tract. Another patient who had ceased treatment with reboxetine due to urinary problems, then subsequently had a suboptimal response to other serotonergic antidepressants, was recommenced reboxetine treatment (4–8 mg) together with tamsulosin and was then free from urinary problems. Similar effects of tamsulosin have also been observed after co-administration with other noradrenergic antidepressants.

Conclusions: Our results suggest that concomitant treatment with tamsulosin and noradrenergic antidepressants should be considered if urinary hesitancy is apparent to such an extent that antidepressant therapy needs to be withdrawn.

NR241 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

CAG Repeats KCNN3 In the Patients with Schizophrenia

Hyo-Jung Ko, M.D., *Department of Psychiatry, Samsung Medical, 50 Ilowon-dong, Kangnam-gu, Seoul 135-710, Korea*; Doh-Kwan Kim, M.D., Shinn-Won Lim, M.A., Min-Young Seo, M.D., Byung-Lo Kim, M.D.

Summary:

Objective: We investigated a possible association between the polymorphic trinucleotide repeat (TNR) expansion in potassium channel gene *KCNN3* and schizophrenia.

Methods: CAG/CTG repeat distribution in *KCNN3, CTG18.1,* and ERDA1 was examined and the copy number of ligation product in repeat expansion detection (RED) was measured in Korean schizophrenics (n = 245) and ethnically matched controls (n = 116).

Results: Longer alleles in the gene *KCNN3* were over-represented in the patients. The frequency of alleles with CAG repeats longer than 19 copy in the *KCNN3* gene was higher in schizophrenics (73.3% vs. 65.1%; p = 0.029, Fisher's exact test). This difference was more prominent in schizophrenics with familial background (p = 0.03, Fisher's exact test). We found no difference in the frequency of longer alleles between negative and positive

subtypes of schizophrenia. Ligation product size in RED and alleles with CAG repeat number in the *CTG18.1* gene was not increased in the patients. The copy number of ligation product in RED was highly correlated with CAG/CTG copies of ERDA1 both in the patient group ($R = 0.45$, $p < 0.001$) and the control group ($R = 0.44$, $p < 0.001$). However, CAG repeat length in the *KCNN3* gene was not correlated with ERDA1 score.

Conclusions: Our results support the hypothesis that the longer allele of *KCNN3* may be considered as a candidate gene for schizophrenia, especially in the cases with familial background. The RED assay results were affected by the CAG copy number of ERDA1.

NR242 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Quetiapine and Risperidone in Outpatients with Schizophrenia: Subanalysis of the QUEST Trial

Rajiv Tandon, M.D., *Department of Psychiatry, University of Michigan, 1500 East Medical Center Drive, UH9C9150, Ann Arbor, MI 48109-0120*

Summary:

Objective: The tolerability and efficacy of quetiapine and risperidone were compared in adult outpatients with schizophrenia.

Methods: In a four-month, multicenter, open-label trial, 751 adult outpatients with psychotic disorders were randomized in a 3:1 ratio (quetiapine:risperidone) and were flexibly dosed. Assessments included the Extrapyramidal Symptoms (EPS) Checklist, the Hamilton Rating Scale for Depression (HAMD), the Clinical Global Impression (CGI), and the Positive and Negative Syndrome Scale (PANSS). A subanalysis was performed on the 251 patients with diagnoses of schizophrenia.

Results: A total of 167 patients were randomized to quetiapine (mean dose 288.1 mg/day) and 51 patients to risperidone (mean dose 5.1 mg/day). At 16 weeks, changes from baseline in the PANSS (positive, negative, total, general psychopathology) scores and HAMD scores were statistically significant ($P < 0.001$) for patients receiving either quetiapine or risperidone, with no significant differences between the two treatments. Patients in both treatment groups showed improvement from baseline in the CGI ratings. Significantly fewer patients receiving quetiapine required adjunctive medication for EPS or had substantial EPS than patients receiving risperidone (3.7% and 7.5% vs 13.3% and 15%, $P < 0.001$ and $P < 0.002$, respectively).

Conclusions: Quetiapine and risperidone are equally effective in the treatment of schizophrenia, and quetiapine produces less EPS than risperidone.

NR243 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Evolution of Plasma HVA Levels in Schizoaffective Disorder

Andre J. Galinowski, M.D., *Hospital Sainte Anne Shu Prof Loo, 1 Rue Cabanis, Paris 75014, France*; Odile Varoquaux, Ph.D., Marie F. Pririer, M.D., Christian Castelnau, M.D., Marie C. Bourdec, Ph.D.

Summary:

Plasma homovanillic acid (pHVA) levels were measured by HPLC at different time points in seven schizo-affective depressed inpatients and four schizo-affective inpatients with a mixed episode, receiving a standardized treatment (lithium, chorpromazine, and clomipramine) during at least four weeks. Plasma HVA levels were also obtained through serial sampling between 8:00 and 14:00 hours at baseline and endpoint, and compared with measurements in normal controls. Subjects were controlled for food intake and motor activity. No significant difference was observed between patients and controls. Under treatment, pHVA levels increased ($p < 0.02$) with clinical improvement (MADRS and PANSS scores) in depressed SA patients. In comparison, pHVA levels tended to remain stable ($p < 0.06$) in the mixed SA subgroup. Although effects of medications prior to the study period were not controlled, results suggest that SA patients, unlike schizophrenic patients receiving antipsychotic drugs, may have normal pHVA levels that do not decline with clinical improvement. Plasma HVA levels tend to vary differently according to mood status. P HVA may help to differentiate SA disorder, an insufficiently defined entity, from schizophrenia.

NR244 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Educational Interventions for the Management of Antipsychotic-Related Weight Gain

Kimberly H. Littrell, N.P., *The Promedica Research Center, 3562 Habersham at Northlake J200, Tucker, GA 30084*; Richard G. Petty, M.D., Nicole M. Hilligoss, M.S., Carol D. Peabody, M.S., Craig G. Johnson, M.D.

Summary:

Background: Recent literature has focused on the weight gain liability associated with atypical antipsychotics. Recommendations are emerging that emphasize the importance of careful monitoring of weight in patients treated with these agents. Furthermore, preliminary data indicate that patients may benefit from interventions that include nutritional counseling and exercise programs to reduce the impact of antipsychotic-related weight gain.

Objective: To determine the effect of a modular educational program on weight gain among olanzapine-treated patients.

Method: Twelve patients (6 M, 6 F) with a DSM-IV diagnosis of schizophrenia or schizoaffective disorder entered this four-month study. All patients began olanzapine treatment at study entry. The patients were then randomized into an intervention group (3 M, 3 F) and a standard care group (3 M, 3 F). The intervention group participated in a one-hour, weekly class that used a modular educational program on nutrition and exercise. The patients' weights and BMIs were measured and recorded monthly.

Results: The mean change in weight of the intervention group was +1 lb. (range: −10.5 to +7.5 lbs.), while the mean change in the standard care group was +6.4 lbs. (range: −13 to +26 lbs.). The mean change in BMI's of the intervention group and standard care group was +0.3 (range: −1.4 to +0.9) and +0.9 (range: −2.6 to +3.4), respectively. Although there was not a statistically significant difference in BMIs (baseline to endpoint) in either group, subjective reports of personal comfort and self-image were notably different. Gender differences were noted in both the intervention group and the standard care group. At endpoint, males gained more weight than females in the intervention group (M = +8 lbs.; F = −0.7 lbs.) and the standard care group (M = +13.7 lbs.; F = −2.5 lbs).

Conclusions: This small, preliminary study suggests that an educational intervention may positively influence antipsychotic-induced weight gain as well as influence feelings of self-image. Larger, extended, controlled trials are needed to more fully understand the impact that educational interventions may have on preventing or limiting antipsychotic-induced weight gain.

NR245 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

The Effect of Olanzapine on Anxiety Among Patients with Schizophrenia

Kimberly H. Littrell, N.P., *The Promedica Research Center, 3562 Habersham at Northlake J200, Tucker, GA 30084*; Richard G. Petty, M.D., Nicole M. Hilligoss, M.S., Carol D. Peabody, M.S., Craig G. Johnson, M.D.

Summary:

Background: Anxiety disorders are extremely common among patients with schizophrenia. Upwards to one-third of patients have some type of comorbid anxiety disorder, yet accurate recognition and treatment of anxiety symptoms continues to be a clinical problem. There is emerging data that suggest that atypical antipsychotics may reduce anxiety symptoms in patients with schizophrenia.

Objective: To determine the effect of monotherapy olanzapine on anxiety among patients with schizophrenia or schizoaffective disorder.

Method: Twenty-four patients (17 M, 7 F) were enrolled in a six-month, open-trial of monotherapy olanzapine. All patients met DSM-IV criteria for schizophrenia or schizoaffective disorder with at least mild anxiety (G-2 $\geq$ 3) at baseline. All patients were receiving conventional antipsychotics at study entry and were cross-titrated to olanzapine (mean dose = 17 mg/day). The patients were evaluated for effects on psychosis and anxiety at baseline, three months, and six months using the Positive and Negative Syndrome Scale (PANSS).

Results: ANOVA results indicate a statistically significant difference in PANSS total scores [$F(2,69) = 9.03$, $p < .001$], PANSS general scores [$F(2,69) = 9.97$, $p < .001$], and PANSS G-2 (anxiety) scores [$F(2,69) = 21.16$, $p < .0001$] between baseline and endpoint. Further analysis of G-2 using Scheffe' tests revealed: (1) statistically significant difference in scores between baseline and three months [$F(2,69) = 9.85$, $p < .001$], (2) between baseline and six months [$F(2,69) = 20.19$, $p < .0001$], and (3) no difference between three and six months [$F(2,69) = 1.84$, $p > .05$].

Conclusions: These preliminary data suggest olanzapine to have a positive effect on anxiety in patients with schizophrenia. Further study with larger, controlled samples is required to better quantify this phenomena.

NR246 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Cigarette Smoking in Schizophrenia and Sensation Seeking

Alain Dervaux, M.D., *Department of Psychiatry, Hopital Sainte Anne, Shu, 1 Rue Cabanis, Paris F-75014, France*; Franck J. Bayle, M.D., Xavier Laqueille, M.D., Marie-Chantal Bourdel, Michelle Leborgne, Jean-Pierre Olie, M.D., Marie-Odile Krebs, Ph.D.

Summary:

Objective: To compare sensation seeking, impulsivity, and anhedonia in a sample of schizophrenic patients with and without current nicotine use.

Method: The Positive and Negative Syndrome Scale, the Fagerstrom Scale, the Barratt Impulsivity Scale, the Zuckerman Seeking Sensation Scale, and the Chapman Physical Anhedonia Scale were used in 100 subjects meeting the DSM-III-R criteria for schizophrenia or schizoaffective disorder.

Results: A total of 67% of the subjects in the study presented current nicotine use. There was a significant different gender distribution: 77.6% of the smoking patients were males compared with 48.5% of the nonsmoking patients ($p = 0.006$). Smoking patients were younger than nonsmoking patients ($p = 0.02$). Adjusted on the basis of age and gender, the mean scores for Sensation Seeking Scale were lower in nonsmoking than in smoking schizophrenic patients (Mean $\pm$ SD, 11.5 ± 5.8 vs 16.6 ± 6.6, ANCOVA, $F = 4.06$, $df = 1,92$, $p = 0.047$). The differences concerned the disinhibition subscale ($F = 8.20$, $df = 1,92$, $p = 0.005$). There were no significant differences in the mean number of hospitalizations, PANSS total score, mean scores for Barratt Impulsivity Scale, and Physical Anhedonia Scale.

Conclusions: Cigarette smoking in schizophrenic patients is associated with different levels of sensation seeking. The disinhibition factor is especially low in non smoking patients.

NR247 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Eye-Tracking Deficits in PTSD with Secondary Psychotic Symptoms

Arleen Cerbonne, M.A., *Department of Psychiatry/Neurology, Tulane University Health Science Center, 1430 Tulane Avenue, TB53, New Orleans, LA 70112*; William J. Evans, Ph.D., Fredric J. Sautter, Ph.D., Justin Wiley, Ph.D., Janet E. Johnson, M.D., Daniel K. Winstead, M.D., Barry D. Schwartz, Ph.D.

Summary:

Objectives: Studies have demonstrated high comorbidity between post-traumatic stress disorder (PTSD) and psychotic symptoms. One way to increase our understanding of this comorbidity is to determine whether patients with PTSD and psychosis show biological and behavioral characteristics that are uniquely associated with PTSD or whether these characteristics are similar to those seen with psychotic disorders.

Method: Patients with PTSD and psychosis, nonpsychotic PTSD, schizophrenia, and healthy control subjects were compared for differences on self-report personality measures, family history of psychiatric disorder, smooth pursuit eye movement (SPEM), and corticotropin-releasing factor (CRF).

Results: PTSD with psychotic symptoms was associated with a paucity of familial schizophrenia and with SPEM deficits that were significantly different from those found in schizophrenia. Patients with PTSD and psychosis showed high levels of CRF that were similar to the levels of CRF found in PTSD.

Conclusions: These data suggest that the psychotic symptoms that co-occur with PTSD may be etiologically different than the psychotic symptoms of the psychotic disorders and they suggest that PTSD with comorbid psychosis may represent a subtype of PTSD.

NR248 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Studies of PTSD with Secondary Psychotic Symptoms

Fredric J. Sautter, Ph.D., *Department of Psychiatry/Neurology, Tulane University Health Science Center, 1430 Tulane Avenue, New Orleans, LA 70112*; Justin Wiley, Ph.D., Arleen Cerbonne, M.A., Gina Manguno-Mire, Ph.D., William J. Evans, Ph.D., Janet E. Johnson, M.D., Barry D. Schwartz, Ph.D.

Summary:

Objectives: Approximately 30% of patients with post-traumatic stress disorder (PTSD) also have a lifetime history of psychosis. The present study was designed to determine if patients with comorbid PTSD and psychosis exhibit abnormalities in smooth pursuit eye movements (SPEM) and whether these SPEM abnormalities are similar to those associated with schizophrenia.

Method: Fourteen patients with PTSD and comorbid psychosis, 14 patients with schizophrenia, and 15 normal control subjects were tested on a pendular smooth pursuit task at frequencies that ranged from 0.3 to 1.1 Hz. Performance data were extracted from each of the five frequencies and separated into 10 discrete components that corresponded to target velocity (i.e., 10 bins).

Results: A repeated measures analysis of variance indicated that the performance of patients with PTSD was significantly different from normal subjects and schizophrenic patients for percentage of time in smooth pursuit ($p = 0.0001$).

Conclusions: The findings suggest an early information processing deficit in PTSD as indexed by SPEM that differs from the

type of deficit found in schizophrenia. These results provide initial evidence that the observed SPEM deficit in PTSD patients with psychosis may involve a different neurophysiologic mechanism than that which underlies schizophrenia.

NR249 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Social Contact and Social Functioning in a Sample of Individuals with Schizophrenia

Prudence Z. Lim, M.P.H., *Health Outcomes, Eli Lilly and Company, Lilly Corporate Center, DC 1850, Indianapolis, IN 46205*; Sandra L. Tunis, Ph.D., Haya Ascher-Svanum, Ph.D., Bruce J. Kinon, M.D.

Summary:

Title: Social Contact and Social Functioning in a Sample of Individuals with Schizophrenia

Authors: Lim PZ, Tunis SL, Ascher-Svanum H, and Kinon BJ.

Introduction: Social isolation is common among individuals with schizophrenia and can negatively impact treatment and outcome (1). The purpose of this analysis was to assess self-reported levels of social contact and social functioning in a sample (N = 529) with schizophrenia or schizoaffective disorder.

Method: Self-reported baseline information from the Lehman Quality of Life Scale and the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36), for participants in a cost-effectiveness trial of antipsychotics, was analyzed.

Results: Over half (52%) reported primarily living independently (over the prior 12 months), 19% reported living with a family member, and 3% reported being homeless. Over one-third (36%) reported that during the past year they got together with a family member less than once/month or not at all. A similar proportion (37%) said they visited with someone (who did not live with them) either less than once/month or not at all. This sample reported clinically significant lower levels (i.e., greater than 5 points) of social functioning when compared to the general population (2).

Conclusions: These results document substantial social isolation and impairments in social functioning for this sample of individuals with schizophrenia. Routinely assessing and addressing the social isolation experienced by many individuals with schizophrenia should be an important element in treatment.

NR250 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Pharmacokinetics of Intramuscular Ziprasidone in Healthy Volunteers

Jeffrey J. Miceli, Ph.D., *Department of Central Research, Pfizer, Incorporated, Building 260, Eastern Point Road, Groton, CT 06340*; Keith D. Wilner, Ph.D., Thomas G. Tensfeldt, M.S.

Summary:

Objective: To evaluate the pharmacokinetics of the intramuscular (Im) formulation of ziprasidone.

Methods: An open, 3-way crossover study of 5 mg IV, 5 mg IM, and 20 mg oral ziprasidone (N = 13) and an investigator-blinded, parallel-group trial of 5-, 10-, and 20-mg IM doses (N = 18) were conducted. Blood samples were collected between 0 and 24 h after IV and IM dosing and for 36 h after oral dosing. Serum concentrations were determined using HPLC.

Results: Mean values for 5 mg IV, 5 mg IM, and 20 mg oral ziprasidone were as follows: C_{max} = 83, 80, and 64 ng/ml, respectively; T_{max} = 1.0, 0.5, and 8.2 h; $AUC_{0-infinity}$ = 217, 223, and 514 ng·h/ml; and elimination $t_{1/2}$ = 3.1, 3.0, and 3.8 h. Mean values for 5-, 10-, and 20-mg IM doses were as follows: C_{max} = 76, 156, and 244 ng/ml respectively; AUC = 229, 463, and 846 ng·h/ml; T_{max} = 0.50, 0.7, and 0.7 h; and $t_{1/2}$ = 2.4, 2.2, and 3.0 h.

Conclusions: In these studies, IM ziprasidone demonstrated complete bioavailability, a T_{max} < 1 h, predictable pharmacokinetics with exposure proportional to dose, and a $t_{1/2} \leq 3$ h. The short T_{max} observed is consistent with the rapid onset of effect seen in clinical trials. The relatively short $t_{1/2}$ allows for a transition to oral drug without concern over persisting drug exposure.

Study supported by Pfizer Inc.

NR251 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Cardiovascular Safety Profile of Ziprasidone: Clinical Development Data

Steven J. Romano, M.D., *Pfizer, Incorporated, 235 East 42nd Street, New York, NY 10017*

Summary:

Objective: To characterize the cardiovascular safety profile of ziprasidone.

Methods: We reviewed electrocardiographic and/or cardiovascular disease risk factor data from short-term (4–6 week) and long-term (≥6 months) studies involving 4,571 patients receiving up to 160 mg/day of oral ziprasidone.

Results: QTc was prolonged a mean 5.9–9.7 msec in fixed-dose trials. QTc > 500 msec was seen in 0.06% of ziprasidone patients versus 0.23% of placebo users. A total of 1.1% of ziprasidone and 0.7% of placebo patients had mean QTc intervals prolonged >60 msec over baseline. A phase I study found no further increase in QTc at steady state with coadministration of a potent metabolic inhibitor. In 1,733 patient-years of exposure, there has been no excess in sudden deaths or syncopy compared with placebo or comparator antipsychotics and no cases of torsade de pointes. Further, no significant cardiovascular events after overdose were observed. In trials, ziprasidone demonstrated a weight-neutral profile. In one short-term study, total cholesterol (TC) ($p < 0.001$), triglycerides ($p < 0.001$), and TC/HDL ratio ($p < 0.01$) improved over baseline.

Conclusions: Ziprasidone has a well characterized cardiovascular safety profile, including low incidence of weight gain and benign effect on lipids. An absence of important drug interactions enhances ziprasidone's overall safety profile.

NR252 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Ziprasidone Versus Olanzapine in Schizophrenia: Results of a Double-Blind Trial

George M. Simpson, M.D., *Department of Psychiatry, LAC/USMC Medical Center, 2020 Zonal Avenue, IRD Room 20, Los Angeles, CA 90033*; Richard L. O'Sullivan, M.D., Cynthia Siu, Ph.D.

Summary:

Objective: To compare the efficacy, tolerability, and safety of ziprasidone and olanzapine in acute inpatients with schizophrenia or schizoaffective disorder.

Methods: In a 6-week, double-blind, multicenter trial, 268 acute inpatients with schizophrenia or schizoaffective disorder were randomly assigned to ziprasidone (40–80 mg b.i.d.) or olanzapine (5–15 mg/day). Primary efficacy evaluations included the BPRS and CGI-S. Secondary assessments included the PANSS. Tolerability and safety measurements included weight, fasting laboratory tests, and treatment-emergent adverse events.

Results: There were no statistically significant differences in BPRS total and core scores, PANSS total scores, or CGI-S (all patients, LOCF) in ziprasidone- and olanzapine-treated patients. Both agents were well tolerated, with movement disorder ratings generally improving with both treatments. Patients receiving olanzapine had significantly greater mean weight gain ($p < 0.001$) and median increases in total cholesterol ($p < 0.001$) and LDL ($p < 0.01$).

Conclusions: Ziprasidone and olanzapine yielded comparable improvement in psychopathology and global illness severity, but there were significant differences favoring ziprasidone in important health parameters.

NR253 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Haloperidol to Ziprasidone Switching Strategies in Schizophrenia

Emmanuel Stip, M.D., *Department of Psychiatry, Louis Hospital Lafont. Fernandseguin, 7331 Rue Hochelaga, Montreal, PQ H1N 3V2, Canada*

Summary:

Objectives: To determine efficacy and tolerability of three strategies for switching from haloperidol to ziprasidone in patients with schizophrenia or schizoaffective disorder.

Methods: In a 6-week study, 54 patients received ziprasidone 40 mg b.i.d. for 2 days, with titration to 80 mg b.i.d. Haloperidol was tapered through three schedules: discontinuation on day 1; 50% of dose on days 1–7, then discontinuation; or 100% of haloperidol dose on days 1 and 2, 50% on days 3–7, and discontinuation. Primary efficacy evaluations included BPRS, CGI-S, and CGI-I. Tolerability assessments included the Extrapyramidal Symptom Rating Scale (ESRS) and the Barnes Akathisia Scale (BAS).

Results: Among all patients (last observation carried forward), symptom control was sustained, with no significant change in BPRS for any strategy. Study completers (N = 40) experienced improved BPRS (–6.0, $p = 0.0003$) and CGI-S (–0.57, $p = 0.0002$). Of all patients, 75% responded to therapy (CGI-I score = 1, 2, or 3). All strategies were well tolerated. Patients experienced improved ESRS (–4.7, $p < 0.0001$) and BAS (–0.61, $p = 0.042$) scores, with no significant differences between strategies. No weight gain was observed. Serum prolactin decreased by a median 2.4 ng/ml.

Conclusions: Switching from haloperidol to ziprasidone through any of three strategies yielded sustained symptom control and improved movement disorder measurements.

NR254 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Randomized Field Study of the Insight Program for the Treatment of Schizophrenia

Douglas Turkington, M.D., *Department of Psychiatry, Roya Victoria Infirmary, U. of New Castle, Queen Victoria Road, New Castle (Tyne) NE1 4LP, United Kingdom*; David G. Kingdon, M.D., Trevor Turner, M.D.

Summary:

Objective: To investigate whether specially trained community psychiatric nurses could successfully deliver cognitive behavior therapy (CBT) and psycho-educational materials to patients with schizophrenia to improve insight and overall symptomatology.

Methods: A randomized trial compared the Insight Programme with treatment as usual in a community sample of schizophrenic patients at six U.K. sites. Patients (N = 257) were randomly assigned to insight intervention and 165 to treatment as usual; 225 and 128 patients, respectively, completed the study. Intervention consisted of six sessions of CBT over 3 months. The main caregiver was offered three sessions. Nurses were given 10 days' intensive CBT training. Primary outcome measures were changes from baseline in insight, overall symptoms, and burden of care.

Results: Patients undergoing CBT experienced significant improvement in insight ($p = 0.001$) and overall symptomology ($p = 0.016$) but not in burden of care or psychotic symptoms. Depression was also significantly improved ($p = 0.013$), with no significant increase in suicidal ideation.

Conclusions: Community psychiatric nurses with appropriate training and supervision can effectively deliver brief CBT intervention to patients with schizophrenia and to their caregivers. Further assessment of results will be carried out 6 months after end of therapy to assess the duration of effects.

Study supported by Pfizer Inc.

NR255 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Improving Insight in Schizophrenia: The Effects of Cognitive-Behavior Therapy and Psychoeducation

Douglas Turkington, M.D., *Department of Psychiatry, Roya Victoria Infirmary, U. of New Castle, Queen Victoria Road, New Castle (Tyne) NE1 4LP, United Kingdom*; David G. Kingdon, M.D., Trevor Turner, M.D.

Summary:

Objective: To establish whether a brief cognitive behavioral intervention as delivered by psychiatric nurses in the community can improve insight in schizophrenia as compared with treatment as usual.

Method: A total of 422 patients with established schizophrenia were randomized to receive either CBT and psychoeducation (257 patients) or treatment as usual (165 patients), 97 carers also received CBT and psychoeducation. Independent raters blind to the patient's treatment condition assessed patients and carers at baseline and at end of therapy (mean = 20 weeks). Insight was rated on the Insight Rating Scale, overall symptoms on the Comprehensive Psychopathological Rating Scale, and the burden of care on the Burden of Care Questionnaire. Clinical significance was set at 25% improvement.

Results: Patients who received CBT and psychoeducation demonstrated a significant improvement in insight ($p = 0.001$), overall symptoms ($p = 0.016$), and in depression ($p = 0.013$) but not in the burden of care ($p = 0.533$). There was no significant increase in suicidal ideation ($p = 0.196$). Overall symptomatology alone has improved to a clinically significant degree.

Conclusions: Community psychiatric nurses can be trained to safely and effectively deliver CBT and psychoeducation to patients with schizophrenia and their carers.

NR256 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Mortality and Cardiovascular Morbidity Among Patients with Schizophrenia

Cheryl Enger, Ph.D., *Department of Epidemiology, Ingenix, One Jackson Square, 8th Floor, Jackson, MI 49201*; Lisa Weaterby, M.S., Robert F. Reynolds, D.Sc., Dale Glasser, Ph.D., Alexander M. Walker, M.D.

Summary:

Objective: To estimate mortality, cardiovascular morbidity, and frequency of new-onset diabetes among patients with schizophrenia.

Methods: Study population included 1,920 patients in UnitedHealthcare research database who received antipsychotic medication between 4/1/95 and 3/31/99, and physician services with an associated diagnosis of schizophrenia. Patients were matched by age, sex, and health plan to 9,600 persons randomly selected from the general membership of UnitedHealthcare. Mortality, cardiovascular morbidity, and new-onset diabetes were determined using National Death Index search and medical claims records.

Results: After adjustment for covariates, risk of death was 4 times greater in the schizophrenia group than in the control group, regardless of whether patients were dispensed a typical or atypical antipsychotic. Schizophrenic patients taking typical antipsychotics had increased risk of myocardial infarction (MI) (RR = 5.34; 95%CI = 1.75–16.30) and arrhythmia (RR = 2.38; 95%CI = 0.54–

10.55) compared to patients without schizophrenia. Schizophrenic patients regularly taking either typical or atypical antipsychotics had increased risk of diabetes (RR = 3.41; 95%CI = 1.62–7.15).

Conclusions: Mortality and cardiovascular morbidity among patients with schizophrenia are significantly elevated compared with rates in matched control subjects. Users of typical and atypical antipsychotics do not differ in their overall mortality or risk of new-onset diabetes. Typical antipsychotics appear to be associated with higher risk of MI and arrhythmia.

NR257 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Increased Cardiovascular Disease in Patients with Schizophrenia

Suellen M. Curkendall, Ph.D., *Department of Research, The Degge Group, 1616 North Fort Myer Drive, Suite 1430, Arlington, VA 22209*; Jingping Mo, Ph.D., Judith K. Jones, M.D., Dale Glasser, Ph.D.

Summary:

Objective: Determine whether patients with schizophrenia are at increased risk of cardiovascular morbidity and mortality compared with the general population.

Methods: Medical claims and death records of 3,022 subjects with diagnostic evidence of schizophrenia between 1994 and 1995 were obtained from Saskatchewan Health. Prevalence and incidence of cardiovascular morbidity and mortality were compared with that in an age/gender-matched population group (N = 12,088), adjusting for risk factors such as hypertension, hyperlipidemia, and serious pulmonary disease.

Results: Prevalence of all cardiovascular comorbidities during 1994–1995 was higher in subjects with schizophrenia than in control subjects. Significantly increased adjusted odds ratios (OR) were seen for arrhythmia (OR = 1.5, CI = 1.2–1.8), syncope (OR = 4.0, CI = 2.0–7.9), stroke (OR = 2.1, CI = 1.6–2.7), transient cerebral ischemia (OR = 2.5, CI = 1.7–3.7), diabetes (OR = 2.1, CI = 1.8–2.4), and heart failure (OR = 1.7, CI = 1.4–2.2). Incidence of cardiovascular outcomes and mortality were computed during 39 months of follow-up (January 1996–March 1999). Adjusted relative risk (RR) was significantly increased for stroke (RR = 1.5, CI = 1.2–2.0), ventricular arrhythmia (RR = 2.3, CI = 1.2–4.3), diabetes (RR = 1.8, CI = 1.2–2.6), heart failure (RR = 1.6, CI = 1.2–2.0), non-suicide mortality (RR = 2.7, CI = 2.2–3.3), and cardiovascular mortality (RR = 2.2, CI = 1.7–2.8).

Conclusions: Persons with schizophrenia appear to be at greater risk for cardiovascular morbidity and mortality than those in the general population.

Study supported by Pfizer Inc.

NR258 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Quetiapine Improves Cognitive Function in Schizophrenia

Herbert Y. Meltzer, M.D., *Department of Psychiatry, Vanderbilt University, 1601 23rd Avenue South, Suite 306, Nashville, TN 37212-8645*; Myung A. Lee, M.D.

Summary:

Objective: To examine the effect of clozapine and quetiapine on working memory after 6 weeks of treatment in patients with schizophrenia.

Methods: To assess the effect of 6 weeks of quetiapine treatment on attention, verbal working memory, executive function, verbal fluency, and motor performance, 19 patients were studied (14 neuroleptic responders and five who were neuroleptic resistant).

Results: Significant improvement was observed in BPRS total score [$p = 0.005$, effect size (ES) = 0.62], and positive symptom subscale score ($p = 0.008$, ES = 0.59), but not withdrawal-retardation (negative symptoms) subscale score. Significant improvement was observed in measures of attention/vigilance (Continuous Performance Test (CPT)-D': $p = 0.02$, ES = 0.70), motor performance (Grooved Peg Board, Dominant Hand: $p = 0.02$, ES = 0.61), and verbal working memory (Auditory Consonant Trigram [ACT]: $p = 0.04$, ES = 0.52). There was a trend for improvement in verbal fluency (Controlled Word Association Test: $p = 0.07$, ES = 0.45). No significant effect on tests of executive function (Wisconsin Card Sorting Test or Trails B) was observed. Improvement in CPT-D' and Grooved Peg Board Test, but not in ACT, was still significant after adjustment for change in BPRS total scores. Improvement in ACT was significantly correlated with improvement in BPRS total scores ($r = 0.56$, $p = 0.01$).

Conclusions: Unlike clozapine, which worsens working memory, quetiapine improved working memory after 6 weeks of treatment in schizophrenia.

NR259 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Long-Term Efficacy of Ziprasidone in Schizophrenia: Results of Two Controlled Trials

Herbert Y. Meltzer, M.D., *Department of Psychiatry, Vanderbilt University, 1601 23rd Avenue South, Suite 306, Nashville, TN 37212-8645*

Summary:

Objective: To evaluate in randomized, double-blind trials, the long-term efficacy and tolerability of ziprasidone in chronic, stable schizophrenia.

Methods: A 28-week, flexible-dose (80–160 mg/d) study versus haloperidol in 301 outpatients, using PANSS, CGI-S, and MADRS. A one-year trial (40 mg/d, 80 mg/d, 160 mg/d) versus placebo in 278 inpatients, employing PANSS, CGI, and GAF, in which patients who met criteria for impending relapse were withdrawn.

Results: 28-week study: Both drugs improved all efficacy variables, but more patients on ziprasidone were classified as negative symptom responders (48% vs 33% for haloperidol, $P < 0.05$). Ziprasidone was superior to haloperidol in all movement disorder assessments. One-year study: Patients in ziprasidone groups had a lower probability of impending relapse at one year than the placebo group ($P \leq 0.002$). Only 6% of ziprasidone-treated patients in the study ≥6 months reached impending relapse, versus 42% of placebo recipients ($P = 0.001$). Ziprasidone had a direct effect on primary negative symptoms ($P = 0.024$). Ziprasidone was indistinguishable from placebo in movement disorders assessments, and was not associated with weight gain or cardiovascular abnormalities.

Conclusion: Long-term therapy with ziprasidone maintains positive symptom control, improves negative symptoms, and reduces risk of relapse, with low incidence of extrapyramidal effects and weight gain.

Study supported by Pfizer, Inc.

NR260 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

FOCIS: An International Survey of Cognitive Dysfunction in Schizophrenia

Bernd Gallhofer, M.D., *Department of Psychiatry, Justus Liebig University, Am Steg 22, Giessen D-35385, Germany*; Michael F. Green, Ph.D., Thomas R.E. Barnes, M.D., Jean-Marie Danion, M.D., Herbert Y. Meltzer, M.D., Christo Pantelis, M.D.

Summary:

Objective: To evaluate psychiatrists' views on the nature of, and treatment strategies for, cognitive dysfunction in schizophrenia.

Methods: A questionnaire, developed in five languages and comprising 27 questions, was distributed to 63,295 psychiatrists worldwide using pre-paid mailing lists or by posting on the internet.

Results: The overall response rate was 4.7%, for a total of 2,696 replies; the largest number of replies (N = 673) came from the United States. Respondents reported that on average, 24% of their patients had a primary diagnosis of schizophrenia. Respondents most commonly (53%) perceived medication to be the cause of cognitive dysfunction in schizophrenia; 83% of these respondent considered conventional antipsychotics to be the primary cause, and 81% considered that atypical antipsychotics might improve cognitive dysfunction. Only 19% considered cognitive dysfunction to be the most important contributor to overall functioning/outcome in stabilized schizophrenic patients.

Conclusions: The results suggest that psychiatrists' awareness of emerging evidence on the nature of cognitive deficits intrinsic to schizophrenia and the potential link between cognitive dysfunction and functional outcomes may be limited, with misattribution of cognitive impairment to conventional antipsychotics. Further education in this area may be warranted.

Study supported by Pfizer Inc.

NR261 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Ziprasidone's Benefits Versus Olanzapine on Weight and Insulin Resistance

Ira D. Glick, M.D., *Department of Psychiatry, Stanford University, 401 Quarry Road, Suite 2122, Stanford, CA 94305-5490*; David Fryburg, M.D., Richard L. O'Sullivan, M.D., Cynthia Siu, Ph.D., George M. Simpson, M.D.

Summary:

Objective: To determine the effects of ziprasidone (ZIP) and olanzapine (OLANZ) on weight, lipids, and metabolic parameters associated with insulin resistance (IR) in schizophrenic patients.

Methods: In a double-blind trial, 268 acute inpatients were randomly assigned to ZIP or OLANZ for 6 weeks. Fasting insulin, glucose, total cholesterol, and triglycerides were measured prerandomization and at last visit. An IR index (HOMA IR = [Ins x Glu]/22.5) was calculated.

Results: From baseline, patients treated with OLANZ had weight gain of approximately 7 lb ($p < 0.001$) and increases in fasting insulin of 36% ($p < 0.001$) and in HOMA IR (log) of 11% ($p < 0.001$). No significant difference was observed in fasting glucose. Total cholesterol and triglycerides increased 9% and 20%, respectively, with OLANZ (both $p < 0.001$). In contrast, ZIP did not significantly alter any of these parameters, and all but glucose were statistically separable (ZIP vs OLANZ, $p < 0.05$).

Conclusions: Within only 6 weeks of treatment, weight, fasting insulin, IR, total cholesterol, and triglycerides rose significantly with OLANZ treatment compared with ZIP. This suggests that OLANZ worsens IR, which may predispose patients to type 2 diabetes mellitus.

NR262 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

The Efficacy and Extrapyramidal Side Effects of the Atypical Antipsychotics

Ira D. Glick, M.D., *Department of Psychiatry, Stanford University, 401 Quarry Road, Suite 2122, Stanford, CA 94305-5490*; John M. Davis, M.D.

Summary:

The choice of drug for treatment of schizophrenia is the most important therapeutic decision made by clinicians. We report here a meta-analysis of the efficacy and extrapyramidal side effects (EPS) of the atypical antipsychotics (risperidone, olanzapine, sertindole, quetiapine, ziprasidone, and aripiprazole) compared with the typical antipsychotics, based on double-blind, random-assignment trials. Some psychopharmacologists believe that typical and atypicals are equally efficacious. The American Psychiatric Association and the Schizophrenia Patient Outcome Research Team recommend either typical or atypical antipsychotics as first line. Others recommend atypicals as first-line treatment. Two meta-analysis techniques were used. The Mantel-Haenszel (1959) method analyzes pooled raw data from treatment responders and nonresponders for each patient. The Hedges-Olkin (1985) method analyzes the combined means and standard deviations (SD). When fixed-dose studies were done, we estimated the dose response curve including the ED50. We found that the data demonstrate that risperidone and olanzapine produce a substantial, clinically meaningful, greater improvement compared with haloperidol. Sertindole, and most of the other atypicals, produced efficacy equal to that of typical neuroleptics.

NR263 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Aripiprazole and Risperidone Versus Placebo in Schizophrenia and Schizoaffective Disorder

William H. Carson, Jr., M.D., *Neurosciences 402, Bristol-Myers Squibb, 5 Research Parkway, Wallingford, CT 06492*; Anutosh R. Saha, Ph.D., Mirza Ali, M.D., Geoffrey C. Dunbar, M.D., Gary Ingenito, M.D.

Summary:

Objectives: To evaluate the efficacy and safety of aripiprazole in patients hospitalized due to an acute relapse of schizophrenia or schizoaffective disorder.

Methods: This multicenter, double-blind, placebo-controlled study involved 404 inpatients with acute exacerbation of schizophrenia or schizoaffective disorder (DSM-IV). All patients had a history of response to antipsychotic therapy. Following a 3–5 day washout period, patients were randomly assigned to receive placebo (N = 103), aripiprazole 20 mg/day (N = 101), aripiprazole 30 mg/day (N = 101), or risperidone 3 mg bid (N = 99) for 4 weeks. Baseline PANSS scores ranged from 92 to 95 in the four treatment arms.

Results: Positive and negative symptoms were significantly reduced in all active treatment groups compared with placebo ($p < 0.02$); earlier improvement in negative symptoms was seen with aripiprazole (week 1). Aripiprazole and risperidone were also well tolerated. Neither drug produced significant extrapyramidal symptoms. Mean plasma prolactin levels showed no change with aripiprazole but increased 5-fold over placebo in the risperidone group. The incidence of QTc prolongation (> 10% over baseline) was similar to placebo in the aripiprazole group, and approximately 2-fold greater than placebo in the risperidone group.

Conclusions: Aripiprazole provides effective treatment for acute relapse of schizophrenia and may have tolerability advantages over available antipsychotics.

NR264 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Quetiapine for Psychosis in Patients with Parkinson's Disease

Vicki J. Roberts, Ph.D., *Department of Neurology, Emory University School of Medicine, 1841 Clifton Road, NE, Atlanta, GA 30329*; Jorge L. Juncos, M.D., C.D. Wood, Ph.D., Rita D. Jewart, Ph.D., Marian L. Evatt, M.D.

Summary:

Objective: To examine the effects of quetiapine on psychosis and cognition in 29 PD patients who received up to 400 mg/day quetiapine, dosed according to clinical response and tolerability.

Methods: This was a 24-week, single-center, open-label study during which we assessed psychiatric, motor, and cognitive func-

tions at baseline and at periodic intervals. Assessments included the Brief Psychiatric Rating Scale (BPRS), Neuropsychiatric Inventory (NPI), Unified Parkinson's Disease Rating Scale (UPDRS), and tests of overall cognition, attention, and memory. Statistical analyses were used to assess change from baseline in psychiatric, motor, and cognitive measures. Additionally, we compared cognitive changes across time between our treatment group and a control group of 12 non-psychotic PD patients.

Results: Compared to baseline, our treatment group exhibited significant improvements in the 24-week BPRS total and NPI psychosis subscale scores, and no decline in UPDRS total/motor subscale scores. On cognitive measures, significant treatment/control group differences emerged only for sustained attention and delayed recall. Specifically, the control group exhibited no change in recall and significant decline in sustained attention, whereas the quetiapine group exhibited significant improvement in recall and nominal improvement in sustained attention.

Conclusions: Quetiapine is effective in improving both cognitive function and psychotic symptoms in PD patients.

NR265 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Do Atypicals Change the Syndrome Profile in Treatment-Resistant Schizophrenia?

Jean-Pierre Lindenmayer, M.D., *N. Kline Institute for Psychiatric Research, New York University, Manhattan Psychiatric Center, Wards Island, New York, NY 10035*; Pal Czobor, Ph.D., Jan Yolayka, M.D., Jeffrey A. Lieberman, M.D., Joseph P. McEvoy, M.D., Leslie L. Citrome, M.D., Brian B. Sheitman, M.D.

Summary:

There has been considerable support for the observation that atypicals have a different pattern of clinical effects than traditional antipsychotics. We are exploring whether this difference can also be seen in patients with treatment-resistant schizophrenia. We are presenting data from two PANSS-based factor analyses (baseline and endpoint) from a prospective, double-blind, randomized 14-week trial in which 157 inpatients with DSM-IV treatment-resistant schizophrenia or schizoaffective disorder were assigned to either clozapine, olanzapine, risperidone, or haloperidol treatment. We found both at baseline and endpoint a five-factor solution based on principal component analysis of the 30 PANSS items and after orthogonal factor rotation. While treatment was associated with an overall modest change, there was a change in the amount of variance explained by the respective factors after treatment. At baseline, the negative factor was followed by the excitement, cognitive, positive, and depression/anxiety factors, which explained 60% of the variance. At endpoint, the largest variance was explained by the cognitive factor followed by the excitement, positive, negative, and depression/anxiety factors, which explained 59% of the total variance. This change meant that negative symptoms contributed less to total psychopathology, while cognitive symptoms were more predominant after treatment with atypicals. We will discuss the implications of these findings in comparison with results from studies with treatment-responsive patients. (Funding: NIMH R10 MH53550 and Lilly and Comp.)

NR266 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Long-Term Benefit of Risperidone Versus Haloperidol for Affective Symptoms in Patients with Schizophrenia and Schizoaffective Disorder

Joyce E. Myers, M.D., *Janssen Research Foundation, 1125 Trenton-Harbourton Road, Titusville, NJ 08560*; Ramy A. Mahmoud, M.D., Samuel J. Keith, M.D., John G. Csernansky, M.D.

Summary:

Background: The effects of long-term treatment with risperidone versus haloperidol on affective symptoms were compared in patients with schizophrenia or schizoaffective disorder.

Methods: In a randomized, double-blind, multicenter trial, 365 patients were treated with risperidone (n = 177) or haloperidol (n = 188) for at least one year. Efficacy assessments included the Positive and Negative Syndrome Scale (PANSS).

Results: Mean modal doses were 4.9 ± 1.9 mg/day of risperidone and 11.7 ± 5.0 mg/day of haloperidol. Patients with schizophrenia receiving risperidone showed greater improvements on the PANSS anxiety/depression cluster ($p < 0.01$) and on individual symptoms including guilt ($p = 0.05$), anxiety ($p = 0.003$), and depressed mood ($p = 0.004$) than haloperidol patients. Among all patients with high baseline scores on the PANSS grandiosity item, risperidone was associated with a greater reduction on the PANSS total score than haloperidol ($p = 0.028$). A possible association between greater improvement in depression and a lower risk of relapse ($p = 0.081$; odds ratio 1.380) was seen in patients receiving risperidone.

Conclusions: Long-term treatment with risperidone was associated with significantly greater improvements in affective symptoms among stable patients with schizophrenia and schizoaffective disorder than in patients receiving haloperidol.

NR267 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Risperidone Versus Olanzapine for the Treatment of Mood Symptoms in Patients with Schizophrenia and Schizoaffective Disorder

Joyce E. Myers, M.D., *Janssen Research Foundation, 1125 Trenton-Harbourton Road, Titusville, NJ 08560*; Ramy A. Mahmoud, M.D., Sally A. Berry, M.D., Robert R. Conley, M.D.

Summary:

Objective: To explore the effects of risperidone and olanzapine on mood symptoms in patients with schizophrenia and schizoaffective disorder, and to correlate symptom changes with measures of outcome.

Methods: An exploratory analysis of mood symptoms from an eight-week, randomized, double-blind study comparing risperidone (n = 188) and olanzapine (n = 189). Efficacy assessments included the PANSS total score, anxiety/depression cluster and item scores (depression, anxiety, guilt, somatic preoccupation), excitement/hostility cluster score, "mania" cluster and item scores (excitement, grandiosity), and Hamilton Depression Rating Scale total score. Correlations between mood symptom improvement and quality-of-life measures (B-QOL) were assessed.

Results: Mean modal doses were 4.8mg/day risperidone and 12.7mg/day olanzapine. Both groups showed significant improvement on all measures of mood symptoms. Risperidone was associated with significantly greater improvement than olanzapine at week 8 on the PANSS anxiety/depression cluster and the depression and grandiosity items ($p < 0.05$). Improvement in the depression item with risperidone positively correlated with improvement on several B-QOL subscales ($p < 0.05$).

Conclusions: Risperidone was associated with greater improvement than olanzapine for depression and grandiosity in these patients. The improvement in depression had a perceived beneficial effect on several aspects of quality of life. Results suggest that risperidone may be superior for affective symptoms in patients with schizophrenia and schizoaffective disorder.

NR268 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Four-Year Clozapine Study in Schizophrenic, Schizoaffective, and Bipolar Psychotic Disorders

Antonio Ciapparelli, M.D., *Department of Psychiatry, University of Pisa, Via Roma 67, Pisa, IT 56100, Italy*; Liliana Dell'osso,

M.D., Adolfo Bandettinidipoggio, M.D., Claudia Carmassi, M.D., Melania Fenzi, M.D., Giovanni B. Cassano, M.D.

Summary:

Objectives: This naturalistic, 48-month follow-up study evaluated the efficacy of clozapine in schizophrenic (32), bipolar (35), and schizoaffective (28) patients selected because of their resistance to classical antipsychotic.

Methods: Clozapine (maximum 600mg/day) was added to ongoing medications. Assessments were held by BPRS, CGI-S, GAF. Improvement was defined as a reduction of more than 50% in BPRS total score maintained for two consecutive evaluations and analyzed by Kaplan-Meier survival curve.

Results: At baseline BPRS and GAF did not differ significantly, while CGI-S was significantly higher among schizophrenics. Bipolars and schizoaffectives reached a BPRS Total Predicted Score more than halved from the baseline by the third and sixth month of evaluation, respectively, while in schizophrenics it occurred after 24 months. After the 48th month, that percentage of improvement increased only in schizoaffectives (86%) and schizophrenics (63%). Bipolars reported significantly lower CGI-S scores than schizoaffectives who showed significantly lower values than schizophrenics. Trend of improvement did not significantly differ among the groups. After 48 months GAF showed an improvement in all groups; only bipolars reached a sufficient social functioning.

Conclusions: All subjects with clozapine therapy showed a significant clinical improvement that was more rapid and higher in bipolar and schizoaffective patients than in schizophrenics.

NR269 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Comparison of Risperidone and Olanzapine in Bipolar and Schizoaffective Disorder

Subhdeep Virk, M.D., *Department of Psychiatry, SUNY Upstate Medical University, 750 East Adams Street, Syracuse, NY 13210*; Prakash S. Masand, M.D., Xiaohong Wong, M.D., Sanjay Gupta, M.D., Thomas L. Schwartz, M.D., Michael Wade

Summary:

Background: While conventional neuroleptics have long been the drugs of choice in patients with bipolar or schizoaffective disorder requiring antipsychotic treatment, atypical antipsychotics offer several advantages, including superior efficacy for negative and mood symptoms and a lower risk of extrapyramidal symptoms (EPS) and tardive dyskinesia (TD). There are, however, few studies of atypical antipsychotics in bipolar or schizoaffective patients.

Methods: We conducted a retrospective chart review of 35 patients with bipolar or schizoaffective disorder seen in three settings. Risperidone and olanzapine were compared for efficacy, tolerability, need for concomitant mood stabilizers, and cost of treatment.

Results and Conclusion: The mean doses were 3.7 ± 3.5 mg/d of risperidone and 12.0 ± 5.4 mg/d of olanzapine. Between-drug differences in patient demographics, psychiatric history, Clinical Global Impressions ratings, or treatment duration were not significant. Side effects, including EPS, akathisia, TD, and precipitation of mania by the respective drug, also showed no significant differences between drugs. Patients in the olanzapine group received a higher dose of concomitant lithium than those in the risperidone group (mean doses: 863 ± 256 mg/d and 1,210 ± 186 mg/d, respectively; $P = 0.03$). The total acquisition cost for olanzapine was $11.84/d versus $5.81/d for risperidone.

NR270 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Treatment Response to Risperidone by African-American and White Patients with Schizophrenia

Rick A. Martinez, M.D., *CNS Medical Affairs, Janssen Pharmaceutica, Inc., 1125 Trenton-Harbourton Road, Titusville, NJ 08560–0200*; Sally A. Berry, M.D., William B. Lawson, M.D.

Summary:

Background and Method: Treatment of schizophrenia in non-white persons is an understudied area of psychiatric research. We conducted post-hoc analyses of data on subsets of African-American and white persons with schizophrenia from three North American clinical trials. In each trial, treatment efficacy was evaluated by means of the Positive and Negative Syndrome Scale (PANSS)

Results: In an eight-week, placebo-controlled trial (Marder & Meibach, 1994), responses to risperidone of 95 African-American subjects were similar to those of 371 white subjects and significantly superior to those of subjects receiving placebo. There was a trend toward greater symptom reductions in African-American than white subjects on three measures: PANSS total, BPRS total, and the thought disturbance item. In an eight-week, double-blind comparison of risperidone and olanzapine (Conley et al, 2000), similar improvements were seen in the two racial groups for both treatments. In a one-year, double-blind study of relapse rates (Csernansky et al, 2000), African-American and white patients had similar relapse rates with fewer relapses among patients receiving risperidone than haloperidol.

Conclusions: The results indicate that African-American patients respond favorably to risperidone treatment and suggest that in some treatment domains African-American subjects may have a better response to risperidone than white subjects.

NR271 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Psychosis of Alzheimer's Disease: Evidence from Community-Dwelling and Nursing-Home Patients

Rick A. Martinez, M.D., *CNS Medical Affairs, Janssen Pharmaceutica, Inc., 1125 Trenton-Harbourton Road, Titusville, NJ 08560-0200*; Ramy A. Mahmoud, M.D., Albert T. Derivan, M.D., Judy Napolitano, M.D.

Summary:

Objective: Determine whether there is a definable psychotic syndrome in elderly patients with Alzheimer's disease (AD) and other dementias.

Methods: Data were derived from a five-month study of community-dwelling patients with mild to moderate dementia (study 1) and a three-month study of nursing-home residents with severe dementia (study 2). Psychosis was defined according to scores on the Neuropsychiatric Inventory or the Behavioral Pathology in Alzheimer's Rating Scale.

Results: Of the 285 placebo patients in study 1, all had AD, and of the 162 placebo patients in study 2, 84% had AD and 16% other dementia. In study 1, 12% of patients showed psychosis before the baseline assessment and 64% had a persistent psychosis for at least one month; 12% of patients without psychosis at baseline developed psychosis. In study 2, 63% of patients had psychosis at baseline, which persisted for at least two weeks in 75%; 17% of patients without psychosis at baseline developed psychosis. Persistent or continuous psychosis was present in 29% of the patients for 12 weeks.

Conclusion: The data support the concept that psychosis of dementia is a clinically definable entity, across the spectrum of AD from mild to severely impaired patients.

NR272 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Assessment of Quality of Life Among Schizophrenia Patients with Deficit Syndrome

Patricia Russo, Ph.D., *ORE, The Medstat Group, 4301 Connecticut Avenue NW, Suite 330, Washington, DC 20008*; Brian Kirkpatrick, M.D.

Summary:

Objective: To determine whether persons with deficit syndrome report higher quality of life than do their non-deficit counterparts.

Methods: Baseline data (QLS scale; mean = 56) from participants in the SCAP study (n = 781) were modeled as a linear function of covariates, including demographic, clinical, medication adherence, and site variables. Presence of deficit syndrome was assigned based on proxy methods (Kirkpatrick B., et al., 1989).

Results: Modeling revealed that deficit syndrome had a negative impact of 4.7 points ($p < .001$) on quality of life score (range 0–120), suggesting that persons with deficit syndrome may experience a significantly lower quality of life than their non-deficit counterparts, all else equal. Those having higher hallucinations/delusions scores ($p < .001$) exhibited lower QLS scores and those with higher functioning scores (GAF; $p < .001$) exhibited higher QLS scores.

Conclusions: Our results suggest that persons with deficit syndrome experience lower quality of life than those who are non-deficit. Although the clinical and functional scores are significant, the impact of deficit syndrome is at least five times greater than that of hallucinations/delusions or GAF.

NR273 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Early-Onset Females with Schizophrenia

Courtenay M. Harding, Ph.D., *Department of Mental Health, Boston University, 940 Commonwealth Avenue, Boston, MA 02215*; Patricia Russo, Ph.D.

Summary:

Objective: To test the hypothesis that persons with disease onset <25 will reflect a similar profile and that they will differ from their later onset (25–45) counterparts.

Methods: Baseline data from the Schizophrenia Care and Assessment Project (n = 1717) were used. Dependent variables were PANSS: (PS), (NS), (GP); MADRS, QLS, GAF, marital status, education. Contrast coding was used to test the relationship ($\mu_1 = \mu_2 < \mu_3 = \mu_4$) between the groups: (onset <25) early females (μ_1; n = 424) and expected males (μ_2; n = 843); (onset 25–45) expected females (μ_3; n = 211) and delayed males (μ_4; n = 239). OLS and logistic regression were applied.

Results: Directionality was supported for NS, QLS, GAF, marital status, and education, i.e., persons with onset <25 had lower scores and were less likely to be married or to have completed high school. Evidence supporting the equality ($\mu_1 = \mu_2$) was observed for GP and education, only. The equality $\mu_3 = \mu_4$, was partially supported (with the exception of GAF, marital status, and QLS), suggesting that those groups reflected a similar profile.

Conclusions: These analyses reveal that the relationship between age of onset, given gender, is more complex than previously thought. The findings suggest that persons with onset at younger age present a more severe profile than their older counterparts.

NR274 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Psychiatric Symptoms and Adverse Events During Antipsychotic Treatment

Hea-Won Kim, Ph.D., *Department of Psychology, Indiana University, 402 North Blackford Street, LD124, Indianapolis, IN 46202*; Sandra L. Tunis, Ph.D., Gary R. Bond, Ph.D., Kriscinda M. Marks, M.S., Piper S. Meyer, M.S.

Summary:

Objective: This analysis assessed psychiatric symptoms and adverse events commonly reported during antipsychotic treatment, including weight gain, among clients with schizophrenia attending psychiatric rehabilitation programs.

Method: Clients being treated with olanzapine ($n = 29$), risperidone ($n = 23$), or traditional antipsychotics ($n = 23$) were interviewed. Median duration on antipsychotic medication across all groups was 14.6 months. Symptoms were measured using five subscales of the Positive and Negative Syndrome Scale (PANSS). Adverse events were reported by clients with an adaptation of the 12-item Subjective Side Effect Rating Scale.

Results: Psychiatric symptoms did not significantly differ by antipsychotic treatment. For seven of 12 adverse events (akinesia, rigidity, tremor, change in appearance, stigma from medications, anticholinergic effects, and sexual dysfunction), a significantly smaller proportion of olanzapine-treated clients reported moderate or serious distress compared with those treated with risperidone or traditional agents. There were no significant differences between medication treatment groups for the remaining adverse events.

Conclusions: In this small community sample of individuals with schizophrenia participating in psychiatric rehabilitation programs, clients on olanzapine reported less distress from adverse events than did clients on other antipsychotics.

NR275 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Anorexogenic Effects of Topiramate in Schizophrenia

Faruk S. Abuzzahab, Sr., M.D., *Department of Psychiatry, University of Minnesota, F282/2A West 2450 Riverside Avenue, Minneapolis, MN 55454-1495*; Victoria L. Brown

Summary:

Method: Twenty outpatients, 14 females and six males, with an average age of 42.45 +/– 8.07 years, who met the DSM-IV criteria for schizophrenia received topiramate for at least three months concomitantly to their neuroleptic medications. Patients were started on the lowest dose of 12.5 mg and gradually increased as tolerated.

Results: At three months the average topiramate dose was 421.5 mg +/– 302.42 mg. The average weight of the 20 patients at pretreatment was 95.13 kg +/– 16.22 kg. After three months of treatment with topiramate the average weight dropped to 91.31 kg +/– 15.8 kg. Using a t-test it was found that with a 95% confidence level the mean weight loss was between 0.89 kg and 6.74 kg after three months, between .05 kg and 10.31 kg for the 13 patients taking topiramate after six months, and between 0 kg and 14.69 kg for the nine patients after nine months.

Conclusion: Although the exact mechanism of topiramate's action is unknown, its unique anorexogenic property, which was observed in convulsive disorder, bipolar disorder, and unipolar depression, is extended through this report to schizophrenia.

Supported in part by the Psychopharmacology and the Pharmacopsychiatry Funds, MN Med. Foundation

NR276 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Pharmacokinetics, D^2 Receptor Occupancy, and Clinical Effects of a Long-Acting Injectable Formulation of Risperidone in Patients with Schizophrenia

Ola Gefvert, Ph.D., *Department of Psychiatry, Central Hospital, Vasteras SE-72189, Sweden*; Svante Nyberg, M.D., Per Persson, M.D., Lars Helklin, Annika Bjorner

Summary:

Background: A risperidone formulation for intramuscular administration is an aqueous suspension microencapsulated into polylactide-co-glycolide polymer whose degradation at the injection site results in release of risperidone over several weeks.

Methods: After five biweekly injections containing 25, 50, or 75 mg of risperidone, plasma concentrations of risperidone and its main active metabolite were determined by radioimmunoassays in 13 schizophrenia patients. D^2 receptor binding was measured by PET in eight of the patients two weeks after the fifth injection (i.e. at steady state).

Results: Among the 11 study completers, PANSS scores remained stable, with no extrapyramidal symptoms except mild akathisia in one patient receiving 75 mg of risperidone. Local tolerance of the injections was good. Plasma concentrations started to increase after injections 2 and 3. Steady state was reached after injection 4. After the last injection, steady-state levels were maintained for four to five weeks and thereafter declined rapidly. D^2 receptor occupancies ranged from 25% to 48%, 59% to 83%, and 62% to 72%, respectively, after the three doses. The curvilinear relationship between receptor occupancy and plasma levels of the risperidone active moiety was confirmed.

Conclusions: Biweekly administration of this atypical long-acting injectable formulation appears to be efficacious and well tolerated.

NR277 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Perception of Facial Emotions in Chronic Schizophrenia

Henry Silver, M.D., *Department of Research, Shaar Menashe Mental Health Center, Mobile Post Hefer, Hadera 38814, Israel*; Nili Shlomo, M.D.

Summary:

Background: Appropriate expression of emotions and correct perception of emotional expression in others are important social skills that may be impaired in schizophrenia and contribute to poor social adjustment. We examined the relationship between expression of emotions as measured by affective flattening and other negative symptoms and their perception. We compared performance on tests of perception of facial emotions with that in other cognitive areas.

Methods: Thirty-six chronic schizophrenic patients on stable doses of atypical antipsychotics were assessed using tests of identification (FID) and discrimination (FDIS) of facial emotional expressions, visual retention (BVRT), and general cognitive function (Mini Mental State Examination, MMSE). Clinical symptoms were assessed with SANS and SAPS. Motor symptoms were assessed with SA and AIMS scales and Finger Tapping Test.

Results: Negative symptoms showed no relation with FID or FDIS. FID showed significant correlation with visual retention and finger tapping but not MMSE.

Conclusion: The ability to identify facial emotional expressions is not related to negative symptoms in chronic schizophrenia and shares common mechanisms with visual reproduction and ability to make rapid motor movements. This suggests common defects in perceptual, timed processes consistent with postulated dysfunction of cortico-subcortical circuits.

NR278 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Perception of Happy and Sad Facial Expressions in Chronic Schizophrenia

Henry Silver, M.D., *Department of Research, Shaar Menashe Mental Health Center, Mobile Post Hefer, Hadera 38814, Israel*; Nili Shlomo, M.D.

Summary:

Background: Schizophrenia patients have impaired perception of emotional expressions, but it is unclear whether this is part of a generalized deficit in cognitive function.

Objective: To test for existence of emotion-specific deficits by studying the effects of valence on recognition of facial emotional expressions.

Methods: Twenty-four male subjects suffering from chronic schizophrenia were examined with the Penn Emotion Acuity Test and the Emotion Differentiation Task. Clinical state was assessed with the Scale for the Assessment of Negative Symptoms and Scale for the Assessment of Positive Symptoms, visual memory with the Benton Visual Retention Test, and motor function with the finger tapping test.

Results: Identification of happy facial expressions showed significant negative correlation with age, cumulative time in hospital, and length of current hospitalization; positive correlations were found with visual retention and finger tapping scores. Identification of sad facial expressions showed significant correlation only with cumulative time in hospital, while identification of neutral facial expressions showed no significant correlations. Discrimination between degrees of happy but not sad facial expression, showed a positive correlation with negative symptoms.

Conclusions: Perception of happy and sad emotion relates differently to significant illness parameters. This difference supports the existence of an emotion-specific deficit in perception of emotions in schizophrenia and of separate channels for processing positive and negative emotions.

NR279 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Favorable Anticholinergic Profile of Olanzapine in Elderly Patients with Dementia

Bruce J. Kinon, M.D., *Lilly Research Lab, Eli Lilly And Company, Lilly Corporate Center, Indianapolis, IN 46285*; Virginia L. Stauffer, Pharm.D., Lynn Wang, M.S., John S. Kennedy, M.D.

Summary:

Objectives: To determine the anticholinergic adverse event profile of olanzapine in elderly patients with dementia.

Methods: Peripheral anticholinergic adverse events were assessed in 82 patients (age ≥ 60) using the Autonomic Symptoms subscale of the Udvalg for Kliniske Undersogelser (UKU) scale. The Mini-Mental State Exam (MMSE) was used to evaluate further cognitive impairment. In addition, serum anticholinergic levels were measured via a radioreceptor assay.

Results: The UKU total score for the subscale showed no difference from baseline to endpoint ($p = 0.17$, LOCF) and no significant worsening on any of the individual items. The MMSE scores increased from 8.7 to 9.4 ($p = 0.15$, LOCF). Serum anticholinergic levels did increase from baseline (0.39 pmol/atropine equivalents) to week 4 (0.55 pmol/atropine equivalents), and week 8 (0.68 pmol/atropine equivalents) ($p < 0.001$ at each time point). Anticholinergic serum levels were not significantly correlated with the UKU autonomic symptoms subscale or the MMSE. The mean daily dose of olanzapine was 5 mg.

Conclusions: The occurrence of anticholinergic adverse events were infrequent, suggesting that olanzapine may have a relatively mild anticholinergic profile in elderly patients with dementia.

Funding provided by Eli Lilly and Company

NR280 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Hyperprolactinemia During Antipsychotic Drug Treatment in Elderly Patients

Bruce J. Kinon, M.D., *Lilly Research Lab, Eli Lilly And Company, Lilly Corporate Center, Indianapolis, IN 46285*; Virginia L. Stauffer, Pharm.D., Lynn Wang, M.S.

Summary:

Objectives: PRL concentrations were measured in elderly schizophrenic patients treated with the novel APD olanzapine (OLZ) compared with haloperidol (HAL) [Study I] and in elderly agitated demented patients switched to treatment with OLZ [Study II].

Methods: Patients ≥ 65 years were identified from Study I, and patients age ≥ 60 years were identified from Study II. Baseline to endpoint PRL concentrations were analyzed in each of the studies.

Results: In Study I, women receiving OLZ (N = 22) had a mean PRL increase of 0.78 ng/ml, versus 5.4 ng/ml for those receiving HAL (N = 8; p = 0.16; within group). In Study II, women not receiving APD therapy prior to study entry (N = 24) experienced a significant increase in PRL ($p < 0.001$; baseline to endpoint) but remained within the normal range. Women entering the study taking RIS (N = 12) returned to the normal range while receiving OLZ. There was no significant increase in PRL when patients were switched from conventional APDs to OLZ (N = 13 women, nine men).

Conclusions: OLZ appeared to be a PRL-sparing APD in the elderly, with only modest PRL increases seen. Conversely, HAL and RIS appeared in general to be PRL-elevating in the elderly.

Funding provided by Eli Lilly and Company

NR281 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Efficacy of Zyprexa Zydis Treatment of Acutely Ill, Noncompliant Schizophrenia Patients

Bruce J. Kinon, M.D., *Lilly Research Lab, Eli Lilly And Company, Lilly Corporate Center, Indianapolis, IN 46285*; Denai R. Milton, M.S., Angela L. Hill, Ph.D.

Summary:

Objectives: To assess the efficacy and safety of the orally disintegrating tablet formulation of olanzapine, which dissolves shortly after contact with saliva, in acutely ill, noncompliant patients.

Methods: Eighty-five acutely ill patients with schizophrenia, schizoaffective disorder, or schizophreniform disorder meeting medication noncompliance criteria (including active or passive refusal; "cheeking/spitting;" inability to swallow tablets) received open-label treatment with olanzapine (10–20 mg/day) in the orally disintegrating tablet formulation for up to 6 weeks. The primary outcome was change from baseline in the Positive and Negative Syndrome Score (PANSS). Secondary outcomes included change in attitude towards medication taking and compliance and change in burden of nursing care. Safety measures included assessments of treatment-emergent adverse events, vital signs, laboratory analyses, and extrapyramidal symptoms.

Results: Significant improvement was demonstrated in PANSS total score from week 1 through end of study ($p < 0.001$). Additionally, significant improvement from baseline to endpoint was seen in medication compliance/attitude and reduced nursing care burden ($p < 0.001$). The drug was well-tolerated.

Conclusions: Orally disintegrating olanzapine, a unique formulation of a novel antipsychotic, demonstrated significant efficacy in acutely ill, noncompliant schizophrenic patients as reflected by improved overall psychopathology and reduced noncompliant attitudes and behaviors. Innovative approaches to reduce medication noncompliance need to be further studied in order to optimize the treatment of schizophrenia.

Funding provided by Eli Lilly and Company

NR282 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Treatment of Agitated Inpatients with Schizophrenia: Effectiveness of Oral Therapy with Olanzapine Versus Typical Antipsychotic Drugs: Europa Study

Fernando Canas de Paz, M.D., *Puerto Somosierra 50, Colmenar 27870, Spain*; Juan C. Gomez, M.D., Antonio Ciudad, M.D., Enrique Alvarez, M.D., Julio B. Bobes, Ph.D., Jose L. Carrasco, M.D., Josep Gaslon, M.D.

Summary:

Objective: Assess effectiveness of oral olanzapine (OLZ) compared to oral typical antipsychotic (APS) in treatment of agitated schizophrenic inpatients.

Method: Observational study of 904 inpatients. Patients entered study when oral olanzapine or oral typical antipsychotic was initiated upon hospital admission. Patients were followed-up during hospital stay. Effectiveness was determined by BPRS, CGI, and NOSIE scores. Agitated patients had BPRS agitation (anxiety, tension, uncooperativeness, hostility, and excitement) scores ≥ 15 at baseline.

Results: 483 patients received olanzapine as monotherapy or in combination with another antipsychotic (olanzapine group); 421 received typical antipsychotics as monotherapy or in combination (control group). In the olanzapine group, 219 patients met the agitation definition versus 229 in the control group. Patients in the control group had significantly greater illness severity at baseline as determined by BPRS positive, CGI, and NOSIE scales. Adjusting for baseline differences, change in clinical scales was significantly greater in the OLZ group compared to the APS group for BPRS total ($p = 0.014$), BPRS positive ($p = 0.008$), BPRS negative ($p = 0.0009$), BPRS agitation ($p = 0.035$), and CGI ($p = 0.0002$) scores. Incidence of treatment-emergent EPS and general adverse events was significantly greater in the APS group compared to the OLZ group ($p = 0.001$).

Conclusions: Olanzapine was associated with greater improvements in agitation and other measures of psychopathology, as well as better tolerability, compared to conventional antipsychotics in acute schizophrenic inpatients.

Funding provided by Eli Lilly and Company

NR283 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Effectiveness and Onset of Action of Olanzapine Versus Typical Antipsychotic Drugs in the Treatment of Inpatients with Schizophrenia: Europa Study

Enrique Alvarez, M.D., *Hospital Saint Pau, 1717 15th Street, Bacelona, Spain*; Juan C. Gomez, M.D., Jose A. Sacristan, M.D., Julio B. Bobes, Ph.D., Fernando Canas de Paz, M.D., Jose L. Carrasco, M.D., Josep Gascon, M.D.

Summary:

Objective: To assess olanzapine (OLZ) compared to typical antipsychotic drugs (APS) in hospitalized schizophrenic patients.

Method: Observational study of 904 patients. Clinical status measured by BPRS, CGI, PGI, and NOSIE. Response definition: baseline-endpoint decrease in BPRS ≥ 40% plus an endpoint BPRS < 18 or an endpoint CGI ≤ 3.

Results: 483 patients received OLZ in monotherapy or in combination, and 421 received APS in monotherapy or in combination. Haloperidol was the most frequent of the APS (76.25% of the patients). OLZ was prescribed in combination with other antipsychotics and with benzodiazepines in 26.5% and 67.7% of the patients, respectively, while haloperidol was used in combination and with benzodiazepines in 50.2% and 53.6% of the patients, respectively. Mean changes in the effectiveness scales, adjusting for baseline differences, were higher in the OLZ group ($p < 0.05$) (except NOSIE p = n.s.). Endpoint PGI score was lower in the OLZ group ($p < 0.001$). Response rate in the OLZ group was higher ($p < 0.001$). Time to response was shorter in the OLZ group ($p < 0.001$).

Conclusions: OLZ was effective in acute hospitalized schizophrenic patients. Greater improvements in clinical scales and in response rate in the OLZ group suggest that olanzapine could be

more effective than APS in the acute treatment of schizophrenic inpatients.

Funding provided by Eli Lilly and Company

NR284 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Intramuscular Olanzapine: Dose-Related Improvement in Acutely Agitated Patients with Schizophrenia

Alan F. Breier, M.D., MC 541, *Eli Lilly and Company, Lilly Corporate Center DC 0538, Indianapolis, IN 46285*; Padraig Wright, M.D., Martin Birkett, M.S., Karena Meehan, M.D., Stacy R. David, Ph.D., Shlomo Brook, M.D.

Summary:

Objective: To assess the efficacy, safety, and dose response relationship of intramuscular olanzapine to treat patients during acute psychosis.

Methods: Patients were randomly assigned to receive up to three injections within 24 hours of olanzapine (N = 185), haloperidol (N = 40) or placebo (N = 45). The primary endpoint was reduction in agitation measured by the PANSS Excited Component (PANSS-EC) at 2 hours post first injection (PFI).

Results: Olanzapine therapy showed a dose-related alleviation of agitation across all treatment groups ($p < 0.001$). Onset of action was rapid, with olanzapine 5, 7.5, and 10 mg groups showing significant improvement versus placebo as soon as 30 minutes after the first injection. All olanzapine and haloperidol groups showed significant improvement versus placebo at 2 hours, and olanzapine 5, 7.5, and 10 mg groups were significantly improved at all measured time points versus placebo. Response rates were higher in all olanzapine and haloperidol groups. The alleviation of acute agitation by olanzapine but not haloperidol was sustained at 24 hrs ($p < 0.05$). Anticholinergics were rarely used. Benzodiazepine use was most common in the placebo group. Hypotension, dizziness, and tremor were the most frequently reported adverse events. EPS improved in olanzapine and placebo groups but worsened in the haloperidol group ($p < 0.05$ vs haloperidol).

Conclusion: IM olanzapine provides a rapid, sustained, safe alleviation of acute agitation in patients with schizophrenia.

Funding provided by Eli Lilly and Company

NR285 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Intramuscular Olanzapine: Efficacy and Safety in Acutely Agitated Patients Diagnosed with Mania Associated with Bipolar Disorder

Karena Meehan, M.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Fan Zhang, Ph.D., Stacy R. David, Ph.D., Mauricio F. Tohen, M.D., Kimberly Koch, M.S., Rosemary Rizk, M.S., Mohammed A. Bari, M.D.

Summary:

Objective: To investigate the effectiveness of IM olanzapine at reducing agitation 2 hours and 24 hours after the first injection as compared to IM lorazepam and IM placebo in patients in the manic or mixed phase of bipolar illness.

Methods: Patients were randomly assigned to receive up to three intramuscular injections within 24 hours of olanzapine (N = 99), lorazepam (N = 51), or placebo (N = 51). The primary endpoint was reduction in agitation measured by the PANSS Excited Component (PANSS-EC) 2 hours after first IM injection.

Results: Patients treated with olanzapine were significantly improved versus lorazepam and placebo for all efficacy scales 2 hours post first injection (PFI). Onset of action was rapid, with olanzapine showing significant improvement versus lorazepam ($p < 0.05$) and placebo ($p < 0.03$) as soon as 30 minutes PFI. For patients with psychotic symptoms, olanzapine was superior to lorazepam on the PANSS-EC and Corrigan Agitated Behavior Scale at 2-hr PFI. 51.0% of lorazepam-treated patients experienced at least one treatment-emergent adverse event whereas olanzapine-treated patients (34.3%) did not significantly differ from placebo (25.5%). Neither active drug showed clinically significant changes for laboratory analyses, vital signs, or ECGs at 24-hr PFI.

Conclusions: IM olanzapine is a rapidly acting effective and safe treatment for acutely agitated patients with bipolar mania.

Funding provided by Eli Lilly and Company

NR286 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Safety and Effectiveness of Olanzapine at Doses of 20mg/Day Versus Typical Antipsychotic Drugs in the Treatment of Acute Schizophrenic Inpatients: Europa Study

Josep Gascon, M.D., *Hospital Mutua, De Tarrasa, Barcelona, Spain*; Antonio Ciudad, M.D., Juan C. Gomez, M.D., Enrique Alvarez, M.D., Julio B. Bobes, Ph.D., Fernando Canas de Paz, M.D., Jose L. Carraslo, M.D.

Summary:

Objectives: Assess the effectiveness and safety of olanzapine with initial dose of 20 mg/day versus typical antipsychotics in the treatment of schizophrenic inpatients.

Methods: Observational study of 904 inpatients. Safety assessed via recording spontaneous adverse events and EPS questionnaire. Clinical evaluations combined with BPRS, CGI-S, NOSIE. Reporting comparative analysis of patients that received olanzapine 20 mg as initial dose in antipsychotic monotherapy (OLZ 20) and a subgroup of patients treated with conventional antipsychotic (APS).

Results: Total of 483 patients received olanzapine as monotherapy or in combination with other antipsychotics (113 were included in the OLZ 20 group), 421 treated with typical antipsychotics as monotherapy or in combination (APS). OLZ 20 patients presented more days of institutionalization in previous year ($p = 0.01$). APS group showed significantly greater appearance or worsening of EPS than OLZ 20 group ($p = 0.001$). Adverse events were significantly fewer in OLZ 20 group than APS patients ($p = 0.001$). Changes in efficacy scales were superior in the OLZ 20 group ($p = 0.006$) than in the APS group for BPRS negative symptoms ($p = 0.006$). In OLZ 20 group the mean final dose was 19.9 mg (SD = 4.85).

Conclusions: OLZ 20 group showed significant improvement of negative symptoms while maintaining a similar effectiveness in global, positive, and agitation symptoms with better tolerance profile.

Funding provided by Eli Lilly and Company

NR287 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Effectiveness and Safety of Different Treatment Regimens of Olanzapine Treatment of Inpatients with Schizophrenia: Europa Study

Juan Gilbert, M.D., *Universidad de Cadiz, Cadiz, Spain*; Antonio Ciudad, M.D., Juan C. Gomez, M.D., Enrique Alvarez, M.D., Julio B. Bobes, Ph.D., Fernando Canas de Paz, M.D., Jose L. Carrasco, M.D.

Summary:

Objective: To assess different doses of olanzapine (OLZ) in hospitalized schizophrenic patients.

Method: Observational study of 904 patients. Clinical status measured by BPRS, NOSIE, and CGI. Safety evaluated by adverse events and EPS. Three groups were defined: those initiated treatment with OLZ 10 mg/day (OZ10, N = 144) or 20 mg/day (OZ20, N = 113) in monotherapy or were given OLZ with a typical

antipsychotic (APS, N = 128) (most frequent patterns of olanzapine use).

Results: The baseline CGI, BPRS total score and BPRS positive subscore were lower in the OZ10 group compared to the OLZ20 and APS group (p = 0.0009). Incidence of adverse events was lower in the OZ10 and OLZ20 group compared to the APS groups (p = 0.036). Incidence of EPS was lower in the OZ10 and OZ20 patients as a group when compared with APS patients (p = 0.007). There were no significant differences in the three treatment groups regarding effectiveness, except for NOSIE, which was favorable to APS when compared to OLZ10 (p = 0.042). For the OZ10 patients, the tendency was to increase the dose (mean = 15.6 mg/day, SD = 5.8; p = 0.0001) meanwhile in OZ20 patients the trend was to maintain (mean = 19.9 mg/day, SD = 4.8).

Conclusions: Effectiveness was similar among the OZ10, OZ20, and APS patient. APS presented a higher incidence of EPS and adverse events. The tendency was to increase the dose for subjects initiated at 10mg/day and to maintain for those initiated at 20 mg/day.

Funding provided by Eli Lilly and Company

NR288 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Safety and Effectiveness of Oral Olanzapine and Oral Typical Antipsychotic Drugs Following IM Treatment with Typical Antipsychotics: Europa Study

Jose L. Carrasco, M.D., *Department of Psychiatry, Fundacion/ Jimenez-Diaz, Avenida Reyes Catolicos 2, Madrid 28040, Spain*; Juan C. Gomez, M.D., Jose A. Sacristan, M.D., Enrique Alvarez, M.D., Julio B. Bobes, Ph.D., Fernando Canas de Paz, M.D., Josep Gascon, M.D.

Summary:

Objective: Assess safety and effectiveness of oral olanzapine compared to oral typical antipsychotics in schizophrenic inpatients initially treated with intramuscular typical antipsychotics.

Method: Observational study of 904 inpatients. Patients entered study when oral olanzapine or oral antipsychotic drug was initiated upon hospital admission. Reporting analysis of patients who received IM antipsychotic prior to initiation of oral treatment. Effectiveness was determined by BPRS, CGI, NOSIE. Safety was determined by emergent EPS.

Results: Total of 164 patients entered study after receiving IM antipsychotic, 68 treated with oral olanzapine as monotherapy or in combination with another antipsychotic (olanzapine group), 96 received typical antipsychotics as monotherapy or in combination (control group). There was a higher percentage of males in olanzapine group (82%) compared to the control group (62%) (p = 0.006). There was no significant difference in change in clinical scales except in BPRS negative symptom subscale, where there was significantly greater improvement in the olanzapine group compared to the control group (p = 0.015). The overall incidence of treatment emergent EPS was significantly greater in the control group compared to the olanzapine group ($p \leq 0.001$).

Conclusions: Oral olanzapine was at least as effective as oral typical antipsychotics as continuation treatment of psychotic schizophrenic inpatients initially treated with IM antipsychotics. Olanzapine was associated with significant improvement in negative symptoms and better tolerability compared to conventional antipsychotics.

Funding provided by Eli Lilly and Company

NR289 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Sertraline Treatment of Depression with Prominent Anxiety Symptoms

Jose L. Carrasco, M.D., *Department of Psychiatry, Fundacion/ Jimenez-Diaz, Avenida Reyes Catolicos 2, Madrid 28040, Spain*; Inmaculada Exposito, Ph.D., Alberto Porras-Chavarino, Ph.D.

Summary:

Objective: To evaluate tolerability and effectiveness of sertraline in a large number of patients with depression and prominent anxiety symptoms treated in primary care settings in daily clinical practice.

Method: In this open-label, non-comparative study, 2.426 depressed (HAM-DO12) outpatients with prominent anxiety symptoms (HAM-AO10) were treated with sertraline (50–200 mg/day) for six months. Patients were evaluated after one, three and six months. Efficacy measures were the score in Hamilton Rating Scale for Depression (HAM-D), Hamilton Rating Scale for Anxiety (HAM-A), and Clinical Global Impression Severity and Improvement (CGI-S, CGI-I).

Results: A total of 1.992 subjects completed the study. The mean final daily dose was 62.1 mg. The mean HAM-D and HAM-A score decreased from 21.6 and 21.5 at baseline to 5.9 and 5.4 after six months of treatment, respectively. At final visit 83.3% of patients were classified as not ill and 92.9% showed a marked improvement.

A total of 151 subjects (8.2%) reported at least one adverse event with the most frequent adverse events being abdominal pain (0.9%) and nausea (0.9%). Only, 2.6% patients discontinued due to adverse events.

Conclusion: Sertraline is a highly effective and well tolerated treatment for depression and anxiety symptoms in patients treated in primary care environment.

This study was supported by a research grant from Pfizer Spain.

NR290 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Treatment of Severely Psychotic Inpatients with Schizophrenia: Effectiveness of Oral Therapy with Olanzapine Versus Typical Antipsychotic Drugs (Europa Study)

Miguel Gutierrez, M.D., *Department of Psychiatry, Hospital de Cruc, Olaguibel 29, Barcaldo Vizcaya, Spain*; Antonio Ciudad, M.D., Juan C. Gomez, M.D., Enrique Alvarez, M.D., Julio B. Bobes, Ph.D., Fernando Canas de Paz, M.D., Jose L. Carrasco, M.D.

Summary:

Objective: Assess effectiveness of oral olanzapine compared to oral typical antipsychotic in the treatment of severely psychotic schizophrenic inpatients.

Method: Observational study of 904 inpatients. Patients entered study when oral olanzapine or oral typical antipsychotic was initiated upon hospital admission. Patients were followed-up during hospital stay. Effectiveness was determined by BPRS, CGI, NOSIE. Patients with prominent positive symptoms defined by baseline BPRS positive (conceptual disorganization, hallucinatory behavior, unusual thought content, suspiciousness) score ≥ 12.

Results: 483 patients received olanzapine as monotherapy or in combination with another antipsychotic (olanzapine group), and 421 received typical antipsychotics as monotherapy or in combination (control group). In the olanzapine group, 352 patients met the prominent positive symptoms definition as did 342 in the control group. Patients in control group had significantly greater illness severity at baseline as determined by BPRS total, BPRS positive, CGI, and NOSIE scores. Adjusting for baseline differences, change in clinical scales was significantly greater in the OLZ group compared to APS patient, for BPRS total (p = 0.0007), BPRS positive (p = 0.011), BPRS negative (p = 0.0017), and CGI (p = 0.0011) scores. Treatment-emergent EPS and general adverse events incidence was significantly greater in the APS group compared to the OLZ group (p = 0.001).

Conclusions: Olanzapine was associated with greater improvements in positive and negative symptoms and with better tolerability compared to conventional antipsychotics in acute severely psychotic schizophrenic in-patients.

Funding provided by Eli Lilly and Company

NR291 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Frequency and Management of Sexual Dysfunction with Antipsychotic Drugs in Schizophrenic Patients: Results from the EIRE Study

Julio B. Bobes, Ph.D., *Department of Psychiatry, University Oviedo, Julian Claveria 6, Oviedo 33006, Spain*; Javier Rejas, M.D., Margarida Garcia, Psy.D., Fernando Rico-Villademoros, M.D., Alberto Porras-Chavarino, Ph.D., Gonzalo Hernandez, M.D.

Summary:

Objective: To assess the frequency and management of sexual dysfunction (SD) with risperidone, olanzapine, quetiapine, and haloperidol in schizophrenic patients.

Methods: A cross-sectional, multicenter study was carried out by 61 Spanish psychiatrists (The EIRE Collaborative Group). Outpatients meeting DSM-IV criteria for schizophrenia and taking a single antipychotic for at least four weeks were consecutively entered into the study. Evaluations comprised demographic and clinical characteristics, CGI-severity scale, and a modified-UKU which included an ad-hoc question to evaluate side-effects management.

Results: A total of 636 evaluable patients (out of 669 recruited) were assessed. The average doses were those seen commonly in the clinical setting: 5.3 mg/d (RIS), 13.5 mg/d (OLAN), 360.5 mg/d (QUE) and 10,6 mg/d (HAL). The frequency of sexual dysfunction (overall and itemized) is shown in the table below. The drug frequency of SD seems to be dose-related and was higher in females. Although uncommon, the action most frequently taken with SD was a dose-reduction.

	HAL(n=131)	OLAN(n=228)	QUE(n=43)	RIS(n=234)
	%	%	%	%
Sexual dysfunction	38.1[a]	35.3	18.2	43.2[a]
Increased sexual desire	1.8	2.6	0.0	1.5
Diminished sexual desire	27.8	36.5[a]	14.3	38.8[a]
♂Erectile dysfunction	30.3	26.3	16.7	32.1
♂Ejaculatory dysfunction	27.3[a]	20.3[a]	11.1[a]	32.6[b]
♀Orgasmic dysfunction	9.1[a]	16.4[a]	0.0[a]	19.0[a]
♀Dry vagina	7.9[a]	10.8[a]	0.0[a]	15.0[a]

[a] χ^2:p<0.05 vs quetiapine; [b] :p<0.05 vs risperidone.

Conclusions: Sexual dysfunction is a frequent side effect of risperidone, olanzapine and haloperidol.

This study was conducted on behalf of the EIRE Collaborative Group.

NR292 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

The Quality-of-Life Scale (QLS) for Schizophrenia: Assessment of Responsiveness to Clinical Change

David Bushnell, M.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Christopher Patrick, Ph.D., M. Martin, Ph.D., Melissa Rody, M.S., Don Buesching, Ph.D., Alan F. Breier, M.D.

Summary:

Introduction: Health status instruments used to monitor change over time should undergo careful evaluation of responsiveness (the ability of an instrument to detect important changes over time) in addition to other psychometric properties.

Objective: To assess the responsiveness of the 21-item clinician-rated Quality of Life Scale (QLS) to detect important clinical change in rating scales used to measure schizophrenia symptomatology.

Methods: A subset of patients (N = 686) from a clinical trial assessing clinical and quality of life outcomes associated with olanzapine and haloperidol in the treatment of schizophrenia were evaluated using the QLS, Brief Psychiatric Rating Scale (BPRS), and Clinical Global Impression (CGI) rating at baseline and 6 weeks. To evaluate responsiveness, changes in QLS total scores were assessed at 20–50% reduction (improvement) in BPRS total scores, and at point changes on the CGI.

Results: The minimal clinically important difference (MCID) for the QLS total score was 2–6 points, corresponding to a 1-point change on the CGI and a 20% improvement in BPRS total scores.

Conclusions: The QLS was shown to be responsive to clinically important changes in standard schizophrenia symptom measures and will be useful in understanding the clinical significance of quality of life results in persons with schizophrenia.

Funding provided by Eli Lilly and Company

NR293 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Preclinical Study of the Mechanisms Underlying Weight Gain with Olanzapine

Mark L. Heiman, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; J. David Leander, Ph.D., Alan F. Breier, M.D.

Summary:

Objective: To study mechanisms responsible for weight gain in rats treated with olanzapine, haloperidol, and risperidone and identify an appropriate intervention.

Methods: Female Sprague-Dawley rats weighing 284 g (SD = 3.2) were injected s.c. with olanzapine, haloperidol, or risperidone (0.1 and 0.3 mg/kg for each drug). Body weight and food intake (FI) were measured daily. Lipid and carbohydrate (CHO) utilization were measured by indirect calorimetry. Body composition was measured by dual energy X-ray absorbometry (DEXA) before and after chronic exposure to olanzapine.

Results: Haloperidol and risperidone stimulated FI and CHO utilization (increase in respiratory quotient, RQ) but spared fat utilization. Similar doses of olanzapine decreased FI and RQ, but rats tended to be sedated. A sustained-release formulation of olanzapine designed to produce blood levels of about 50 ng/ml for 14 days had the same effects with less sedation. Such adiposity and decreased lipid utilization was attenuated by sibutramine (15 mg/kg).

Conclusion: Data indicate that olanzapine, haloperidol, and risperidone can stimulate adiposity. Antipsychotics may antagonize at least one neurotransmitter intimately involved in regulating energy balance at the hypothalamic level, which presents as hyperphagia and sparing of fat utilization. Since sibutramine opposes such actions, the gain in body fat can be spared.

Funding provided by Eli Lilly and Company

NR294 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Replacement of Depot Antipsychotic Therapy with Oral Ziprasidone

Steven R. Hirsch, M.D., *Department of Psychiatry, Imperial College, St. Dunstan's Road, London W6 8RP, United Kingdom*

Summary:

Objectives: To evaluate the efficacy and tolerability of switching to oral ziprasidone in patients with chronic schizophrenia or schizoaffective disorder who had been receiving an antipsychotic by depot intramuscular injection.

Methods: In a 12-week, open-label study, 28 patients received 40 mg ziprasidone (b.i.d.) for 2 days and 40–80 mg (b.i.d.) thereafter. Primary efficacy evaluations included the BPRS, CGI-S, and CGI-I scales. The Drug Attitude Inventory (DAI) and Patient Preference Scale (PPS) were also completed. Safety assessments included the Extrapyramidal Symptom Rating Scale (ESRS) and Barnes Akathisia Scale (BAS) as well as adverse event and ECG monitoring.

Results: Among all patients (last observation carried forward), symptom control was sustained at 12 weeks, with no significant change in BPRS. Study completers (N = 15) demonstrated significant improvement from baseline on BPRS (–3.6; $p < 0.05$). Fifty-two percent of all patients were identified as responders to ziprasidone (CGI-I score = 1 or 2). The DAI and PPS indicated preference for oral ziprasidone. Safety analysis of all patients showed significant improvement in ESRS (mean change = –2.2, $p = 0.014$). Ziprasidone was generally well tolerated. There were no clinically significant ECG abnormalities and minimal (<1 kg) weight gain.

Conclusions: In this study, switching from depot antipsychotic to oral ziprasidone resulted in continued symptom control and significantly improved EPS.

NR295 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Timing of Intervention and Long-Term Clinical Outcome in Schizophrenia

David J. Meagher, M.D., *Department of Psychiatry, Regional Hospital, Dooradoyle, Limerick, Ireland*; John Quinn, M.D., Stephanie Bourke, M.D., Patrice Murphy, M.D., Anthony Kinsella, M.S.C., Sally Linehan, M.D., John L. Waddington, D.Sc.

Summary:

Objective: The timing of intervention is increasingly considered as an important determinant of outcome in schizophrenia. This work investigates outcome in an elderly population who first became unwell in the pre-neuroleptic era and have experienced prolonged duration of initially untreated psychosis (DIUP).

Method: 82 patients with DSM-IV schizophrenia [48M, 34F; mean age = 71.6 years; mean duration illness = 47.5 years; mean DIUP = 9.2 years] were assessed. The relationship between DIUP and performance on PANSS, Social and Adaptive Functioning Evaluation (SAFE), and a neuropsychological battery [MMSE, EXIT, Praxis Test, Digit Span, Delayed Word Recall Test (DWRT)] were assessed by multiple regression analyses.

Results: DIUP significantly predicted the severity of negative [$\beta = 0.86$; $p < 0.001$] rather than positive symptoms. Performance on the DWRT was significantly predicted by DIUP [$\beta = 0.22$; $p < 0.001$], an effect that endured when the possible confounding effect of negative symptom severity was accounted for. DIUP also predicted performance on the SAFE, but this relationship was confounded by the association between DIUP and negative symptom severity.

Conclusions: More prolonged DIUP is associated with poorer long-term psychopathological, neuropsychological, and socioadaptive outcome although the basis of this association remains to be determined.

NR296 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Olanzapine Versus Risperidone Treatment of Schizophrenia: A Comparison Study

Karen Rascati, Ph.D., *Department of Pharmacology, University of Texas at Austin, Austin, TX 78712-1074*; Beth L. Barber, Ph.D., Maureen J. Lage, Ph.D.

Summary:

Objective: The purpose of this retrospective study is to examine both schizophrenia-related costs and total costs among Texas Medicaid patients who have been diagnosed with a schizophrenic disorder and have been initiated on one of two atypical antipsychotic therapies (olanzapine or risperidone).

Methods: From January 1996 to August 1999 medical and prescription utilization and cost data were retrieved for 3,072 schizophrenic patients who were initiated on regimens of olanzapine or risperidone. Multivariate analysis was used to control for a wide range of factors (drug choice, patient demographics, region, health conditions, and treatment patterns) that may influence schizophrenia-related costs and total costs. Estimation was conducted via a two-stage instrumental variable model.

Results: The mean unadjusted total schizophrenia-related cost per patient per year was $4,973, and the total cost per patient per year was $7,335. Although the daily drug costs associated with olanzapine were higher than risperidone and patients taking olanzapine on average stayed on therapy longer than those taking risperidone, when looking at total schizophrenia-related costs (medical plus prescription utilization), there was no significant difference between drug groups (olanzapine $101 lower, p = 0.7063). Additionally, receipt of olanzapine was associated with significantly lower total costs (including drug costs) compared to risperidone ($693 lower costs, p = 0.0383).

Conclusion: This study used data from clinical practice in a Texas Medicaid population to examine the schizophrenia-related costs (and total costs) for schizophrenic patients who received olanzapine versus risperidone. When schizophrenia-related costs (including drug costs) were studied, there was no difference in costs for patients receiving olanzapine versus risperidone. When total costs (including drug costs) were examined, receipt of olanzapine was associated with significantly lower costs.

NR297 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Caudate Nucleus and Lateral Ventricle Volume in First-Episode Schizophrenia: An MRI Study

James J. Levitt, M.D., *Department of Psychiatry, Brockton VAMC, 940 Belmont Street, # 116A, Brockton, MA 02301*; Robert W. McCarley, M.D., Ron Kikinis, M.D., Aleksandra Ciszewski, B.A., Ferenc A. Jolesz, M.D., Dean F. Salisbury, Ph.D., Martha E. Shenton, Ph.D.

Summary:

Objective: A growing appreciation has emerged for the role of the basal ganglia in cognitive functioning. Cognitive circuits anatomically link the frontal lobe to subcortical structures. Pathology in any of the core components of these circuits, such as in the caudate nucleus, may thus result in similar neurobehavioral syndromes. Typical neuroleptic medications, however, have been reported to increase striatal volume. The time course of this effect, however, has not been well characterized. To understand the time course of such an effect we have performed longitudinal MRI scans in first-episode (FE) schizophrenic (SZ) subjects, with minimal previous neuroleptic exposure at the time of their first scan, at two time points, 18 months apart.

Method: We measured the caudate nucleus, using MRI scans obtained on a 1.5 Tesla magnet, in nine right handed male FE subjects, with minimal neuroleptic exposure (a mix of typical and atypical neuroleptics), and in nine matched normal controls (NCLs). For the measurement of specific regions of interest higher spatial resolution SPGR images (1.5 × .9375 × .9375 mm voxels) were used. For whole brain measurements, used to correct for head size, 3mm spin echo double axial images were obtained.

Results: We have so far only analyzed Time 1 scans. T-tests revealed no group differences between FE SZs and NCLs in absolute volume of left or right caudate nucleus (4.6 vs. 4.7 ml.;

4.8 vs. 4.7 ml, $p \geq 0.8$) or in relative volumes ($p \geq 0.6$). Similarly, we found no group differences in absolute (5.5 vs. 4.6 ml; 4.9 vs. 4.6 ml, $p \geq 0.3$), or relative volume ($p \geq 0.3$), in contiguous lateral ventricles.

Conclusions: The failure to show group caudate nucleus volumetric differences, at time 1, may be because of our small sample size or because the intrinsic group difference is hidden by the enlarging effect on striatal structures of even a short period of neuroleptic exposure.

NR298 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Auditory P3 and Personality Traits in Schizophrenia Compared with Normals

Ronald J. Guerrera, M.D., *Department of Psychiatry, Brockton DVAMC, 940 Belmont Street, # 116A, Brockton, MA 02301*; Margaret Niznikiewicz, Ph.D., Paul G. Nestor, Ph.D., Martha E. Shenton, Ph.D., Ileana Berman, M.D., Christopher Allen, Robert W. McCarley, M.D.

Summary:

Objective: To compare the relationship of auditory P3 event-related cortical potential amplitude with major personality dimensions in individuals with schizophrenia and healthy controls.

Method: Nineteen medicated clinically stable outpatients (15M, 4F; mean age ± SD = 40.2 ± 8.4 years) with DSM-IV chronic schizophrenia, and 11 healthy controls (7M, 4F; mean age ± SD = 39.2 ± 9.0 years), gave written informed consent. EEG data were collected with a 64-channel array and referenced off-line to a common reference. Peak P3 amplitude was measured at each lead within a 275–550 msec latency window, post-stimulus. The NEO Five-Factor Inventory measured neuroticism (N), extraversion (E), openness (O), agreeableness (A), and conscientiousness (C). NEO scale scores and P3 amplitudes were correlated by subject group; all significantly ($p \leq .01$) correlated lead-scale pairs in either group were included in a Principal Components Analysis (PCA), by group.

Results: Peak P3 amplitude at 14 leads correlated significantly with one or more NEO scales. The first PCA component in each subject group accounted for about one-third of variance; in both groups this component contained the highest loading for C and was dominated by positive loadings for frontal leads. The pattern of loadings for other personality dimensions differed somewhat between groups on this component. The highest loading for N occurred on a subsidiary component in both groups, and was negatively associated with identical left temporal leads in each case.

Conclusions: These preliminary results suggest that the topographic relationship of P3 amplitude to major personality dimensions is similar in patients with schizophrenia and healthy controls, although some unexplained differences exist.

NR299 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Abnormal Personality Traits in Schizophrenia Are Related to Cognitive Deficits

Ronald J. Gurrera, M.D., *Department of Psychiatry, Brockton DVAMC, 940 Belmont Street, #116A, Brockton, MA 02301*; Paul G. Nestor, Ph.D., Christopher Allen, Brian F. O'Donnell, Ph.D., Robert W. McCarley, M.D.

Summary:

Objective: To examine the contribution of neuropsychological function to major personality traits in patients with schizophrenia, which differ significantly from those in healthy controls (Gurrera et al, 2000).

Method: Patients with DSM-IV schizophrenia (N = 30) and healthy controls (N = 48) completed the Trail Making Test (TMT), Wisconsin Card Sort (WCS), and NEO Five Factor Inventory (NEO-FFI) after giving written informed consent.

Results: As expected, subject groups showed distinct personality profiles, indicated by a highly significant Group x Personality Trait interaction ($F_{[4,77]} = 11.14$, $p = .000$). Patients scored significantly higher on neuroticism and lower on extraversion, openness, agreeableness, and conscientiousness. Expected group differences were also found on measures of attention (TMT) and executive function (WCS). Neuropsychological measures correlated with NEO scale scores in both groups, such that poorer cognitive performance generally was correlated with higher scores on neuroticism and lower scores on extraversion, openness, agreeableness, and conscientiousness in patients and controls. Correlation patterns differed slightly between groups. Repeated measures MANCOVA, with NEO scales as the within-subjects factor and neuropsychological measures as covariates, found no group difference in personality trait profile ($F_{[4,63]} = .84$, $p = .487$).

Conclusions: The cognitive functions indexed by these neuropsychological measures are significantly correlated with broad personality dimensions in healthy individuals as well as those with schizophrenia. Personality trait profiles do not differ significantly between these groups when neuropsychological performance is statistically controlled.

NR300 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Safety and Tolerability of Short-term Risperidone Treatment in Adolescents With a Family History of Schizophrenia

Tyrone D. Cannon, Ph.D., *Department of Psychology, University of California at Los Angeles, 1285 Franz Hall, Box 156304, Los Angeles, CA 90095-1563*; Matti O. Huttunen, M.D., Minna Dahlstrom, M.D., Ilkka Carmo, M.D., Pirkko Rasanen, M.D., Alo Juriloo, M.D.

Summary:

Objective: The authors sought to determine the safety and tolerability of short-term treatment with a low dose of risperidone in adolescents with prodromal symptoms and a family history of schizophrenia.

Method: Four prodromal high-risk adolescents and six first-episode patients with schizophrenia were treated with average doses of 1.0 and 1.8 mg of risperidone, respectively, in an eight to 12-week, open-label trial.

Results: The study drug was well tolerated, with no significant treatment-related adverse events noted. Rated severity of thought and behavior disturbances declined by about 30%, and performance on a test of verbal learning improved by about 100%, during eight to 12-weeks of treatment in both prodromal and first-episode patients, changes that achieved statistical significance despite the small sample sizes.

Conclusions: Short-term treatment with a low dose of risperidone appears safe for use and may be associated with improvement in behavioral and neurocognitive functioning in adolescent patients with prodromal symptoms of schizophrenia. A definitive test of whether the benefits observed in prodromal patients are due to medication and whether pharmacological intervention in this phase may prevent the initial psychotic episode, will require a larger, longer-term, randomized placebo-controlled, double-blind clinical trial.

Research supported by Janssen Pharmaceutica.

NR301 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Planum Temporale and Inferior Parietal Volumes in Paranoid Schizophrenia

Kathryn J. Kotrla, M.D., *Department of Psychiatry, Baylor College of Medicine, One Baylor Plaza, BCM350, Houston, TX*

77030-3411; Angela B. Lane, M.S., David M. Corey, Ph.D., John Langdoc, B.S., Stephen R. Kirkham, M.D., Pedro Diaz, M.D., Janet E. Johnson, M.D., Anne L. Foundas, M.D.

Summary:

Objective: The planum temporale (PT) is anatomically close but functionally distinct from the posterior ascending ramus (PAR). The PT is important in auditory processing and language; the PAR contributes to directed visual attention. Since thought disorder has been associated with atypical PT anatomy, we hypothesized that patients with paranoid schizophrenia, without thought disorder, would not show atypical PT anatomy, but would show atypical PAR anatomy.

Method: The MRIs from 12 age- and parental education-matched, right-handed male controls were compared with 12 patients with paranoid schizophrenia. SCID diagnoses were made, and symptoms quantified with the SANS and SAPS. Brain volume measurements were made using NIHImage.

Results: There was a nonstatistically significant trend for a smaller PT and PAR in schizophrenia, a trend toward a larger left PT, and no interhemispheric PAR size difference. Patients versus controls showed significantly different asymmetry quotient distributions of the PT and PAR with PAR anatomy more variable in the patients.

Conclusions: In a well-controlled comparison of controls and individuals with paranoid schizophrenia, atypical PT anatomy was not found in schizophrenia. In contrast, patient PAR anatomy was more variable, suggesting that higher-order parietal lobe structures may be selectively involved in this group without thought disorder.

NR302 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Adjunctive Anticonvulsant Use in First-Episode Schizophrenia

Theodore T. Kolivakis, M.D., *Department of Psychiatry, Allan Memorial Institute, 1025 Pine Avenue West, Montreal, QC H3A 1A1, Canada*; Howard C. Margolese, M.D., Linda Beauclair, M.D., Guy Chouinard, M.D.

Summary:

Studies suggest a beneficial effect of adjunctive anticonvulsants in schizophrenia independent of anti-aggressive effect. No studies have evaluated anticonvulsants on outcome of early psychosis. We reviewed 20 patients, 16 men and four women (mean age: 24.95 ± 4.57), with schizophreniform disorder (9) and early paranoid schizophrenia (11), enrolled in a randomized study comparing risperidone and haloperidol. Adjunctive anticonvulsant use and outcome was examined. Retention rate was compared with historical cohorts. A total of 17/20 patients (85%) received anticonvulsants [valproic acid (11), lamotrigine (13), gabapentin (11), and > 1 anticonvulsant (12)]. Retention rates were 19/20 (95%) at eight weeks and 16/18 (89%) at one year. Average time in trial was 23.0 ± 12.2 months for the whole group, and 22.8 ± 12.0 months for those on anticonvulsants. Mean PANSS at baseline was 80.7 ± 17.3, eight weeks 62.8 ± 13.3, and one year 74.6 ± 20.2. Mean CGIs at baseline was 4.8 ± 0.8 and one year 3.7 ± 1.1. A superior retention rate compared with other studies of shorter duration was demonstrated (95% vs 74.5%). In fact the retention rate at 23.9 months was higher than pooled data of historical cohorts at six to eight weeks (80% vs 74.5%). Furthermore, our retention rate at six weeks was superior to another study in first-episode patients (95% vs 74.7%). We propose a role for adjunctive anticonvulsants in early schizophrenia, through prevention of kindling or lowering the required dose of antipsychotics.

NR303 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Antipsychotic Medication: Impact on Coronary Artery Disease Risk Factors

Donna A. Wirshing, M.D., *Department of Psychiatry, GLAVA Health Systems, 11301 Wilshire Boulevard, Building 210 B151, Los Angeles, CA 90073*; William C. Wirshing, M.D., Laura Meng, Pharm.D., Jennifer Boyd, Pharm.D., Jake Ballon, B.S.

Summary:

Objective: Novel antipsychotic medications (NAPDs) such as clozapine (CLOZ), and olanzapine (OLZ) have been linked with increases in weight and dysregulation of glucose control. We retrospectively examined 590 clinical charts to compare weight gain, glucose, cholesterol, and triglycerides—risk factors for coronary artery disease.

Method: 215 subjects' clinical records had adequate data to be included in the study (CLOZ (N = 39), OLZ (N = 32), risperidone RIS (N = 49), quetiapine QUE (N = 13), haloperidol HAL (N = 41), or fluphenazine FLU (N = 41)). Weight, glucose, cholesterol, and triglyceride data were obtained.

Results: Patients in all groups were overweight (BMI > 25). We found statistically significant differences in total cholesterol ($F = 2.9$, $p = 0.03$, $df = 4, 137$) and triglycerides ($F = 6.6$, $p = 0.0001$, $df = 4, 115$) among the NAPDs. CLOZ, OLZ, and HAL groups had statistically significant increases in glucose levels. CLOZ and OLZ groups had statistically significant increases in triglycerides. OLZ, RIS, and QUE groups all showed significant decreases in LDL.

Conclusions: The NAPDs offer a favorable EPS profile but have their own side effects. Weight gain, glucose elevation, and dyslipidemias may be linked phenomena. The NAPDs differ in their effects on these parameters. Clinicians need to be aware of these potential side effects and intervene to prevent the risk of coronary artery disease.

NR304 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

The Community Re-Entry Program for Schizophrenia: Correlates of Treatment Response

Donna A. Wirshing, M.D., *Department of Psychiatry, GLAVA Health Systems, 11301 Wilshire Boulevard, Building 210 B151, Los Angeles, CA 90073*; William C. Wirshing, M.D., Elizabeth Rossoto, Ph.D., Lorena Gonzalez, B.A., Jennifer Watson, Jake Ballon, B.S., Cyrus McNally

Summary:

Objective: The goal of this study are to compare psychoeducational classes occurring during brief hospitalizations. These classes were aimed at decreasing rehospitalization and increasing compliance with medication and outpatient appointments. At the time this program began, only 45% of patients discharged made it to their first appointment.

Method: 94 patients with DSM-IV-diagnosed schizophrenia or schizoaffective disorder were randomly assigned to the Community Re-Entry Program (CREP) (N = 47) or to a series of Illness Education (IE) classes (N = 47). All subjects were given both a pre-test and a post-test of their knowledge of illness-pertinent issues within the CREP training module as well as neuropsychiatric testing.

Results: The CREP group learned more than the IE group on three out of the areas of knowledge pertinent to making and keeping appointments. Learning correlated with performance on a neurocognitive test, the CVLT ($r = 0.41$ $p = 0.004$). 73% of CREP patients made it to their appointments compared to 67% of the IE patients. There was a medium effect ($w = 4$) of RIS on making appointments for the IE group.

Conclusions: During brief hospitalizations both psychoeducational interventions positively impacted patients' ability to make

their first appointment. Neurocognitive and medication factors may also influence outcome.

NR305 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

An Educational Videotape to Enhance Schizophrenia Patients Knowledge of Informed Consent

Donna A. Wirshing, M.D., *Department of Psychiatry, GLAVA Health Systems, 11301 Wilshire Boulevard Building 210 B151, Los Angeles, CA 90073*; Robert Kern, Joseph Ventura, Ph.D., Curley L. Bonds, M.D., MaryJane Robertson, Ph.D., Jennifer Boyd, Pharm.D., Jim Mintz, Ph.D.

Summary:

Objective: The ability of patients with schizophrenia to give informed consent for clinical trials has been a subject of some scrutiny. The goal of this ongoing project was to develop an educational intervention that enhances schizophrenia patients' participation and understanding of the informed consent process.

Methods: Patients were asked to participate in clinical trials for schizophrenia and were randomly assigned to view a videotape about the informed consent process or a control videotape prior to consenting to the clinical trial. A quiz about the informed consent procedure was given before and after the videotape intervention.

Results: Thus far 14 patients have viewed the informed consent videotape (ICV) and six patients have viewed the control videotape. The ICV group had statistically significant improvements on their knowledge quiz regarding the informed consent process compared to the control group ($F = 13.03$, $df = 1,18$, $p = 0.002$). Scores for the experimental group rose from 84% correct to 90% correct. The control group's scores were 79% correct for both pre and post tests.

Conclusions: These preliminary results suggest that an educational videotape can enhance schizophrenia patient's knowledge of the informed consent process. The results also suggest that the patients sampled thus far already have a reasonable fund of knowledge regarding the informed consent process, even prior to our intervention.

NR306 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Mental Well-Being Among Caregivers of People with Schizophrenia

John Travers, M.D., *CNS, AstraZeneca Pharmaceuticals, 1800 Concord Pike, FOC 1, Box 15437, Wilmington, DE 19850-5437*; Richard E. White, Ph.D., Audra N. Boscoe, M.P.H., Diana McDonnell, A.B.

Summary:

Objective: Schizophrenia severity, and its effect on caregivers' mental health, may be critical to patients' quality of care. This research therefore assessed how schizophrenia symptoms affect caregivers' mental well-being.

Methods: In June 2000, 376 schizophrenia caregivers from national support groups completed self-administered questionnaires. Mental well-being was measured using the SF-12. Schizophrenia symptoms were evaluated as a four-level variable: high negative/high positive (35%), high negative/low positive (17%), low negative/high positive (10%), and low negative/low positive (38%). To control for confounders to caregivers' well-being, caregivers' demographics and involvement, and patients' demographics and time with schizophrenia, linear regression was used.

Results: The mean SF-12 was 48.7 (SD = 10.6). In bivariate, chi-squared analysis, caregivers' mental well-being decreased as schizophrenia symptoms increased ($p < 0.001$). Controlling for confounders, symptom severity remained significant. Caregivers of patients with *low* positive and negative symptoms had average SF-12 scores six points higher than those caring for patients with *high* symptoms ($p < 0.001$). Even caregivers of patients with only high positive symptoms scored about five points higher ($p = 0.015$). Caregivers of patients with high negative symptoms did not differ from those with both high negative and positive symptoms ($p = 0.616$).

Conclusion: Medications and strategies that help control patients' symptoms, especially negative symptoms, can also help caregivers experience more positive well-being.

NR307 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

The Association of Antipsychotic Medication Use with Productive Activity Among Schizophrenia Patients

Amy L. Grogg, Ph.D., *Department of Outcome Research, Janssen Pharmaceuticals, 1125 Trenton-Harbourton, Titusville, NJ 08560*; Susan C. Bolge, M.A., Ramy A. Mahmoud, M.D.

Summary:

Objective: To evaluate the association of antipsychotic medication on the productivity of people with schizophrenia.

Methods: Schizophrenia patients (N = 390) identified through the National Alliance for the Mentally Ill (NAMI) and community mental health centers, completed self-administered questionnaires in June 2000. Those reporting any paid employment, volunteer work, or school were considered productive. To determine the effect of antipsychotic medications on productive activity, a logistic regression was used, controlling for severity, demographics, and other prescription medications. The Psychological General Well-Being Scale (PGWB) was used as a surrogate measure for severity.

Results: Fifty-three percent of respondents participated in at least one productive activity in an average week. Thirty-three percent engaged in paid employment, 26% in volunteer work, and 9% were in school. Less severe respondents were more likely to be productive ($p = 0.001$). Although risperidone users were more severe than conventional antipsychotic users (PGWB scores of 60.7 versus 66.4, respectively), this did not negatively affect productivity. Fifty-eight percent of risperidone users were productive compared to 49% of conventional antipsychotic patients. Logistic regression revealed risperidone as the only conventional or atypical antipsychotic that was significantly associated with increased productive activities ($OR = 1.85$, $p = 0.047$).

Conclusion: Risperidone use had a positive impact on the productivity of people with schizophrenia.

NR308 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Catatonia in Chinese Patients with Chronic Schizophrenia

Gabor S. Ungvari, M.D., *Department of Psychiatry, Chinese University, Prince of Wales Hospital, Shatin, N.T., Hong Kong, SAR, China*; Siu-Kau Leung, M.D., Fung-Shing Ng, M.D.

Summary:

Objective: To determine the frequency of catatonia in Chinese patients with chronic schizophrenia and its association with sociodemographic, clinical, and treatment variables and to describe distinct catatonic syndromes occurring in chronic schizophrenia.

Method: A cross-sectional assessment of a randomly selected cohort of patients (N = 225; 160 men, 65 women age = 42 years [SD = 7]; length of illness: 20 years [SD = 7]; antipsychotic dose: 812 mg chlorpromazine equivalent [SD = 595]) with a DSM-IV schizophrenia and standard rating instruments for catatonia, drug-induced signs/symptoms, and psychotic, depressive, and obsessive-compulsive symptoms were employed.

Results: Using a narrow definition of catatonia, which required the presence of four or more signs and symptoms on the Bush-

Francis Catatonia Rating Scale, 62 subjects (27.6%) formed the catatonia group with a number of catatonic signs/symptoms (6.5, SD = 1.9). Most frequent catatonic signs and symptoms were mannerisms, mutism, posturing, grimacing, and immobility. Catatonic subjects had significantly more negative symptoms, akinesia, and more severe illness globally than their non-catatonic counterparts. There were no differences between the two groups with respect to other clinical, demographic, or treatment variables. Factor analysis of catatonic signs and symptoms yielded four factors: immobility-mutism, excitement-impulsivity, mannerism-stereotypy, and obedience-mitgehen.

Conclusions: Catatonia constitutes a distinct symptom cluster in schizophrenia; however, the present study failed to validate a separate catatonia subtype of schizophrenia.

Target Audience(s): Psychiatrists and allied mental health professionals

NR309 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Insight and Psychopathology in Schizophrenia

Serge M. Sevy, M.D., *Psychiatric Research Department, Hillside Hospital, 75-79 263rd Street, Glen Oaks, NY 11004*; Laurie J. Polubinsky, M.D., Kay Nathanson, M.P.H., Xavier Amador, Ph.D.

Summary:

Objective: To examine the relationship between insight and the positive, negative, excited, depressed, and cognitive dimensions of symptoms in patients with a diagnosis of schizophrenia.

Methods: 98 patients with a diagnosis of schizophrenia were assessed with PANSS and SUMD—revised version. PANSS data were analyzed based on a five-factor model defined by Kay and Sevy (1990).

Results: Percentage of patients having a moderate or severe lack of awareness was 32.7% for illness, 58.2% for symptoms, 18.4% for treatment response, and 41.8% for social consequences. Lack of awareness for symptoms was significantly correlated with all five symptom factors. Lack of awareness for the illness and unawareness of treatment response were only correlated with the positive dimension, while unawareness of social consequences was correlated with both positive and excited dimensions.

Conclusion: Poor insight is a common feature of schizophrenia and has a complex relationship to other symptoms of the illness. Our results suggest that some aspects of insight are more closely tied to positive symptoms than other aspects. Treatment studies that measure insight could answer the question of whether these deficits in awareness improve along with positive symptoms.

NR310 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Gene Environment Interaction in Schizophrenia Risk: Traumatic Brain Injury

Cheryl M. Corcoran, M.D., *Department of Psychiatry, NYSPI, 1051 Riverside Drive, Unit 2, New York, NY 10032*; Dolores Malaspina, M.D.

Summary:

Introduction: Traumatic brain injury (TBI) is associated with increased risk for schizophrenia. There are three models for an association: 1) TBI interacts with genetic vulnerability to cause schizophrenia; 2) The vulnerability for schizophrenia comprises a vulnerability to incur TBI; or 3) TBI produces a disorder that resembles schizophrenia, i.e., a phenocopy. An examination of TBI and schizophrenia in pedigrees with variable genetic risk can clarify the nature of their association.

Methods: We examined the association of prior TBI and schizophrenia in individuals from 1) 1,271 schizophrenia ("high genetic risk") families; and 2) 561 bipolar ("low genetic risk") families. Families were identified by the NIMH Genetics Initiative; each had at least two first-degree relatives with the respective core disorders. Diagnoses were made using the Diagnostic Interview for Genetic Studies (DIGS), which also queries for TBI.

Results: Compared with healthy relatives, in a combined pedigree sample, schizophrenia patients had an odds ratio (OR) of 3.32 (95% CI = 1.77–6.22) for TBI, confirming an overall TBI-schizophrenia association. The odds ratio for TBI for schizophrenia patients was 4.27 (95% CI = 1.40–13.0) in schizophrenia pedigrees and 0.75 (95% CI = 0.10–5.93) in bipolar pedigrees. This finding suggests that TBI and genetic vulnerability may have synergistic effects on schizophrenia risk.

NR311 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Advancing Paternal Age, New Mutations, and Schizophrenia Risk

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Summary:

The major source of new mutations in the human is advancing paternal age. There is overwhelming evidence supporting a genetic contribution to schizophrenia, but it is unclear how the disease is maintained in the population, given the low fertility of affected individuals. An association of schizophrenia risk with advancing paternal age would suggest that new mutations contribute to the risk for schizophrenia. This study was conducted through record linkage of a birth cohort of 87,907 individuals born in Jerusalem in 1964–1976 to the Israeli Psychiatric Case Registry. We detected 1,337 individuals who had a psychiatric hospital admission before 1998; 658 of them had a schizophrenia diagnosis. We used proportional hazards models to estimate the independent and combined effects of parental ages on the schizophrenic patients' age at first admission to the hospital with any psychiatric diagnosis, adjusting for gender and ethnic group. We found that each decade of the father's age multiplied the odds ratio (relative risk) for schizophrenia by 1.41 (95% = 1.21 – 1.65), an effect not seen in the patients with other psychiatric diagnoses. This data supports the hypothesis that new autosomal mutations in men substantially contribute to schizophrenia risk.

NR312 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

A Retrospective Economic Evaluation of Olanzapine Versus Risperidone Treatment of Schizophrenia

Zhongyun Zhao, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*

Summary:

Objectives: The purpose of this study was to assess the 1-year direct schizophrenia-related treatment costs, mental health care costs, and total health care costs for patients diagnosed with schizophrenia who initiated therapy with either olanzapine or risperidone.

Methods: A retrospective analysis of the integrated medical and pharmacy claims of a large, geographically diverse, commercially insured population was conducted. A previously validated algorithm to identify schizophrenic subjects was used for patient selection. The confirmed schizophrenia patients who began treatment with either olanzapine or risperidone were included. Treatment course and associated schizophrenia-related, mental health care, and total health care costs during the subsequent 12-month period were examined using univariate and multivariate methods.

Results: Nine hundred eighty-five (985) patients initiated on a regimen at risperidone and 348 initiated on a regimen at olanzapine met inclusion criteria. The mean dose was 4.02 and 10.49 for risperidone and olanzapine patients, respectively. Patients taking olanzapine versus risperidone stayed on therapy longer during the 12-month observation period (217 days versus 181 days, $p < 0.0001$). Although pharmaceutical costs were significantly higher for the olanzapine patients, their medical costs were significantly lower than those taking risperidone. After adjusting for differences in patient demographics, disease severity, and comorbidities, olanzapine patients had significantly lower mental health care costs including drug costs ($1,827 less, $p < 0.03$) and lower total health care costs ($1,834 less, $p < 0.05$). The schizophrenia-related costs (including drug costs) were not statistically significantly different, although numerically the risperidone patients incurred $740 more per patient than patients taking olanzapine ($p = 0.26$).

Conclusions: The findings in this study suggest that the initial selection of atypical antipsychotic for the treatment of schizophrenia matters, as olanzapine offset its acquisition cost by reducing medical costs and demonstrated significant mental and total health care cost savings over risperidone.

NR313 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Cost Analysis of Olanzapine Versus Risperidone Treatment of Uncontrolled Schizophrenia

Zhongyun Zhao, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*

Summary:

Objectives: This study compares the 1-year direct schizophrenia-related treatment costs, mental health care costs, and total health care costs of schizophrenia patients initiating a regimen at olanzapine versus risperidone.

Methods: The integrated medical and pharmacy claims of a large, geographically diverse, commercially insured population were used to conduct this analysis. Patients who initiated treatment with either olanzapine or risperidone and had one inpatient or two outpatient services for schizophrenia within 30 days prior to initiation of drug of interest were included in this analysis. Treatment course and associated schizophrenia-related, mental health care, and total health care costs during the subsequent 12-month period were examined using univariate and multivariate methods.

Results: Four hundred thirty-one (431) patients initiated on a regimen at risperidone and 142 initiated on a regimen at olanzapine met inclusion criteria. The mean dose was 4.34 and 11 for risperidone and olanzapine patients, respectively. During the 1-year period after initiation of drug of interest, olanzapine patients (compared with risperidone patients) were less likely to be hospitalized and had shorter mean length of hospital stays for schizophrenia-related causes, mental health care causes, and all causes. Although pharmaceutical costs were significantly higher, medical costs were significantly lower for patients taking olanzapine compared to those taking risperidone. Univariate and multivariate analyses (controlling for potential confounding factors such as patient demographics, disease severity, and comorbidities) consistently demonstrated that olanzapine patients had significantly lower schizophrenia-related costs ($2,839 less, $p < 0.011$), mental health care costs ($3,744 less, $p < 0.004$), and total health care costs ($4,674 less, $p < 0.001$) than those patients taking risperidone.

Conclusions: The findings revealed significant differences between olanzapine and risperidone in the treatment of schizophrenic patients in clinical practice. Olanzapine patients incurred lower costs (lower schizophrenia-related, mental health care, and total health care costs). The lower costs were inpatient driven by fewer hospitalizations and shorter length of hospital stays in the olanzapine treatment group.

NR314 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Health Care Resource Use Among Caregivers of People with Schizophrenia

Richard E. White, Ph.D., *CNS, AstraZeneca, 1800 Concord Pike, Box 15437, FOC 1, Wilmington, DE 19850-5437*; John Travers, M.D., Audra N. Boscoe, M.P.H., Diana McDonnell, A.B.

Summary:

Objective: With increasing medical costs, the health of schizophrenia caregivers cannot be ignored. This research therefore evaluated healthcare resource use among caregivers of people with varying severities of schizophrenia.

Methods: In June 2000, 376 schizophrenia caregivers from national support groups completed self-administered questionnaires. They reported whether they were hospitalized (17%), visited the ER (19%), or had physicians' appointments (48%) in the past 6 months. Caregivers rated schizophrenia severity by reporting how often (on a scale from zero to four) their patient experienced 23 problems. Scores were then computed as the overall mean. Logistic regression was used to control for other variables that confound resource use-caregivers' demographics and SF-12, and patients' demographic data, length of illness, and antipsychotic use.

Results: Controlling for confounders, caregivers of people with severe schizophrenia were almost three times more likely to have been hospitalized ($OR = 2.8$, $p < 0.001$) or to have visited an ER ($OR = 3.1$, $p < 0.001$) in the previous 6 months. The effect of severity on the number of physician visits was not significant ($p = 0.798$).

Conclusion: Medication and other strategies that help control patients' severity or help maintain people at lower severity may reduce caregivers' use of hospitals and emergency rooms and ultimately lower the overall costs associated with treating schizophrenia.

NR315 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Prevalence of Diabetes in Schizophrenia Patients Treated with Antipsychotics

Daniel E. Casey, M.D., *Mental Health Department, Portland VA Medical Center, 3710 SW U.S. Veterans Hospital Road, Portland, OR 97201*; Erica M. Danielson, B.S., Naomi B. Fishman

Summary:

Patients with schizophrenia are often described as being at greater risk for diabetes mellitus (DM) than the general population. This has been attributed, in part, to higher rates of obesity and higher body mass indices (BMI). With the wide adoption of atypical antipsychotics, and the potential for substantial additional weight gain that is associated with certain agents, the rate of weight-induced DM may be higher than previously observed. Additionally, early evidence suggests that some antipsychotics may produce adverse effects on glucose metabolism even in the absence of weight gain. Surprisingly little is known about the actual prevalence of DM with either typical or atypical antipsychotics in various populations. To address this issue, the prevalence of DM was determined by reviewing the clinical records of patients with the diagnosis of schizophrenia at the Portland, Oregon VA Medical Center to identify those with a concurrent diagnosis of DM. Drug treatment records were also reviewed to determine which antipsychotic medicines patients were taking at the time of the survey. The DM prevalence and mean ages of schizophrenia patients treated with

an antipsychotic are presented. For the typical antipsychotic agents: haloperidol, N = 3/47 (6.4%), age = 66.3 years; perphenazine, N = 3/42 (7.1%), age = 45.7 years; chlorpromazine, N = 2/18 (11.1%), age = 46.0 years; thioridazine, N = 4/20 = (20%), age = 61.0 years. For the atypical antipsychotic agents: risperidone, N = 6/73 (8.2%), age = 57.2 years; quetiapine, N = 2/16 (12.5%), age = 47.5 years; clozapine, N = 5/31 (16.1%), age = 58.8 years; olanzapine, N = 33/194 (17.0%), age = 57.9 years. These results compare with the rates in the general population of 3.9% for 40–49 year olds, 6% for 50–59 year olds, and 12.6% for 60–69 year olds. Thus, agents that are traditionally associated with higher amounts of weight gain, such as the typical agents of chlorpromazine and thioridazine as well as the atypical agents quetiapine, clozapine, and olanzapine are associated with a higher than average prevalence of diabetes. The clinical consequences of these findings will be discussed.

NR316 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Use of Somatic Health Care Services Among Persons with Severe Mental Illnesses

Faith Dickerson, Ph.D., *Sheppard Pratt, 6501 North Charles Street, Baltimore, MD 21204*; Janine C. Delahanty, M.A., Lorraine O'Donnell, M.S., Alicia Lucksted, Ph.D., Lisa B. Dixon, M.D.

Summary:

Objective: We studied the utilization of somatic health services among persons with severe mental illnesses. We hypothesized a lower utilization of these services among persons with schizophrenia versus those with affective disorders.

Methods: The sample (N = 200; mean age = 44, SD = 9) was equally divided among schizophrenia, schizoaffective disorder, bipolar disorder, and major depression and drawn from suburban and urban psychiatric clinics. Participants completed an interview with items derived from the NHANES and NHIS national surveys.

Results: Consistent with the study hypothesis, patients with schizophrenia and schizoaffective disorder were less likely to have seen a medical specialist in the last year than affective disorder patients (24 versus 41%) and were also less likely to have consulted a practitioner of complementary or alternative medicine (8 versus 27%). Reported barriers to health care among the entire sample included inability to afford dental care (35.7%) or prescription drugs (22.5%) and transportation problems leading to a delay in medical care (14%). These findings will be compared to published norms based on demographically matched persons in the general population.

Conclusion: Results of this study suggest specific deficits in the somatic health care received by persons with severe mental illnesses that may impact on their health and quality of life.

NR317 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Comparative Weight Change with Atypical Antipsychotic Treatment

Kashinath B. Patil, M.D., *Department of Psychiatry, University of Rochester, 36 Forest Meadow Trail, Rochester, NY 14624*; Terrance J. Bellnier, M.P.A., Shyam D. Karki, Ph.D., Sampath K. Neerukonda, M.D.

Summary:

Objective: We propose to evaluate weight change risk factors associated with atypical antipsychotic treatment.

Method: We conducted a retrospective review of 316 charts. Patients with DSM-IV Schizophrenia were randomly selected and matched for age and sex with a control group. Data were analyzed to determine differences in maximal weight change, duration, pretreatment weight, average dose, and sex in patients receiving five different drug treatments (clozapine: N = 42, olanzapine: N = 46, risperidone: N = 44, quetiapine: N = 44, and haloperidol [control]: N = 46) for 6 months.

Results:

Subject Characteristics: Meanage: 46 years, SD = 12; 148 were male.

Weight Change (kg): Clozapine: 6.9 (SD = 4.3), olanzapine: 4.3 (SD = 4), risperidone: 2.2 (SD = 2.6), quetiapine: 2.9 (SD = 2.5), haloperidol: 1.9 (SD = 2.2). Weight gain for clozapine ($t = 6.99$, $df = 86$, $p < 0.0001$, olanzapine ($t = 3.63$, $df = 90$, $p < 0.0001$), and quetiapine ($t = 2.05$, $df = 88$, $p = 0.021$) were significant. All groups reached maximal weight change by 20 weeks (SD = 4).

Risk Factors: Pretreatment weight, daily dose, and sex had no effect on weight change. Weight gain with clozapine ($t = 1.01$, $df = 40$, $p = 0.159$) persisted after nutritional counseling.

Conclusion: Clozapine caused the most and risperidone the least weight gain. Pretreatment weight, duration, average dose, and sex may not be risk factors. Nutritional counseling may reduce the risk of gaining weight.

NR318 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Orienting Response and Task Performance in Schizophrenia and Mania

David B. Schnur, M.D., *Department of Psychiatry, Mt. Sinai School of Medicine, 79-01 Broadway, Elmhurst, NY 11373*; Scott P. Smith, Ph.D., Alvin S. Bernstein, Ph.D., Sachidanand Peteru, M.D., S. M. Ahmed, M.D.

Summary:

Objective: We have previously reported that the finger pulse amplitude response (FPAR) component of the orienting response (OR) was reduced in schizophrenic and bipolar manic patients. As an extension of that study, we now examine FPAR change and task performance longitudinally to evaluate diagnostic differences in the relationship between OR and information processing.

Method: FPAR to tones requiring foot-pedal release was obtained during two testing sessions separated by a 3-week interval in 20 schizophrenic, 14 manic, and 24 control subjects.

Results: A repeated measures ANOVA indicated a significant interaction between FPAR change and diagnosis on task performance accuracy ($p < 0.0001$). Follow-up analyses revealed a significant effect of FPAR change on task performance in the schizophrenic group ($p = 0.01$); increased FPAR was associated with increased accuracy and decreased FPAR with decreased accuracy. Moreover, changes in number of errors across sessions was negatively correlated with FPAR change ($p < 0.05$). Relations between FPAR and task performance were less consistent among the bipolar and control subjects.

Conclusions: Heightened FPAR appears to be associated with task performance improvement in schizophrenic patients. These data support the view that OR reductions may be associated with information processing deficits in schizophrenia.

NR319 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Diffusion Tensor Imaging in Kraepelinian Schizophrenia

Lina S. Shihabuddin, M.D., *Department of Psychiatry, Mt. Sinai School of Medicine, One Gustave Levy Place, Box 1505, New York, NY 10029*; Monte S. Buchsbaum, M.D., Adam M. Brickman, B.A., Jimcy Platholi, M.A., Rachel Bloom, B.A., Kenneth L. Davis, M.D.

Summary:

Background: Kraepelinian patients are a subtype of schizophrenic patients characterized by a progressive clinical course, poor outcome, and often dementia. Non-Kraepelinian schizo-

phrenic patients on the other hand, have a better outcome and a relatively static course. Diffusion tensor MR imaging was used to assess white matter tract integrity in these two groups of patients. Through the quantification of directionality of restricted anisotropy, this technique allows the direct assessment of both large axons stretching from frontal regions to the striatum, as well as interhemispheric connectivity.

Methods: Structural MRI with diffusion tensor imaging was obtained from 13 Kraepelinian schizophrenic patients and 24 non-Kraepelinian schizophrenic patients. The SPGR anatomical sequence acquired 124 1.2-mm thick slices and the diffusion tensor sequence acquired 14 5-mm thick slices. Anisotropy (i.e., white matter alignment) was analyzed and compared between the two groups.

Results: Kraepelinian patients showed lower levels of anisotropy than non-Kraepelinian schizophrenic patients in the genu of the corpus callosum and in white matter bundles interior to the frontal pole (Brodmann's area 10).

Conclusions: These findings demonstrate less organized and coherent white matter in Kraepelinian schizophrenia as compared to non-Kraepelinian schizophrenia. Less white matter tract integrity may help account for the poorer outcome in Kraepelinian schizophrenic patients and may be indicative of an underlying neurodegenerative abnormality in this subtype. It further suggests that poorer outcome schizophrenia may be characterized by more dysfunctional patterns of neuronal connectivity.

NR320 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Olanzapine Affects Neurocognitive Function in Medication-Refractory Schizophrenia

Robert C. Smith, M.D., *Department of Psychiatry, New York University Medical School, P.O. Box 316, Hewlett, NY 11557*; Jean-Pierre Lindenmayer, M.D., Amaresh Khandat, M.D., Maurico Infante, M.D., Abhay Singh, M.D.

Summary:

In addition to disabling symptoms, chronic schizophrenia is characterized by neurocognitive and neurological deficits that may be more closely related to underlying pathology and social functioning. To assess the efficacy of olanzapine on clinical improvement and neurocognitive functioning in chronic nonresponding schizophrenic patients, we conducted a double-blind study of olanzapine and haloperidol, with open-label olanzapine follow-up of up to 40 mg/day. Assessments included a variety of neurocognitive tests and quantitative clinical scales at baseline and several time points during the drug trial. Results with a sample of 34 patients showed that compared to haloperidol, olanzapine significantly improved performance on the Wisconsin Card Sorting Task (WCST) at the end of the double-blind phase compared to baseline testing. There were nonsignificant trends for more improvement with olanzapine than haloperidol on some other measures of verbal learning and memory at the end of the double-blind phase. At the end of the open-label olanzapine treatment phase, performance on several verbal memory tests from the RANDT and Sternberg memory task is were improved over baseline. Olanzapine improved visual-spatial memory at the end of the open olanzapine phase, but there were no differences between olanzapine and haloperidol after only 8 weeks of the double-blind treatment. Olanzapine tended to improve verbal fluency. Olanzapine's-effects on improving neurocognitive performance were not strongly correlated with its effects on changes in rating scale clinical symptom scores. The effects of olanzapine on performance on the WCST, RANDT, and Sternberg memory and visual-spatial memory tasks suggest that olanzapine may have ameliorative effects on neurocognitive functions involving verbal memory, visual-spatial memory, and executive functions. The lack of significant correlations between the effects of olanzapine on neurocognitive and clinical improvements suggest that these may be separate domains of clinical effects. (Supported by a grant from Lilly Pharmaceuticals)

NR321 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Hyperglycemia in Schizophrenic Patients Treated with Olanzapine and Clozapine

Robert C. Smith, M.D., *Department of Psychiatry, New York University Medical School, P.O. Box 316, Hewlett, NY 11557*; Jean-Pierre Lindenmayer, M.D., Amaresh Khandat, M.D., Benidicto Parker, M.D., Abhay Singh, M.D.

Summary:

There are case reports of hyperglycemia in patients receiving olanzapine, but no published larger series to begin to provide prevalence estimates. This study examined glucose levels in 51 schizophrenic patients who participating in research studies, and extended these findings with a chart study sample. Three of 55 patients (5.5%) showed persistent, clinically significant, glucose elevation of glucose values over baseline during treatment with olanzapine, and five patients showed a transient elevation in glucose > 140 mg/dl, which returned to normal values during continued treatment with olanzapine. Patients had statistically significant higher maximum glucose values during treatment with olanzapine compared with pre-olanzapine baseline. Glucose increases were not related to olanzapine dose or weight change. Blacks and Hispanics tended to show an increase in maximum glucose on olanzapine, whereas whites did not. In the routinely treated patient study (i.e.-chart review) rates of hyperglycemia were also low. Mean glucose levels in olanzapine and clozapine treated patients were all within normal limits and below 100 mg/dl. 4% of olanzapine patients and 2% of clozapine patients had mean glucose levels ≥ 140mg/dl. 8.1% o patients treated with olanzapine and 10% of patients treated with clozapine had at least borderline or very mildly elevated glucose levels (i.e.->110 mg/dl). Mean cholesterol and triglyceride level in clozapine and olanzapine patients were within the normal range. Rates for evelated triglycerides were much higher, 17% in the olanzapine patients and 26% in the clozapine patients. The rates for hyperglycemia in our olanzapine patients are not higher than the rates of diabetes in epidemiological surveys in U.S. adults (7.8%). However, elevated triglyceride levels may be a more important prevalent abnormality.

Supported by a grant from Lilly Pharmaceuticals And NIMH grant R10-MH53550.

NR322 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Current Combination Antipsychotic Use in Psychiatric Inpatients

Fraca Centorrino, M.D., *Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02478*; Jessica L. Goren, Pharm.D., James P. Kelleher, M.D., John Hennen, Ph.D., Samy E, B.A., Marion C. Eakin, M.D., Ross J. Baldessarini, M.D.

Summary:

Objective: To test the hypothesis that simultaneous treatment with more than one antipsychotic drug is associated with longer hospitalization.

Method: From medical records during hospitalizations at McLean Hospital (March–May, 1998), polytherapy cases were matched with controls by diagnosis, sex, and approximate age. Length-of-stay (LOS) was the outcome measure in a random-effects multivariate regression analysis that included age, sex, and diagnosis (clustering within case-control pairs).

Results: Treatment with >1 antipsychotic was encountered in 27% of antipsychotic-treated patients (N = 90), matched with N = 90 controls. Among subjects, 59% were women; 67% were diag-

nosed with schizophrenia-like, 22% bipolar, and 11% major depressive disorders. Age averaged 39.8 ± 13.8 (cases) and 40.9 ± 14.2 years (controls; NS). LOS averaged 36.7 ± 31.4 days (cases) and 17.8 ± 14.5 days (controls) (multivariate-z = 6.92; p < 0.0001). Final total chlorpromazine-equivalent doses (mg/day) were 429 ± 605 (cases) vs. 304 ± 329 mg/day (controls; NS).

Conclusion: Combination-antipsychotic treatment was strongly associated with longer hospitalization, independent of sex, age, and primary diagnosis, but did not lead to significantly increased total dosing. Polytherapy may reflect illness severity.

NR323 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Evidence of Efficacy of Risperidone in Schizophrenia

John M. Davis, M.D., *Department of Psychiatry, University of Illinois, 1601 West Taylor Street, Chicago, IL 60612*; Nancy Chen, M.D.

Summary:

Background: Stimulated by the need pointed out by Dawkins et al (1999) and Remington and Kapur (2000) to develop a clinical profile of the new atypical antipsychotic drugs and by the critiques of Mattes (1997, 1998), analyses were performed to define the clinical profile of risperidone.

Methods: Data from the North American risperidone trial were reanalyzed and a meta-analysis of the results of 11 controlled trials of risperidone was performed.

Results and Conclusions: Risperidone was superior to haloperidol to an equal degree in patients with and without the deficit syndrome, in patients with paranoid and nonparanoid schizophrenia, in treatment-resistant and treatment-responsive patients (patients hospitalized for longer and shorter periods), and in patients with or without weight gain. Moreover, risperidone was more effective than haloperidol on symptoms nonresponsive and responsive to haloperidol; its effects on negative symptoms were independent of its effects on extrapyramidal symptoms; and it was found to have beneficial effect on depression in schizophrenia. According to the meta-analysis, risperidone was consistently more effective than conventional antipsychotics in the treatment of both positive and negative symptoms.

NR324 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Diabetic Ketoacidosis in Patients with Schizophrenia Disorders

Enrico Cagliero, M.D., *MGH Diabetes Center, 50 Staniford Street, Boston, MA 02114*; David C. Henderson, M.D., David M. Nathan, Ph.D.

Summary:

Use of atypical antipsychotic agents has been linked to increased incidence of diabetes mellitus in patients with schizophrenia, and cases of diabetic ketoacidosis (DKA) have been described in such patients. We identified patients with a diagnosis of schizophrenic disorders, diabetes, and DKA attending a large urban teaching hospital between 1/95 and 1/01. The prevalence of diabetes in 3,753 schizophrenic patients was 11.2%, compared with 4.5% in the general hospital population (n = 642,823), confirming the high frequency of diabetes in these patients. Fifteen patients with schizophrenic disorders had DKA, and chart review showed that six developed DKA without a prior diagnosis of diabetes. The incidence of DKA in the schizophrenic patients without a prior diagnosis of diabetes, all of whom were on atypical antipsychotic agents (four on olanzepine, one on clozapine, and one on clozapine and risperidone) was 10.6/10,000 patient year, nearly ten-fold higher than that reported in a non-diabetic population (1.4/10,000). Their age was 37 ± 8 years (mean ± SD), body mass index (BMI) was 30.2 ± 5.4, four were males, four were Caucasian, one African American, and one Hispanic. At the time of presentation with DKA mean glucose was 812 ± 350 mg/dl, pH 7.23 ± 0.24, bicarbonate 14.5 ± 5.96 mmol/L, and hemoglobin Alc (HbAlc) 12.25 ± 1.29%. After 2.2 ± 1.5 years of follow-up, only one patient required long-term insulin therapy, excluding the diagnosis of type 1 diabetes for most, and HbA1c decreased to 7.72 ± 1.84. In conclusion, patients with schizophrenic disorders have a very high incidence of DKA. The cases were observed only in patients treated with atypical antipsychotic agents, supporting a link between the use of these drugs and severe abnormalities of glucose metabolism.

NR325 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Cognition in Kraepelinian Schizophrenia

Adam M. Brickman, B.A., *Department of Psychiatry, Mt. Sinai, One Gustave Levy Place, Box 1505, New York, NY 10029*; Philip D. Harvey, Ph.D., Lina S. Shihabuddin, M.D., Olga G. Berwid, B.A., Janah T. Boccio, B.A., Joseph I. Friedman, M.D., Kenneth L. Davis, M.D.

Summary:

Background: The clinical heterogeneity of schizophrenia has prompted many attempts to establish valid subtypologies. The classification system of "Kraepelinian" and "non-Kraepelinian" schizophrenia is based on analysis of longitudinal self-care deficits. Kraepelinian schizophrenics have had unremitting symptomatology and have been dependent on others for life necessities for at least five continuous years. Kraepelinian schizophrenia is marked by a degenerative course and often results in long-term institutionalization. In contrast, non-Kraepelinian schizophrenics have better outcome and more static course. Several clinical differences between the two groups exist. This study examined cognitive functioning to further elucidate neuropsychological differences between the two groups.

Methods: 26 Kraepelinian schizophrenics and 26 non-Kraepelinian patients were tested with a brief neuropsychological battery, including the Calfornia Verbal Learning Test (CVLT), Trailmaking Test, and a test of verbal fluency. The two groups were similar in gender, age, and duration of illness. Analysis of covariance was used to assess differences in total learning on the CVLT over five trials; duration of illness and age were held as covariates. Analyses on the other tests are underway and will be presented.

Results: Kraepelinian schizophrenics recalled significantly fewer words (mean ± sd = 30.46 ± 2.58) than non-Kraepelinian patients (mean ± sd = 38.85 ± 2.58) [F(1,48) = 5.13; p < 0.05].

Conclusions: These findings further support the validity of the Kraepelinian/non-Kraepelinian classification and suggest a unique cognitive profile for each group.

NR326 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Prevalence of Risk Factors for Coronary Heart Disease in Schizophrenia

Haya Ascher-Svanum, Ph.D., *Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46285*; Sandra L. Tunis, Ph.D., Lim Prudence, M.P.H., Ralph D'Agostino, Ph.D., James Hunt, B.A., Patrick McCollam, Ph.D., Coleen Baker, B.S.

Summary:

Background and Purpose: The comorbidity of schizophrenia and coronary heart disease has been previously reported. The purpose of this analysis was to assess the prevalence of specific coronary risk factors in a sample (n = 529) with schizophrenia or schizoaffective disorder, and to suggest treatment implications.

Method: Screening laboratory tests and physical examination, and baseline self-report data for participants in a cost-effectiveness trial of antipsychotics were used to assess age- and gender-specific prevalence of seven established coronary heart disease

risk factors. These were cigarette smoking, elevated systolic blood pressure, high level of total cholesterol, diabetes mellitus, obesity, sedentary lifestyle, and ECG abnormalities.

Results: The sample included 328 men and 197 women, with an average age of 42. Most (88%) were taking conventional antipsychotics at screening. Compared with the general adult U.S. population, prevalence rates were high for most risk factors examined; particularly for sedentary lifestyle (72%), cigarette smoking (61%), and obesity (32%, body mass index > 30).

Conclusions: Individuals with schizophrenia may have an elevated risk for coronary heart disease. Comprehensive treatment would include cardiac risk assessment and the facilitation of preventive measures, including assisting patients to make more healthy choices in habits and lifestyle.

NR327 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Associations Between EEG Alpha Power and Visuospatial Functions in OCD

Yong-Wook Shin, M.D., *Department of Psychiatry, Snu Hospital, 28 Yeongundong, Jongrogu, Seoul 110-744, Korea*; S. J. Park, I. K. Ryoo, M.D., K. S. Ha, M.D., Jun-Soo Kwon, M.D.

Association between EEG alpha power and visuospatial functions in Obsessive-compulsive disorder

YW Shin, SJ Park, IK Ryoo, KS Ha, JS Kwon.

From the Department of Psychiatry, Seoul National University Hospital and Neuroscience Institute, SNU-MRC, Seoul; Korea

Summary:

Objective: To determine whether EEG alpha power is correlated with measures of visuospatial functions in obsessive-compulsive disorder (OCD) patients.

Method: Electroencephalograms (EEGs) were recorded from 23 patients meeting DSM-IV criteria for OCD. All patients completed Rey-Osterrieth Complex Figure Test (RCFT). After quantitative analysis of EEG (fast Fourier transformation, FFT) over the frontal, temporal, parietal, and occipital regions (Fp1, Fp2, T3, T4, P3, P4, O1, and O2), we regressed the log transformed absolute power values of alpha frequency band, age, and IQ onto each RCFT index (copy score, immediate recall, delayed recall) to identify the region that showed correlation.

Results: RCFT copy scores were explained by alpha waves on the frontal region (F1, F2) and right temporal region (T4), and the correlations between alpha wave and copy score were positive on the left side and negative on the right side. In the case of immediate and delayed recall score, no correlation was found.

Conclusion: Visuo-constructional ability represented by RCFT copy score was correlated with frontal activation (as measured by decreased alpha power), which suggests visual memory deficit in OCD patients is mediated by executive function deficit. An opposite direction of correlation between right and left frontal area is an indirect evidence of the possibility that right hyperfrontality in OCD is a compensatory mechanism.

NR328 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Voxel-Based Morphometry Analysis of Gray Matter in First-Episode Schizophrenia

Robert W. McCarley, M.D., *Department of Psychiatry, Harvard/ VA Medical School, 940 Belmont street, Brockton, MA 02301*; Marek Kubicki, Ph.D., Elizabeth David, B.A., Dean F. Salisbury, Ph.D., Martha E. Shenton, Ph.D.

Summary:

It has been proposed that VBM analysis of structural MRI data affords a more rapid and extensive survey of gray matter abnormalities in schizophrenia than ROI analysis, the current gold standard. Unfortunately, VBM has generally not been validated by comparison with ROI analyses.

We thus used SPM99 implementation of VBM to compare a group of 16 first-episode (FE) right-handed schizophrenics with 18 normal controls matched for age and handedness. Our previous ROI study found these subjects to have decreased left superior temporal gyrus (STG) gray matter volume (Hirayasu et al., AJP, 1998). For VBM, our original structural images (1.5 mm thick, 256 x 256 SPGR) were normalized to the T1 weighted 1 x 1 x 1mm SPM99 template, segmented, smoothed, and then subjected to an ANCOVA, with group as the between factor, and global gray matter intensity as a covariate.

After transforming to the unit normal distribution (Z) and correcting for total volume, only the left STG region was significant, a finding consistent with the ROI finding. In a second, less stringent analysis, we thresholded the images on $Z = 4.2$ ($p < 0.0001$ uncorrected), and then corrected for peak value of Z or spatial extent, whereupon we found significance bilaterally in anterior cingulate gyri and insula (not examined with ROI), but not in medial temporal lobe or parietal angular gyrus where ROI analysis showed differences. These findings suggest the importance for comparison of VBM findings with traditional ROI analyses until the reasons for differences are determined. The VBM findings point to additional brain areas that should be further investigated with traditional ROI analysis.

NR329 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Age and Melancholia Influence Cerebral Metabolism in Major Depression

Sidney H. Kennedy, M.D., *Department of Mood and Anxiety, CAMH-Clarke Site, 250 College Street, Room 1125, Toronto, ON M5T 1R8, Canada*; Shahryar Rafi-Tari, M.S.C., Jeffrey H. Meyer, M.D., Helen S. Mayberg, M.D., Kenneth R. Evans, Ph.D., Franco J. Vaccarino, Ph.D.

Summary:

Objective: To evaluate the effect of age, diagnostic subtype, and prior treatment, on positron emission tomograph by using [18F] fluorodeoxyglucose (PET/FDG) in major depression.

Method: Scans were obtained on 67 male subjects, aged 18–60 years who met DSM-IV criteria for major depressive episode with HRSD ≥18 and were free of antidepressants for at least four weeks. These data were analyzed using statistical parametric mapping (SPM 99).

Results: There was a significant negative correlation between age and metabolism, bilaterally, in the anterior prefrontal cortex (BA 9, 44) and anterior cingulate (BA 24, 32). A positive correlation with age was observed in the right hippocampus and bilaterally in the medial globus pallidus. When subjects were grouped as melancholic (n = 38) or nonmelancholic (n = 28) and compared, significant left sided increases in metabolism were found in posterior insula, parietal (BA 40), and premotor (BA 6) cortices in the melancholic group. These latter differences remained significant when age was entered as a "covariate of no interest." There was no significant relationship between prior treatment status and metabolism.

Conclusion: The importance of age and diagnostic subtyping may explain variances in resting cerebral metabolism in previous studies of major depression.

NR330 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Brain Metabolic Correlates of Increased Urge to Smoke Cigarettes

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M.D., Lewis R. Baxter, M.D., Anna R. Childress, M.D., Murray E. Jarvik, M.D.

Summary:

Background: Brain mediation of craving for addictive substances other than cigarettes (cocaine, opiates, and alcohol) has been studied using positron emission tomography (PET) and other functional brain imaging techniques. When subjects with these other addictions are presented with drug-related cues compared with neutral cues, activation of the anterior cingulate gyrus (AC), anterior temporal pole/amygdala, orbitofrontal cortex (OFC), and lateral prefrontal cortex (PFC) has been reported. Positive correlations between strength of craving and OFC, lateral PFC, and insular activity have also been reported.

Method: Forty otherwise healthy subjects (20 heavy smokers and 20 nonsmoking controls) underwent two ^{18}F-fluorodeoxyglucose (FDG)-PET scans 10 days apart in randomized order. During one scan, subjects were presented with neutral cues (an educational nature video and a pen). During the other, subjects were presented with cigarette-related cues (a video of people smoking in a variety of situations and a cigarette).

Results: Heavy smokers and nonsmoking controls had similar clinical states during both scans other than a significantly increased mean urge to smoke in the heavy smokers when presented with cigarette-related cues ($p = .008$). Heavy smokers (but not nonsmoking controls) had increased regional brain metabolism in the cigarette-related cue state in the ventral (and dorsal) AC. Heavy smokers also had increased metabolism in the medial temporal lobe and OFC during presentation of cigarette-related cues. In the heavy smoker group, positive correlations between mean urge to smoke and regional brain metabolism were found in the anterior insula, ventral AC, posterior OFC, and lateral PFC.

Conclusions: In heavy smokers, widespread limbic and paralimbic activation (in the AC, medial temporal lobe, and OFC) is associated with exposure to cigarette-related cues. In addition, activation of limbic and prefrontal cortical regions is strongly positively correlated with increased urge to smoke. These findings are similar to craving for other addictive substances, such as cocaine, opiates, and alcohol.

Acknowledgments: Funded by the Tobacco-Related Disease Research Program, a VA Career Development Award, and the National Alliance for Research in Schizophrenia and Depression.

NR331 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Structural Imaging: Can It Detect Early Premorbid Experienced Stress?

H. Stefan Bracha, M.D., *NC-PTSD, Veterans Adminstration, 1132 Bishop Street, Suitte 307, Honolulu, HI 96813-2830*; Norman Flaxman, D.M., Nora Harmsen, D.D.S., Jeffrey W. Weiser, M.D., Maurice A. Sprenger, M.D., Tyler Ralston, B.A., Ziva Bracha, M.D.

Summary:

Current estimates of experienced stress during early brain development are dependent almost exclusively on retrospective self-report. Corroboration of premorbid stress during early life by interviews remains difficult and labor intensive. A fresh biotechnological approach for estimating stress during early life needs to be added to the psychiatric research armamentarium. Even a rough imaging estimate of severe autonomic perturbations during infancy and childhood stress may be useful.

Method: Episodes of vagal suppression during early deleterious experiences (during prolonged sympatho-adrenal activations) are accompanied, as a rule, by slowing of trophic parasympathetic functions to the ameloblast tissue of unerupted molars. Ameloblast stress lines (ASL) are chronological structural rings in human dental enamel. The markings are conceptually akin to tree rings, which are markers of prior environmental adversity in forestry science.

Results: Ameloblast stress line scores are significantly higher in VA research participants with PTSD ($n = 8$) versus 38 controls ($p = 0.001$ Wald-Wolfowitz test). Pearson Correlation coefficient of ASL is high (0.805, $p = 0.000$, $N = 34$).

Conclusions: If validated by our ongoing studies, enamel-imaging techniques may provide estimates of neurobiologically relevant early life adversity experienced by psychiatric research participants.

Funded by a VA Merit Award, NARSAD and Stanley foundations, and SPS Japan.

NR332 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Cortical Motor Activation in Neuroleptic-Induced Parkinsonism: An MRI Study

Laurent Scmitt, M.D., *Department of Psychiatry, Chu Casselardit, Place Baylac, Toulouse 31059, France*; Christine Sarramon, M.D., Kader Boulanouar, Ph.D., Nelly Fabre, M.D., Francois Chollet, M.D., Olivier Rascol, M.D.

Summary:

Objective: In previous studies using functional MRI, a cortical motor reorganization has been shown in akinetic patients with Parkinson's disease (PD). The purpose of this study was to determine if a similar pattern was seen in patients with neuroleptic induced-parkinsonism.

Method: We have studied six right-handed schizophrenic patients (mean age = 36 years SD = 5), chronically treated with typical neuroleptics without current delusion and exhibiting mild akineto-rigid parkinsonism (UPDRS score = 17, SD = 4). Patients were compared to six matched healthy subjects. Subjects were asked to perform a complex sequential movement (right hand). All subjects underwent fMRI on a 1.5-T MR scanner with Echo Planar Imaging.

Results: Compared to control subjects, schizophrenic patients exhibited a relatively decreased activity in the supplementary motor area (SMA) and in the left primary sensorimotor cortex. Concomitantly the patients exhibited a significant bilateral relative increased activity in the inferior parietal and in the anterior cingulate cortex.

Discussion: Like in PD we observed a decreased activation of the SMA and an increased activity in the parietal and anterior cingulate cortices. However unlike in PD a decreased activation in the sensorimotor cortices was shown in the schizophrenic patients, suggesting a different functional disturbance in the cortical motor circuitry.

NR333 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Frontal Lobe Gray Matter Volume and Biochemical Differences in Bipolar Disorder

Nathan F. Dieckmann, B.A., *Department of Psychiatry, Stanford University, 401 Quarry Road, Stanford, CA 94305*; Po W. Wang, M.D., Nadia Sachs, M.Eng., Courtney M. Rennicke, B.A., Debbie Tate, Anil Patwardhan, Terence A. Ketter, M.D.

Summary:

Objective: To compare brain volumes and chemistry in 10 bipolar disorder patients (BP) and 10 age and sex-matched, healthy control (HC) subjects.

Method: Subjects received magnetic resonance imaging (MRI) and spectroscopy (MRS) scans on a 1.5-Tesla General Electric Signa scanner. MRS was assessed in bilateral 8cc dorsolateral prefrontal (DLPF) voxels. Volumetric analysis of MRI data used *Brainimage* software (Reiss et al., 1997) and Talaraich atlas-based lobular parcellation methods.

Results: DLPF N-acetyl aspartate (NAA) tended to be lower in BP than in HC subjects, as previously reported (Winsberg et al., 2000). Right DLPF NAA correlated with right frontal lobe gray matter in HC subject ($r = 0.66$, $p < 0.04$) but not in BP ($r = 0.33$). Correlations between left DLPF NAA and left frontal lobe gray matter also tended to differ in HC subjects ($r = 0.52$) and BP ($r = 0.17$). In addition, left/right frontal lobe gray matter ratios tended to be lower in BP (0.96) than in HC subjects (1.01, $p < 0.10$).

Conclusions: In this preliminary analysis, we found evidence suggesting related structural and functional frontal lobe abnormalities in BP compared to HC subjects. These findings may be particularly robust as they emerged in this initial sample, while differences in ventricular and cerebellar volumes, which were expected in view of prior studies, were not significant.

(supported by Stanley Foundation Research Awards Program)

NR334 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Structural Brain Abnormalities in First-Episode Schizophrenia

Eva Ceskova, M.D., *Faculty Hospital, Jihlavska 2, Brno-Bohvnice, Brno 63900, Czechoslovakia*; Petr Urobar, M.D., Marta Ondrusova, M.D.

Summary:

Objectives: To compare the CT parameters in the first-episode with the control group, to follow their development and to find significant correlations.

Method: In 100 patients hospitalized for the first time with first-episode schizophrenia, the following parameters were determined: clinical (PANSS, CGI), biochemical (cortisolemia, prolactinemia), neuropsychological (attention and memory), neurological (Neurological Evaluation Scale for soft signs), six quantitative CT parameters. The same re-evaluation was done after one year.

Results: In average no significant differences between the CT parameters in first-episode schizophrenics and the control group were found and no changes after one year were observed. No significant correlation between recorded CT parameters, symptomatology, severity of illness, biochemical, or neuropsychological and neurological parameters were found.

Conclusions: The structural abnormalities in first -episode schizophrenia are too subtle to be of diagnostic value. If present, they may be independent nonspecific markers, which could be important in connections with other variables for the treatment reactivity and outcome of the disorder. This implies that the multidimensional statistical methods should be used.

NR335 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Neurocognitive Advantages of Quetiapine

Dawn I. Velligan, Ph.D., *Department of Psychiatry, University of Texas H.S.C., 7703 Floyd Curl Drive, San Antonio, TX 78229-3900*

Summary:

Objective: To examine the effectiveness of quetiapine versus conventional antipsychotics in improving cognitive and functional outcomes.

Methods: In an ongoing study, 40 stable outpatients with schizophrenia were randomly assigned to continue conventional antipsychotics or switch to quetiapine. Neurocognitive and functional measures were obtained at study entry, 3 months, and 6 months. Data analysis was conducted by a blinded statistician. Group differences were examined using repeated measures analyses of covariance for mixed models on the first 33 patients.

Results: Global level of cognitive function and verbal memory improved in the quetiapine group relative to the standard treatment group ($p < 0.01$ and $p < 0.03$, respectively) over the 6-month period. There was a trend for improvement in executive functions in the quetiapine group relative to standard treatment. Adaptive function and community adjustment improved a greater extent in the quetiapine group ($p < 0.02$).

Conclusions: Although the data are preliminary, results for neurocognitive variables were similar to those found in efficacy studies of quetiapine. Neurocognitive advantages of quetiapine relative to conventional antipsychotics may be reflected in important improvements in community adjustment.

NR336 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Concurrent Validity of Neuropsychological Tests of Executive Functioning: Telephone Versus In-Person Administration

Tina L. Harralson, Ph.D., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, room 762, Philadelphia, PA 19104*; Tiffany A. Purnell, B.A., Lyn Harper-Mozley, Ph.D., Sarah Speranza, B.A.

Summary:

Objective: The purpose of this study was to examine the concurrent validity, telephone vs. in-person administration, of four neuropsychological measures that have been associated with executive functioning and memory. Screening for impairment in executive functioning could help identify patients who may have problems adhering to treatment regimes.

Method: This sample included 45 older adults responding to newspaper ads (mean age = 73.7 years; 27% minority; 47% women). Persons were randomly assigned to receive either an in-person or a telephone assessment first. Measures included the nine-item California Verbal Learning Task (CVLT), the Wechsler Digit Span (Digit Span; total of forward and backward recall), a semantic fluency task (animal naming from the Boston Diagnostic Aphasia Examination), and the Trail Making Test (TMT-A, TMT-B; time in seconds). Concurrent validity coefficients were calculated using intra-class correlation (ICC) and corresponding 95% confidence intervals (CI).

Results: There were no statistically significant differences between the neuropsychological measures by sex, race, education, marital status, or age. Results are as follows: CVLT total correct on trials 1–5, ICC = .63 (CI: 0.41, 0.79); CVLT total number of clusters for trials 1–5, ICC = .62 (CI: 0.39, 0.78); sum of forward and backward correct on Digit Span, ICC = .38 (CI: 0.10, 0.61); animal naming: ICC = .65 (CI: 0.44, 0.79); orally administered TMT-A: ICC = .65 (CI: 0.44, 0.79), and TMT-B: ICC = .71 (CI: 0.53, 0.83). The ICCs between written and orally administered TMT-A & B were not significant. However, oral TMT-A was moderately correlated with written TMT-A ($r = .30$, $p = .08$) and oral vs. written TMT-B was significantly correlated ($r = .57$, $p < .001$).

Conclusions: Concurrent validity of the telephone vs. the inperson administered neuropsychological tests were good with the exception of Digit Span and TMT written vs. oral.

NR337 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Cognitive Deficits of Traumatic Brain-Injured and Schizophrenia Patients on the Neuropsychological Tests

Min-Cheol Park, M.D., *Department of Neuropsychiatry, Wonk Wang Psychiatric Hospital, Dongsan-Dong 144-23, Iksan, Chonbuk 570-060, Korea*; Chong-Ho Park, M.D., Sang-Woo Oh, Ph.D., Sang-Yeol Lee, M.D.

Summary:

Objectives: This study was to investigate the impairments of intelligence, memory, and executive function of the traumatic brain-injured (TBI) patients and schizophrenics.

Methods: Sixty-seven traumatic brain-injured patients, 30 schizophrenics, and 30 normal persons were performed the K-WAIS, WMS, WCST. The data were analyzed by paired t-test, ANOVA, and scheffe test.

Results: (1) There were significant differences between premorbid IQ and current IQ in groups of TBI patients (frontal, nonfrontal, normal brain MRI) and schizophrenics. (2) Groups of TBI patients scored 10 over than normal control group in verbal IQ, and groups of TBI patients and schizophrenics scored significantly lower than normal controls in performance IQ and full-scale IQ. (3) Groups of TBI patients and schizophrenics scored significantly lower than normal controls in personal and current information, mental control, logical memory, visual reproduction, associate learning, and memory quotient of the WMS. (4) Frontal lesion group scored higher than nonfrontal lesion group in number of trials administered and failure to maintain set of the WCST.

Conclusions: TBI patients and schizophrenics showed impairment of general intelligence, memory, and executive function. TBI patients and schizophrenics showed lower current IQ than premorbid IQ. TBI patients were impaired in verbal IQ and performance IQ, but schizophrenics showed lower performance IQ than verbal IQ.

NR338 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

The Pharmacologic Risk Factor for NMS Induced by Novel Antipsychotics

Brendan T. Carroll, M.D., *Department of Psychiatry, VA Medical Center-Chillicote, 17273 State Route 104, #116A, Chillicote, OH 45601*; Kevin T. Graham, B.S., Arthur Thalassinos, M.D.

Summary:

Objective: Neuroleptic malignant syndrome is a rare phenomenon that appears to be related to several clinical risk factors including catatonia, extrapyramidal disorders, structural brain damage, dehydration, and agitation. NMS induced by the novel antipsychotics (i.e., clozapine and others) may be due to a pharmacologic risk factor and the presence of comodulating medications, such as SSRIs and lithium.

Methods: Based on our model for the pathogenesis of NMS and catatonia (Carroll, CNS Spectrums, 2000), we developed a risk factor coefficient to calculate and compare the risk of NMS among available novel antipsychotics. This formula incorporates the receptor affinities of these agents plus any comodulating medications. Seventy-five (75) patients who reported to the Neuroleptic Malignant Syndrome Information Service (NMSIS) were reviewed to investigate the relationship between the calculated pharmacologic risk factor and various case details.

Results: Review of the 25 patient with consultant-defined NMS revealed that a significant number occured in the presence of novel antipsychotics (N = 15). Furthermore, the presence of 5-HT1A enhancing agents (lithium, N = 7 and SSRIs, N = 8) appeared to increase the risk.

Conclusions: If NMS is caused by a variety of overlapping factors, then the pharmacologic risk factor may play a minor role. The pharmacologic risk factor should be included in the pathogenesis of NMS associated with both novel and standard antipsychotics.

NR339 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Use of Quetiapine in Patients with Huntington's Disease

Menekse Alpay, M.D., *Department of Psychiatry, Massachusetts General Hosptial, Fruit Street, Boston, MA 02114*

Summary:

Background: Huntington's disease (HD) is a rare, autosomal dominant neurodegenerative disease; it presents in mid-life, with involuntary choreic movements, psychiatric symptomd, and cognitive decline. Characteristic neurologic symptoms include chorea, dystonia, and parkinsonian features. Approximately 10% of HD patients develop psychosis at some point during their illness. Although antipsychotics are commonly used in the treatment of chorea, psychosis, and agitation, there is a paucity of data about the use of newer atypical antipsychotics in this population. Hypokinesia and worsening dystonia with typical neuroleptic medications are detrimental to the patients major side effect. Atypical agents are superior to typical agents due to their lower risk of extrapyramidal side effects.

Objective: This study examines use of quetiapine, a newer atypical neuroleptic, in patients with HD.

Method: A consecutive case series of six patients with HD and psychosis were treated with quetiapine.

Results: Psychiatric symptoms of all patients significantly improvement without worsening of parkinsonian symptoms, dystonia, and voluntary movements.

Conclusion: To our knowledge this is the first case series of successfully treated HD patients for psychosis/agitation with quetiapine. Quetiapine was helpful for psychotic symptoms (e.g., paranoid delusions), agitation, irritability, and insomnia. Our data suggest that quetiapine is very well tolerated in HD patients without worsening the disease while treating their psychosis.

NR340 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Prevalence of Psychosocial Interventions Concomitant with Risperidone Treatment of Schizophrenia Outpatients

Michael Linden, M.D., *Department of Psychiatry, Free University, Eschenaulee 3, Berlin 14050, Germany*

Summary:

Background: There is sound scientific evidence that the course of schizophrenic disorders can be improved by concomitant psychosocial interventions. There are almost no data on the utilization of such interventions in routine care.

Method: In an ongoing, two-year, prospective drug utilization observation study on risperidone, 456 psychiatrists countrywide gave detailed information on the treatment of 886 schizophrenic outpatients. They were asked whether additional to prescribing risperidone psychosocial interventions also were applied.

Results: 56.3% of patients were treated with psychosocial intervention; 28.4% received psychotherapeutic interventions such as formal psychotherapy (17.7%), educational training (9.0%), family treatment (5.9%), or attended self-help groups (5.8%), 39.3% received social support, i.e. had contact to sociopsychiatric services (23.7%), got work therapy (11.3%), lived in sheltered housing (10.4%), or attended day/night clinics (3.7%). Patients who received psychotherapeutic interventions are significantly better off than those receiving social support.

Conclusion: This is the largest available study on the utilization of psychosocial treatment for schizophrenic patients in psychiatric routine care. In every second pattent psychiatrists combine prescribing of risperidone with some form of psychosocial intervention. Further analyses of the data will test whether this can improve the two year course and overall treatment outcome.

NR341 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

The Impact of Childhood Abuse on Adult Mental Health

Patrick J. Gibbons, M.B., *Department of Psychiatry, Tralee General Hospital, Kerry, Ireland*; Hilda F. De Arevalo, B.A., Mauricio M. Monico

Summary:

Introduction: Existing studies of the long-term psychological effect of childhood sexual abuse largely fail to control for the potential confounding effect of other forms of childhood abuse (Rind & Tromovitch, 1998, Benchman et al, 1992).

Objective: To assess the long-term psychological impact of childhood sexual abuse in a community sample, while controlling for the effect of co-occuring childhood physical and emotional abuse.

Method: The participants were a representative quota sample of 714 students at the Technological University of El Salvador. Childhood trauma was assessed retrospectively using the Spanish versions of the Childhood Abuse and Trauma Scale (Sanders et al, 1995), administered as an anonymous questionnaire, and validated by a semi-structured interview using the Childhood Experiences of Care and Abuse (Bifulco et al. 1994). The General Health Questionnaire (Goldberg & Hülier, 1979) was administered as a measure of current psychological health. The psychological impact of each form of abuse was assessed by partial correlation of abuse subscales with the total GHQ-28 score.

Results: The prevalence and severity of the different types of abuse as well as the overall correlation of abuse with psychological distress was similar in both males and females. However, males were more specifically affected by parental antipathy and emotional neglect, while females were also affected by sexual abuse and parental discord.

Conclusion: Childhood abuse is associated with adult mental ill health, but male and female victims appear to vary in their sensitivity to different forms of childhood abuse.

NR342 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Quality of Life in Family Caregivers of the Chronically Mentally Ill

Alison M. Heru, M.D., *Department of Psychiatry, Brown University/Butler Hospital, 345 Blackstone Boulevard, Providence, RI 02906-9980*; Christine E. Ryan, Ph.D., Kimberly Vlastos, B.A., Dorota Gawlas, M.D.

Summary:

Objective: Families who care for their chronically mentally ill relative at home are at increased risk for psychiatric morbidity. Caregiving is associated with increased burden, depressive symptoms, and impaired functioning.

Method: Caregivers of patients with chronic mental illness rated depressive symptoms, quality of life, perceived burden, reward, and family functioning. 43 subjects completed the acute phase of this 12-month study.

Results: Subjects were predominantly male (56%), spouses (65%), with a mean length of caregiving of 7.4 (SD = 7.6) years, with a median length of 4 years. Caregivers rated their social, physical, and emotional health as significantly poorer than normal subjects taken from a community sample (all p values < 0.001). Caregiver's mental health, energy/vitality, ($p < 0.001$) and bodily pain ($p < 0.05$) were also significantly worse than community subject norms. Ten of 18 caregivers who completed the CESD had scores that met the cut-off associated with a diagnosis of major depression. Reporting poor family functioning was related to the presence of depressive symptoms in the caregiver.

Conclusion: The chronically mentally ill rely upon their families for immediate care in the home. Mental health professionals must ensure that these caregivers do not suffer from depression, excessive burden, and impaired functioning.

NR343 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Creativity Enhancement in Bipolar Patients More Specific Than in Creative Discipline Graduate Students

Bibi Das, *Department Of Psychiatry, Stanford University, 401 Quarry Road, Room 2131, Stanford, CA 94305-5723*; Connie M. Strong, M.S., Nadia Sachs, M.Eng., Jenny Mongkolcheep, B.S.C., Matthew Schumacher, B.A., Po W. Wang, M.D., Terence A. Ketter, M.D.

Summary:

Objective: To assess creativity in 48 euthymic bipolar patients (BP), 25 euthymic unipolar patients (UP), 47 healthy controls (HC), and 22 creative controls (CC). The latter included eight fine arts (FACC), seven writing (WCC), and seven product design (PDCC) graduate students.

Method: Subjects were administered Barron-Welsh Art Scale (BWAS), Adjective Check List Creative Personality Scale (ACL-CPS), and Torrance Test of Creative Thinking, Figural (TTCT-F) and Verbal (TTCT-V) versions.

Results: BWAS was higher in BP (27.5, $p < 0.001$) and CC (26.4, $p < 0.01$) than in HC (18.8); and in BP compared with UP (21.3, $p < 0.05$). High BWAS in FACC (32.9) drove the CC advantage, and exceeded that of PDCC (24.6, $p < 0.05$) and WCC (20.7, $p < 0.01$). TTCT-F was higher in CC (117.2) than in BP (106.7, $p < 0.04$), and UP (104.4, $p < 0.01$). High TTCT-F in PDCC (128.0) drove the CC advantage, and tended to exceed that of FACC (113.5, $p < 0.05$) and WCC (110.7, $p = 0.10$). CPS-ACL and TTCT-V did not differ between groups.

Conclusion: BP but not UP had creativity enhancement, which was more specific than that of CC, and the latter had subgroup effects, suggesting mechanistic commonalities and dissociations underlying creativity in BP, CC, and subgroups of CC.

(Supported by NARSAD and Stanley Foundation)

NR344 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Creativity and Temperament Relationships in Mood Disorder and Creative Subjects

Connie M. Strong, M.S., *Department of Psychiatry, Stanford University, 401 Quarry Road, Room 2124, Stanford, CA 94305-5723*; Bibi Das, Nadia Sachs, M.Eng., Claudia M. Santosa, M.A., Po W. Wang, M.D., Terence A. Ketter, M.D.

Summary:

Objective: To assess relationships between creativity and temperament/personality across 48 euthymic bipolar patients (BP), 25 euthymic unipolar patients (UP), 47 healthy control subjects (HC), and 22 creative discipline graduate student control subjects (CC).

Method: Subjects were administered the Adjective Check List Creative Personality Scale (ACL-CPS), Barron-Welsh Art Scale (BWAS), and Torrance Test of Creative Thinking, Verbal (TTCT-V) and Figural (TTCT-F) creativity ratings to assess creating the NEO Personality Inventory, Cloninger's Temperament and Character Inventory, and Akiskal's Affective Temperament Scale were Administered to assess temperment/personality.

Results: Controlling for age, gender, and subgroup effects, ACL-CPS score correlated with openness ($r = 0.477$), extraversion ($r = 0.316$), lack of neuroticism ($r = -0.185$); Novelty seeking ($r = 0.414$), lack of harm avoidance ($r = -0.254$), self-directedness ($r = 0.182$); lack of dysthymia ($r = -0.407$), lack of irritability ($r = -0.189$), and hyperthymia ($r = 0.188$). BWAS correlated with cyclothymia ($r = 0.256$) and neuroticism ($r = 0.163$). TTCT-V correlated with openness ($r = 0.175$), and TTCT-F did not correlate with temperament/personality measures.

Conclusion: ACL-CPS was most closely related to openness (consistent with prior studies), novelty seeking, and lack of dysthy-

mia. BWAS was most closely related to cyclothymia and neuroticism. TTCT-V was modestly related to openness. Thus, temperament/personality contributed to enhancement of different aspects of creativity to varying extents.

(Supported by NARSAD and The Stanley Foundation)

NR345 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Health Economic Evaluation of Quetiapine and Risperidone in the QUEST Trial

Jamie Mullen, Ph.D., *AstraZeneca, 1800 Concord Pike, Box 15437, Wilimington, DE 19850-5437*

Summary:

Objective: To assess the cost-effectiveness of quetiapine.

Methods: Comparative cost-effectiveness was assessed in a supplemental analysis of a 4-month, multicenter, open-label, randomized trial comparing the efficacy and safety of quetiapine with risperidone. Mild, moderate, and severe health state profiles were constructed using cluster analysis of patient PANSS scores. Patients were categorized into one of three states based on overall PANSS scores at baseline and at 2 and 4 months or LOCF. Difference in expected utilities from baseline was calculated. Patients who were in a mild or moderate health state at baseline improved; there were no statistically significant differences in performance between groups. For patients with severe symptoms at baseline, more quetiapine than risperidone patients improved to less severe health states at 2 months, 4 months, and LOCF.

Results: Average daily doses were 253.9 mg for quetiapine and 4.4 mg for risperidone, yielding average daily costs to U.S. consumers of $6.38 and $7.85. At average U.S. retail, quetiapine reduces cost by $1.47 per day, or $536.55 annually.

Conclusions: In severe patients, quetiapine treatment results in significant clinical benefits, effectiveness, and cost savings compared with risperidone. In mild and moderate patients, quetiapine is cost saving while achieving similar clinical benefits.

NR346 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Comparison of Managed Care Charges Among Patients Receiving SSRI Treatment for PMDD

Jean Endicott, Ph.D., *Department of Psychiatry, NY State Psychiatric Institute, 1051 Riverside Drive, Unit 123, New York, NY 10032*; Trent McLaughlin, Ph.D., Amy Grudzinski, Pharm.D.

Summary:

Objective: To determine the impact on managed care charges of selecting sertraline, fluoxetine, paroxetine, or citalopram as first-line pharmacotherapy for newly diagnosed PMDD.

Methods: A retrospective analysis of the PharMetrics' Integrated Outcomes database was performed that included patients 18 years of age or older, newly diagnosed with PMDD between 07/98 and 06/99, and who initiated therapy with an SSRI within 30 days. Patients with documented previous mental disorders or treatment were excluded. PMDD-related treatment charges for the 6-month period following treatment initiation were compared using log-linear regression.

Results: 1,413 patients were included in the analysis (sertraline: N = 519; fluoxetine: N = 532; paroxetine: N = 276; citalopram: N = 86). During the study period, PMDD-related charges ranged from $126 (sertraline) to $217 (paroxetine) per patient. After controlling for differences in age, managed care plan, pretreatment history of resource utilization, physician specialty type, index RX year, and switching/augmentation, fluoxetine, paroxetine, and citalopram patients incurred 16%, 32%, and 58% higher PMDD-related charges, respectively, than patients initially treated with sertraline ($p < 0.05$ for all comparisons).

Conclusion: After rigorously controlling for other variables, initial treatment of PMDD with sertraline was associated with significantly lower disease-related charges than fluoxetine, paroxetine, or citalopram.

NR347 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Comparison of Emergency Room and Inpatient Care Resource Utilization Among Patients Treated with SSRIs for Panic Disorder

Sean Sullivan, Ph.D., *College of Pharmacy, University of Washington, Box 357630, Seattle, WA 98195-7630*; Peter P. Roy-Byrne, M.D., Amy Grudzinski, Pharm.D., Lynn Okamoto, Pharm.D.

Summary:

Objective: To determine the impact of selecting an SSRI as first-line pharmacotherapy for newly diagnosed panic disorder on utilization of emergency room (ER) or inpatient (HOSP) care.

Methods: A retrospective analysis was conducted of all patients 18 years or older who were newly diagnosed with panic disorder between 07/98 and 06/99 in the PharMetrics' Integrated Outcomes database and who had initiated therapy with sertraline (SER), fluoxetine (SER), paroxetine (PAR), or citalopram (CIT) within 30 days. Patients were followed for 6 months from the initial diagnosis to capture utilization of medical services. Outcome measures included the mean number of ER or HOSP claims per patient.

Results: 446 patients were included in the analysis (SER = 143, FLU = 73, PAR = 206, CIT = 24). The mean number of ER/HOSP claims per patient for the 6-month period prior to and following the panic disorder diagnosis and initiation of SSRI therapy are shown below:

	SER	FLU	PAR	CIT
Pre Period — Mean (SD)	0.27 (1.1)	0.21 (0.7)	0.29 (0.7)	0.17 (0.5)
Post Period — Mean (SD)	0.16 (0.6)*	0.26 (0.9)	0.45 (1.7)*	0.25 (0.20)

* $p<0.05$ for SER versus PAR

Conclusion: Patients initially treated with sertraline had fewer emergency room visits or inpatient stays than similar patients treated with other SSRIs.

NR348 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Analysis of Managed Care Charges for Patients with Depression Initiating Therapy on Sertraline, Nefazodone, and Mirtazapine

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Summary:

Objective: To determine the impact on managed care charges of selecting sertraline, nefazodone, or mirtazapine as first-line pharmacotherapy for patients with newly diagnosed depression.

Method: We performed a retrospective database analysis of adult patients diagnosed with depression who initiated therapy between 07/98 and 06/99, excluding patients with documented previous mental disorders/treatment. Depression-related treatment charges for the 6-month period following treatment initiation were compared using log-linear regression.

Results: 19,129 patients were included in the analysis (sertraline: N = 15,222; nefazodone: N = 3,100; mirtazapine: N = 914). Mean depression-related charges ranged from $960 / patient (sertraline) to $2,380 / patient (mirtazapine). After controlling for differences in age, gender, managed care plan, pretreatment history of resource utilization, physician specialty type, index RX year,

and switching/augmentation, nefazodone and mirtazapine patients incurred 13% and 32% higher depression-related charges, respectively, than patients initially treated with sertraline ($p < 0.05$ for both comparisons). Nefazodone and mirtazapine patients incurred 26% and 43% higher medical (non-pharmacy) depression-related charges ($p < 0.05$ for both comparisons) and 2% and 36% higher total charges than sertraline patients during the study period ($p < 0.05$ mirtazapine versus sertraline).

Conclusion: After rigorously controlling for other variables, initial treatment of depression with sertraline was associated with lower total charges than either nefazodone or mirtazapine.

NR349 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Comparison of Depression-Related Treatment Charges for Patients Treated with Sertraline or Citalopram in a Managed Care Population

Trent McLaughlin, Ph.D., *Department of Outcome Research, NDC Health, 2394 East Camelback Road, Phoenix, AZ 85016*; Amy Grudzinski, Pharm.D.

Summary:

Objective: To examine differences in depression-related charges among newly diagnosed patients treated with either sertraline or citalopram.

Method: A retrospective database analysis was conducted of adult patients diagnosed with depression who initiated therapy between 07/98 and 06/99. Patients with documented previous mental disorders/treatment were excluded. Depression-related treatment charges for the 6-month period following treatment initiation were compared using log-linear regression.

Results: 15,222 sertraline and 3,175 citalopram patients met the inclusion criteria. After controlling for patient age, gender, managed care plan, pretreatment history of resource utilization, physician specialty type, and index RX year, citalopram patients had approximately 22% higher depression-related charges than the sertraline cohort (beta coefficient: 0.22, $p < 0.0001$).

Conclusions: Despite the lower acquisition cost of citalopram, initial treatment of major depression with this agent was associated with higher treatment costs compared to sertraline.

NR350 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

An Algorithm for Identifying Depression and Appropriate Medication

Stewart Levine, M.D., *Beth Israel Medical Center, First Avenue at 16th Street, New York, NY 10003*; Moon Leung, Ph.D., Jodi Cohn, Ph.D., Jurgen Unutzer, M.D., Timothy Schwab, M.D., Daniel D. Anderson, M.D.

Summary:

Underdiagnosing of depression, inappropriate prescribing of psychotropic medication (particularly benzodiazepines [BZD]), and increasing costs of psychotropic medications are pressing concerns in today's managed care settings. A multifactorial algorithm was designed to monitor the accuracy in diagnosing depression and selection of appropriate antidepressant medication. The algorithm can further assist in identifying roles for consultation-liaison psychiatrists.

The algorithm draws on four data sources—pharmacy, claims and encounter data, annual health screening, and comprehensive assessment data. The algorithm was applied to a sample of 40,000 older people in a Social HMO, a Medicare managed care program designed to maintain individuals at home. Twenty three percent of the subjects were frail and nursing home certifiable (NHC). Prescribing patterns were analyzed for appropriate/inappropriate medication usage and further sorted by type of provider. Overall costs by drug class were tabulated.

Findings consistently indicated underdiagnosing of depression. Psychotropics were generally prescribed by primary care providers; less than 5% were written by psychiatrists. Costs of the nearly 51,000 psychotropic prescriptions increased 27% over the previous year. Drug costs for the NHC group were nearly 50% more than the non-NHC group. Analysis of prescribing patterns indicated that anti-anxiety and sedatives/hypnotics represented 19% of all psychotropic prescriptions written, despite evidence that long-term administration (>2 weeks) of BZDs is contraindicated in older people.

Subsequent studies will focus on refining the algorithm as well as monitoring behavior and prescribing patterns of primary care physicians. A model will also be structured for appropriate consultation-liaison roles for psychiatrists to improve quality of care for this frail population.

NR351 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Treatment Course and Changes for Depressed Patients Treated with Sertraline, Venlafaxine, and Venlafaxine Extended Release in the Managed Care Setting

Robert Hirshfeld, M.D., *Department of Psychiatry and Behavioral Sci., University of Texas Medical Branch, 301 University Boulevard, Galveston, TX 77555-0188*; Michael Eaddy, Pharm.D., Amy Grudzinkski, Pharm.D.

Summary:

Objective: To determine the impact on treatment course and depression-related charges of selecting sertraline (SER), venlafaxine (VEN), or venlafaxine sustained-release (VXR) as first-line pharmacotherapy for newly diagnosed patients.

Method: Retrospective database analysis of adult patients diagnosed with depression who initiated therapy during 07/98–06/99. Patients with documented previous mental disorders/treatment were excluded. Depression-related treatment charges for the six-month period following treatment initiation were compared using log-linear regression. Cohorts were comparable with respect to prescribing physician (psychiatry vs. other).

Results: A total of 19,129 patients were included in the analysis (SER = 15222; VEN = 1032; VXR = 2875). VXR patients were more likely to augment therapy compared with VEN or SER (18% vs. 13% and 12%; $p < 0.05$). VEN patients were more likely to switch to other medications than VXR or SER (33% vs. 21% and 16%; $p < 0.05$). After controlling for differences in age, gender, managed care plan, pre-treatment history of resource utilization, physician specialty type, index RX year, and switching/augmentation, VEN and VXR patients incurred 13% and 30% higher depression-related charges, respectively, than patients initiated on SER ($p < 0.05$ for both comparisons).

Conclusion: Treatment of depression with sertraline was associated with a simpler treatment course (i.e. significantly less augmentation/switching), and lower depression-related charges than venlafaxine or sustained release venlafaxine.

NR352 Tuesday, May 8, 12:00 p.m.-2:00 p.m.

Comparative Cost-Effectiveness of Atypical Antipsychotics in Severe and Persistently Mentally Ill Patients with Schizophrenia and Schizoaffective Disorders

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Summary:

Objective: To evaluate the relative cost effectiveness of clozapine, olanzapine, and risperidone.

Method: An open-label, prospective, intent-to-treat effectiveness study with treatment-refractory patients was conducted for clozapine (N = 119), olanzapine (N = 120), and risperidone (N = 118). A sample of 50 patients were randomly selected from each study and matched for age, sex, ethnicity, diagnosis, and baseline Brief Psychiatric Rating Scale (BPRS) score. Cost effectiveness was determined by the ratio of cost change in BPRS for each drug after 6 months of treatment. A sensitivity analysis was conducted to determine the validity of the variables used.

Results:

Mean prescription costs: Clozapine = $17.44, SD = 6.4; olanzapine = $13.96, SD = 4; and Risperidone = $9.21, SD = 2.4.

Mean (and 95% CI) cost/change in BPRS: Clozapine: $2.91 ($1.20–$4.40), olanzapine: $2.41 ($1.36–$3.46), and risperidone: $4.13 ($2.90–$5.40). The mean difference between cost change in BPRS for risperidone and olanzapine was –$1.72 ($–3.54–$0.10) (t = –2.12, df = 98, p = 0.036).

Sensitivity Analysis: The results of a multidirectional change in drug dose and effectiveness were as predicted, confirming validity of both variables used to determine cost effectiveness ratios.

Conclusion: Olanzapine in our population of severe and persistently mentally ill patients was the most cost-effective alternative. Simple cost effectiveness evaluations should be made at every health care organization before deciding on the formulary status of newer drug treatments.

NR353 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Comparative Efficacy and Tolerability of Quetiapine at High and Low Doses

Michael J. Reinstein, M.D., *Department of Psychiatric Research, Forest Foundation, 4755 North Kenmore Avenue, Chicago, IL 60640*; John G. Sonnenberg, Ph.D., Maxim A. Chasanov, M.D., Sangarapillai C. Mohan, M.D., Shephali A. Patel, M.D., Rad Gharavi, M.D., Lynne E. Jones, R.N.

Summary:

Objective: In this single-blind, non-randomized, 10-week, prospective comparison study, the efficacy and tolerability of quetiapine at high and low doses was assessed in subjects diagnosed with schizophrenia and schizoaffective disorders.

Methods: 15 subjects taking high a doses of quetiapine were compared to 15 subjects receiving low doses. Side effects were determined through group comparisons of adverse treatment events. Efficacy was determined by group comparisons of change from baseline on the PANSS and Ham-D. High dose was defined as 1200 mg per day and low dose as 600 mg per day or less.

Results: The high- and low-dose groups were statistically equivalent in regards to tolerability. The high- and low-dose groups differed with regard to efficacy, with both groups showing improvement but the high-dose group showing a trend toward greater improvement than the low-dose group.

Discussion: The study results suggest that quetiapine is an antipsychotic agent equally as safe and possibly more effective for treating subjects at daily doses of 1200 mg as compared with 600 mg or less. Treating physicians should consider using quetiapine at higher doses when they believe current doses are insufficient at controlling symptom acuity.

This research was supported in part from a grant by AstraZeneca Pharmaceutical Company.

NR354 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Oxcarbazapine and Divalproex Sodium: A Comparison of Efficacy and Side Effects for Mania

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Summary:

Objective: This open-label, non-randomized, 10-week, prospective study compared oxcarbazapine (OXC) to divalproex sodium (DS) for subjects under treatment for mania. OXC is an approved anticonvulsant with possible antimanic properties. If OXC has no higher side effect profile than DS, and if both control mania equally, then OXC may be an alternative treatment for mania.

Methods: 30 subjects taking OXC were compared with 30 receiving DS. Subjects were assessed at baseline, week 5, and week 10. Mania was assessed using the CARS-M. Side effect measures included weight, mental status, and adverse treatment event reporting.

Results: The two study groups were statistically equal in the control of mania. DS was associated with higher weight gain. OXC was associated with higher MMSE scores.

Discussion: The preferred results of weight and cognition for OXC in comparison to DS suggest that OXC merits further study for antimanic potentials.

This research was supported by a grant from Novartis Pharmaceuticals Company.

NR355 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Chronobiological TSH, Prolactin Responses to TRH, and Prognosis of Depression

Fabrice Duval, M.D., *Department of Psychiatry, Centre Hospitalier, 27 Rue du 4eme RSM, Rouffach 68250, France*; Marcelo Valdebenito, M.D., M. Claude Mokrani, Ph.D., Paul Bailey, M.D., Jose Monreal, M.D., Marc-Antoine Crocq, M.D., Jean-Paul Macher, M.D.

Summary:

Objectives: Studies of the therapeutic predictive value of the TRH test, performed in the morning, are inconsistent. The aim of this study was to examine the relationship between morning and evening thyrotropin (TSH) and prolactin (PRL) response to TRH tests prior to antidepressant treatment and 12-month outcome.

Methods: TSH and PRL responses to 8 a.m. and 11 p.m. TRH tests (200 μg, IV) were examined, on the same day, in 63 drug-free DSM-IV euthyroid major depressed inpatients and 50 hospitalized control subjects. Patients were subsequently treated with either 1) amitriptyline (N = 23), 2) the selective serotonin (5-HT) reuptake inhibitor fluoxetine (N = 22), or 3) the 5-HT uptake-enhancing drug tianeptine (N = 18). Outcome was assessed during 12 months of treatment.

Results: Clinical efficacy did not differ across the three antidepressant drugs. Compared with control subjects patients demonstrated lower TRH-TSH test responses at 8 a.m. and 11 p.m. (both $p < 0.0001$). Pretreatment TSH responses did not differentiate between treatment responders, treatment nonresponders, and healthy control subjects at any of the three time points investigated (6 weeks, 6 months, 12 months). However, decreased 11 p.m. PRL responses were associated with good clinical outcome (all $p < 0.017$), while patients with poorer outcome had 11 p.m. PRL responses comparable with control subject.

Conclusions: Blunted evening pituitary TRH receptor responsiveness (possibly secondary to endogenous TRH hypersecretion) may predict good clinical outcome. Dissociation between 11 p.m. TRH-induced TSH and PRL stimulation, which is predictive of poorer outcome, might be secondary to a deficit in central dopaminergic function, in which case treatment with dopaminergic drugs might be indicated.

NR356 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Increased ACTH Suppression Following DST in Adolescents with PTSD

Fabrice Duval, M.D., *Department of Psychiatry, Centre Hospitalier, 27 Rue du 4eme RSM, Rouffach 68250, France*; Marie S. Guillon, M.D., Marc-Antoine Crocq, M.D., Paul Bailey, M.D., Jean-Paul Macher, M.D.

Summary:

Objectives: Individuals with postraumatic stress disorder (PTSD) demonstrate a more robust suppression of adrenocorticotropin (ACTH) and cortisol in response to the dexamethasone suppression test (DST) than normal control subjects. However, there are few studies of adolescents.

Methods: Dexamethasone, 1 mg orally, was given at 11 p.m.; the following day, cortisol and ACTH levels were measured at 8 a.m., 4 p.m. and 11 p.m. Eight adolescent inpatients with DSM-IV PTSD (seven female, one male; mean age ± SD, 17.1 ± 2.4 years) were compared with eight adolescent hospitalized control subjects (six female, two male; age, 15.6 ± 2.7 years). All patients were drug-naive. The causative trauma had been sexual abuse in all cases and had occurred 4.5 ± 4.5 years earlier. Clinical assessment included the Impact of Event Scale, Stanford Acute Stress Reaction Questionnaire, Beck Depression Inventory, and Coping Inventory for Stressful Situations.

Results: Post-DST mean ACTH levels (average of the three samples) were significantly lower in PTSD patients (4.4 ± 2.1 pg/ml) than in control subjects (8.5 ± 4.9 pg/ml; $p = 0.011$). Post-DST mean cortisol levels were lower in patients than in control subjects; however, the difference was not significant. No correlations were found between these endocrine parameters and the scale and questionnaire scores nor with time elapsed since trauma.

Conclusions: These preliminary results show that the hyptothalamic-pituitary-adrenal axis abnormality of PTSD is already present in adolescents, despite the relatively short period elapsed since trauma. These results are compatible with the hypothesis of an upregulation of glucocorticoid receptors possibly acting as a buffer to protect CNS structures from the effect of stress.

NR357 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Dopaminergic and Serotonergic Function in Untreated Schizophrenia

Fabrice Duval, M.D., *Department of Psychiatry, Centre Hospitalier, 27 Rue du 4eme RSM, Rouffach 68250, France*; M. Claude Mokrani, Ph.D., Paul Bailey, M.D., Jose Monreal, M.D., Marcelo Valdebenito, M.D., Marc-Antoine Crocq, M.D., Jean-Paul Macher, M.D.

Summary:

Objectives: The aim of this study was to examine the relationships between the dopaminergic (DA) and serotonergic (5-HT) systems in schizophrenia.

Methods: Prolactin (PRL), adrenocorticotropin (ACTH), and cortisol responses to the selective 5-HT releasing agent D-fenfluramine (D-FEN, 45 mg, p.o.) and the direct DA receptor agonist agent apomorphine (APO, 0.75 mg, s.c.) were measured in 31 drug-free schizophrenics patients (SPs) and 23 hospitalized control subjects (HCs).

Results: Pituitary-adrenal responses to APO and D-FEN were positively correlated (cortisol: $r = 0.38$; $N = 54$; $p < 0.006$, ACTH: $r = 0.30$; $N = 54$; $p < 0.03$). SPs showed significantly lower APO-induced ACTH and cortisol stimulation than HCs (all $p < 0.03$). SPs with a history of suicide attempt ($N = 11$) showed significantly lower D-FEN-induced PRL stimulation compared to SPs without such a history ($p < 0.01$) and to HCs ($p < 0.0001$). In the group of SPs without history of suicide attempt: 1) paranoid SPs ($N = 12$) showed lower APO-induced ACTH and cortisol stimulation than disorganized SPs (all $p < 0.01$), 2) disorganized SPs ($N = 8$) showed higher D-FEN-induced cortisol stimulation than paranoid SCZs ($p < 0.02$), and 3) predominance of positive symptoms was correlated with lower D-FEN-induced ACTH-cortisol stimulation and lower APO-induced ACTH-cortisol stimulation (all $r > 0.45$; $N = 20$; $p < 0.005$).

Conclusions: These findings indicate that DA and 5-HT systems exert reciprocal regulatory actions at the hypothalamic-pituitary level. It is suggested that 1) decreased D2-like receptor function (possibly secondary to increased DA activity) is associated with paranoid schizophrenia subtype, 2) enhanced 5-HT tone is associated with disorganized subtype, and 3) decreased central 5-HT tone is associated with suicidal behavior independent of schizophrenia subtypes.

NR358 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Diagnosis of Bipolar II Disorder

Franco Benazzi, M.D., *Department of Psychiatry, National Health Service, Via Pozzetto 17, Cervia, RA 48015, Italy*

Summary:

Objective: To test sensitivity and specificity for bipolar II diagnosis of clinical markers of bipolar II: atypical features, depressive mixed state, young age at onset, recurrences, and interpersonal rejection sensitivity.

Method: Consecutive unipolar (major depressive disorder, dysthymic disorder) ($N = 64$) and bipolar II ($N = 97$) major depressive episode (MDE) psychoactive drug-free outpatients, presenting spontaneously for depression treatment, were interviewed (with relatives) with the Structured Clinical Interview for DSM-IV Axis I Disorders during their first visit. Depressive mixed state was defined as MDE with two or more, or with three or more (DMX3) concurrent hypomanic symptoms. Logistic regression was used. Two-tailed $p < 0.05$.

Results: DMX3 and atypical features had the highest specificity (92.1%, 82.8%) and predictive power (0.69, 0.64) but had low sensitivity (46.3%, 45.3%). Concurrent presence of DMX3 and atypical features increased sensitivity (67.0%), reduced specificity (76.5%), and increased predictive power (0.75). Age at onset, recurrences, and interpersonal rejection sensitivity, concurrent with DMX3 and atypical features, increased only slightly predictive power.

Discussion: Two cross-sectional features of MDE, like DMX3 and atypical symptoms, may strongly support bipolar II diagnosis, which, when based only on history of hypomania, may have low reliability.

NR359 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Depressive Morbidity and Response to Citalopram in Perimenopausal Women

Nora Belso, M.D., *XIII Department, National Institute of Psychiatry, Huvosvolgy U. 116, Budapest 1021, Hungary*; Kitty Kiss, M.B., Zoltan Rihmer, M.D., Mandor Tuzko, M.D., Ferenc Paulin, M.D.

Summary:

The objective of this study was to investigate the prevalence of depressive disorders and response to citalopram among perimenopausal women visiting two menopause clinics in Budapest, Hungary.

Methods: 185 consecutive outpatients were screened using the short Beck Depression Inventory. Persons with medium or severe depression were investigated by a psychiatrist. For patients with DSM-IV unipolar major depression who provided informed consent, a 6-week open trial with citalopram (20–40 mg daily) was

started, The severity of depression was measured by the 17-item Hamilton Depression Rating Scale (HDRS) at baseline and at weeks 3 and 6. The primary outcome measure was the rate of responders at week 6 (more than 50 percent drop in the total HDRS score at week 6 compared to baseline).

Results: 185 consecutive outpatients were screened, 48 (26 percent) had medium or severe depression, and 37 met the diagnosis of DSM-IV unipolar major depression. Citalopram treatment was started in 30 patients, and 21 (70 percent) finished the trial. The rate of responders at week 6 was 13/21 (62 percent).

Conclusions: Depressive disorders are quite common among perimenopausal women visiting menopause clinics, and the majority of those with depression respond well to citalopram.

NR360 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Platelet 5HT-2 Receptors in Depression

Sumant Khanna, M.D., *Department of Psychiatry, N. I. M. H. A. N. S., P O Box 2900 Hosur Road, Bangalore 560029, India*; T. A. Sunitha, M.S.C.

Summary:

Depression is perceived as a serotonin deficiency syndrome, and many biological markers have been studied to elucidate the site of dysfunction in depression. Use of platelets as a model to study the central serotonergic dysfunction has been well established.

Objectives: The current study aims at studying the platelet 5-HT2 receptors in patients with depression and compared to normal healthy controls. The study group included 30 patients with major depression without psychotic symptoms and 23 normal healthy controls.

Methods: Fasting blood was drawn from the subjects between 8–9 AM in EDTA, and the separation of platelet pellets was done immediately. Radioreceptor assay with [^{3}H] LSD as the 5-HT2 ligand was carried out, on the crude platelet membranes. Bmax and Kd were estimated by Scatchard plot analysis. Student t-test was done to compare the binding indices of the two groups.

Results: Bmax, representative of the receptor density, did not differentiate between the two groups; Kd, which describes the receptor affinity to the ligand, also did not differentiate between the depressed patients and normal controls. Age and severity of the illness did not correlate with the binding indices.

Conclusion: Our results did not show an increase in the density of 5-HT2 receptors, as suggested by some of the earlier reports. This could be due to factors such as suicidality. 5-HT2 receptors are considered as a potential marker for suicide, which was also supported by our study as the patients with high suicidal ideation showed an increase in Bmax of 5-HT2 receptors. Another possible explanation could be the heterogeneity in the clinical population.

NR361 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Factor Structure of OCD: From a National French Survey of 3,500 Patients

Elie G. Hantouche, M.D., *Department of Psychiatry/Mood Center, Pitie-Salpetriere Hospital, 43 Bd Hopital, Paris 75013, France*; Frederic J. Kochman, M.D., Jean-Francois Allilaire, M.D., Jules Angst, M.D.

Summary:

Background: Recognition of obsessive-compulsive disorder (OCD) in everyday practice is a difficult task, especially in primary care. In this context, a recent survey was undertaken on a national level with the participation of more than 650 clinicians. The aim of the survey, called "AR-TOC," was to show the feasibility of screening OCD in patients presenting with "resistant anxiety."

Results: Data are presented for a cohort of 5919 patients. They showed the presence of OCS (obsessive-compulsive syndrome) in 13.9% and of OCD in 45.2% ("probable OCD" in 31.2% and "definite OCD" in 14%). Principal component analyses were conducted in 3498 cases presenting with OCS or OCD. These analyses concerned the clinical data derived from clinician-rated (OCD Screening Questionnaire [OCD-SQ]) and self-rated (Maudsley Obsessive-Compulsive Inventory [MOCI]) questionnaires. The results were concordant with the dimensional approach of OCD by identifying clinically meaningful separated subtypes. Three factors were isolated from the OCD-SQ ("compulsive," "obsessive," and "mixed" subtypes); four factors were identified from the MOCI ("property cleaning," "checking," "waste of time," and "pure obsessions." Factorial scores derived from the MOCI were capable of differentiating significantly the different diagnoses of OC phenomena (OCS, probable OCD, and definite OCD).

Conclusion: "AR-TOC" succeeded in showing the feasibility of screening OCD in patients suffering from resistant anxiety. Moreover, using dimensional analyses resulted in the characterization of separate subtypes based on the dominant obsessive and/or compulsive symptomatology.

NR362 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Hidden Bipolarity in OCD

Elie G. Hantouche, M.D., *Department of Psychiatry/Mood Center, Pitie-Salpetriere Hospital, 43 Bd Hopital, Paris 75013, France*; Frederic J. Kochman, M.D., Hagop S. Akiskal, M.D.

Summary:

Background: OCD and depression are frequently comorbid. Clinical data are largely focused on depressive comorbidity. According to the literature, OCD with comorbid depression tends to be severe and chronic. In practice, treating resistant or severe OCD sufferers revealed many cases who seem to have an authentic OCD with a hidden comorbid bipolar disorder. An Italian study (N = 315) showed a comorbidity rate of 16% for bipolar disorder (primarily BP-II).

Methods: Using new instruments, we undertook a study among the members of the French association of patients suffering from OCD (AFTOC). From a total sample of 780, 453 files (58%) were returned and analyzed: 76% had suffered from a major depression (83% had recurrent episodes), and 17% had attempted suicide.

Results: After systematic search for hypomania (according to DSM-IV), 11% of the total sample were classified as bipolar (3% as BP-I and 8% as BP-II). Twenty percent had been treated with mood stabilizers; moreover, 38% of patients taking antidepressants had shown hypomanic switches. Furthermore, the Hypomania Checklist of Angst showed that 29.8% scored ≥10. The use of the self-rated questionnaire for Cyclothymic Temperament showed that 50% had obtained a score ≥10. Both thresholds for hypomania and cyclothymia had been previously validated by Hantouche et al. (1998). Our analyses finally showed that anger attacks (according to the Fava criteria) and suicide behavior in OCD were mainly linked to co-existing soft bipolarity.

Conclusion: These data extend clinical studies on bipolar-OCD comorbidity and implicate cyclothymia in hostile suicide attempts in this population.

NR363 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Maternity Blues and Post-Natal Depression

Nathalie Olivier-Lambert, M.D., *Department of Child Psychiatry, USN B, 6 Rue du Professeur Laguesse, Lille 59037, France*; Patrick G. Devos, Ph.D., Xavier Codaccioni, M.D., Daniel D. Bailly, M.D.

Summary:

Objective: To investigate the possible link between maternity blues and post-natal depression.

Method: 235 women who had delivered a live baby completed three short questionnaires on their fourth day post-partum. The first requested information concerning their sociodemographic situation, health problems, delivery, and the infant. The two other questionnaires were the Blues Questionnaire (BQ) and the Edinburgh Postnatal Depression Scale (EPDS). The EPDS was then mailed to the mothers for completion 6 weeks after delivery; a stamped addressed return envelope was provided.

Results: At the fourth day post-partum, 115 women (48.9%) exhibited a clinically significant episode of maternity blues (BQ ≥ 7), and there was a significant positive correlation between BQ and EPDS scores (r = 0.64). Occupational activities, primiparity, a delivery more difficult than expected, and unsatisfactory interactions with the baby were all significantly associated with a BQ score ≥7. One hundred forty-eight women completed the EPDS at 6 weeks post-partum. Among them, 24 (16.2%) exhibited a probable post-natal depression (EPDS ≥ 11). Marital disharmony and previous use of psychotropic drugs were significantly associated with an EPDS score ≥11. Both the fourth day post-partum BQ and EPDS scores were found to be weakly correlated with the 6-week post-partum EPDS score (r = 0.32 and r = 0.44, respectively).

Conclusions: Maternity blues and post-natal depression appear to be two different clinical states.

NR364 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Efficacy of Risperidone Add-On to Mood Stabilizers in Acute and Continuation Treatment of Mania

Lakshmi N. Yatham, M.B., *Department of Psychiatry, University of British Columbia, 2255 Wesbrook Mall, Vancouver, BC V6T 2A1, Canada*

Summary:

Objective: To determine the efficacy and safety of the addition of risperidone to mood stabilizers for treatment of acute mania.

Method: Subjects (Bipolar I) with manic episodes (N = 106) who gave written informed consent were recruited. All subjects were taking one to two mood stabilizers (lithium, carbamazepine, valproate) at initiation of risperidone (range 0.5–4mg). No other antipsychotic or ongoing benzodiazepine therapy was allowed.

Results: There were significant mean decreases in YMRS scores from baseline (27.1 ± 7.5) to week 1 (–10.2, $p < 0.001$), week 3 (–17.3, $p < 0.001$), and week 12 (–22.1, $p < 0.001$). Mean YMRS score decreased to 16.9 (week 1), 9.8 (week 3), and 5.0 (week 12). Response rates (≥50% reduction in YMRS scores from baseline) at 1, 3, and 12 weeks were 30%, 66%, and 88%, respectively. Significant mean-decreases in HAM-D 21 mean scores from baseline (12.3) were observed at week 3 and week 12 (–5.7, $p < 0.001$). No significant changes in extrapyramidal symptoms were noted between baseline and endpoint. The mean daily dose of risperidone was 2 mg.

Conclusion: Findings suggest that the addition of risperidone to mood stabilizers is safe and effective for acute and continuation treatment of mania.

NR365 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Comparative Efficacy of Typical and Atypical Antipsychotics Add-On to Mood Stabilizers in the Treatment of Acute Mania

Lakshmi N. Yatham, M.B., *Department of Psychiatry, University of British Columbia, 2255 Wesbrook Mall, Vancouver, BC V6T 2A1, Canada*; Debra Miller, Raymond W. Lam, M.D.

Summary:

Objective: To determine the comparative efficacy of atypical vs typical antipsychotic add-on therapy to mood stabilizers in acute mania through retrospective chart review in a clinically relevant, naturalistic setting.

Method: Patients admitted to the UBC Hospital over a 30-month period were separated into three groups according to the medications used: (1) mood stabilizer and typical antipsychotic, (2) mood stabilizer and atypical antipsychotic, or (3) combination: mood stabilizer plus typical antipsychotic, then switched to risperidone or olanzapine within 1 week. The atypical group was further subdivided into risperidone and olanzapine subgroups. Outcome was measured using clinical global impression (CGI-S and I) ratings generated by review of clinical information in the chart.

Results: Patients treated with typical antipsychotics were more severely ill on admission and at discharge than those treated with atypical antipsychotics. Patients in the atypical ($p < 0.001$) and combination groups ($p < 0.05$) showed significantly greater clinical improvement at discharge than those patients treated with typical antipsychotics. This difference was also significant in the subset of patients with psychotic features ($p < 0.03$). Risperidone and olanzapine were associated with fewer extrapyramidal side effects than typical antipsychotics.

Conclusions: These results suggest that atypical antipsychotics are an excellent choice as add-on therapy to mood stabilizers for the treatment of patients with mania.

NR366 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Clinical Predictors of Complete Suicide in Bipolar Disorder

Shang-Ying Tsai, M.D., *Department of Psychiatry, Taipei Medical College Hospital, 252 Wu Hsing Street, Taipei 110, Taiwan*; Hsin-Chien Lee, M.D., Chian-Jue Kuo, M.D., Chiao-Chicy Chen, Ph.D.

Summary:

Objective: Bipolar patients in Taiwan have long-term outcome and suicide risk comparable to Western patients despite markedly lower comorbidity of substance use disorders [1, 2]. Thus, risk factors of suicide identified from Taiwanese bipolar samples may be less influenced by substance abuse.

Method: All acute inpatients with bipolar disorder were followed from date of admission after January 1, 1985 until December 31, 1996 by record linkage to the Death Certification System in Taiwan. Nineteen female and 24 male patients died by suicide and were matched with one living bipolar individual for age, sex, and date of admission as a control. Demographic and clinical data were collected from the medical records.

Results: The latency period from the presumed time of onset to suicide averaged 12.2 years. Conditional logistic regression revealed a strong association of suicide with onset with mood-congruent psychotic features (95% CI for odds ratio (OR) = 0.04–0.74), positive first-degree family history of successful suicide (95% CI for OR = 1.39–163.5), and making a suicide attempt at least once in 7 years of illness (95% CI for OR = 1.03–23.83).

Conclusions: Those bipolar disorder patients having a first-degree family history of suicide and having at least one suicide attempt in 7 years of illness are likely to commit suicide. The symptomatology at onset may differentiate subgroups of bipolar patients with various levels of suicide risk.

NR367 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Parasuicidal Behavior: Repeaters Versus Nonrepeaters

Aranzazu Sanchez, M.D., *Department of Psychiatry, Oviedo University, Julian Claveria 6-3, Oviedo 33006, Spain*; Jose A.

Blanco, M.D., Juan I. Franch, Ph.D., M. Jesus Rojas, M.D., Pilar A. Saiz, Ph.D., Julio B. Bobes, Ph.D., Valentin J.M. Conde, Ph.D.

Summary:

Objectives: To analyze the sociodemographic, psychological, and biological differences between parasuicidal repeaters (R) and nonrepeaters (NR).

Subjects / Method: Fifty-eight persons who attended the Valladolid University Hospital (Spain) due to parasuicidal behavior between February 1999 and June 1999.

Evaluation: Ad hoc protocol, Hamilton Depression Rating Scale (HDRS), Plutchik's Impulsivity Scale (IS), Hopelessness Scale (HS), and lipidic profile (total-cholesterol, LDL-chol, HDL-chol, triglycerides).

Results: Age- R: 34.64 (12.64), NR: 33.81 (15.17) (p = .225); Females- R: 19 (76.0%), NR: 16 (59.3%) (p = .199); SES: Low- R: 18 (72.0%), NR: 14 (53.8%) (p = .180); Family relationships: Good or acceptable- R: 8 (33.3%), NR: 17 (65.4%) (p = .024); Religious practice: Moderate- R: 7 (29.2%), NR: 9 (47.4%) (p = .506); Previous family suicide attempts- R: 4 (17.4%), NR: 0 (0%) (p = .045); Somatic Illness: R: 19 (76.0%), NR: 14 (53.8%) (p = .098); Total-cholesterol <149 mg/dl- R: 6 (27.3%), NR: 7 (35.0%) (p = .588); IS ≥ 20- R: 9 (37.5%), NR: 5 (25.0%) (p = .375); HS > 8- R: 15 (62.5%), NR: 7 (35.0%) (p = .069); HDRS > 18- R: 21 (87.5%), NR: 14 (70.0%) (p = .152).

Conclusions: In our study repetition of attempted suicide is associated with bad family relationships and previous family suicide attempts.

NR368 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Clozapine Low Doses in Refractory Bipolar Disorder

Rodrigo Paz, M.D., *Neuropsychiatric Center of Santiago, Portugal #128, Santiago, Chile*; Danilo W. Quiroz, M.D., Jose A. Bitran, M.D., Luis E. Hormazabal, M.D., Rodrigo C. Labarca, M.D.

Summary:

Objective: To evaluate the efficacy and safety of low doses of clozapine in the treatment of bipolar disorder refractory to conventional strategies.

Methods: Patients were recruited at the Jose Horwitz Psychiatric Institute, Santiago, Chile. Subjects included patients with bipolar disorder type I, diagnosed according to DSM-IV criteria, refractory at least to lithium, valproic acid, and conventional antipsychotics. Clinical Global Impression Scale (GCI), number of admissions to clinical guards, and working status, before and after treatment, were used as measure of clinical improvement. Clozapine was used as an add-on treatment.

Results: Of the 18 patients, 14 were men, and four were women. Most patients (14) were rapid cyclers. The average length of illness was 22.6 ± 12.4 years. The average clozapine dose was 118 ± 71 mg/day. Clozapine treatment resulted in a decrease in CGI from 6.3 ± 0.87 to 2.3 ± 1.59. Before clozapine, patients registered on average 2.7 ± 1.4 admissions in the last 2 years. With clozapine only three hospitalizations had been reported (average 0.2 ± 0.4). Of previously unemployed patients, 61.5% (8/13) returned to work. Three patients had no response to clozapine. The rest continued taking clozapine for an average of 18 months.

Conclusions: In this open study, clozapine, at low doses, had mood stabilizer properties.

NR369 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Mianserin Augmentation, Sertraline Dose Increase, or Extended Duration of Treatment in Patients with Major Depression Nonresponding After Six Weeks of Sertraline Treatment: A Randomized, Double-Blind Study

Rasmus W. Licht, M.D., *Psychiatric Hospital A, Skovagervej 2, Risskov 8240, Denmark*; Susanne Qvitzav, M.D.

Summary:

Objective: The aim of this study was to evaluate a strategy of sertraline dose increase and a strategy of adding mianserin, which enhances noradrenergic neurotransmission, in patients with major depression nonresponding to six weeks of open treatment with sertraline according to a fixed dosing schedule.

Method: Adult patients with DSM-IV major depressive disorder scoring at least 18 on the 17-item Hamilton Depression Scale (HDRS) were included. Patients who after four weeks of treatment with 50 mg/day of sertraline had not achieved a 50% reduction on the HDRS were treated with 100 mg/day of sertraline for an additional two-week period. The patients who had still not achieved a 50% reduction on the HDRS were then randomized to double-blind treatment for an additional five weeks with either 100 mg/day of sertraline plus placebo (time effect), 200 mg/day of sertraline plus placebo, or 100 mg/day of sertraline plus 30 mg/day of mianserin.

Results: Of 1,629 patients included, 60% responded after six weeks of open treatment and 22% dropped out, leaving 295 patients (18%) for randomization. Of these, 253 (86%) completed the five weeks of double-blind treatment. In the intention-to-treat-analysis, continuing the treatment with 100 mg/day of sertraline resulted in response in 70% of the nonresponders, which was similar to the response rate (67%) obtained in the patients who had mianserin added. However, increasing the sertraline dose to 200 mg/day resulted in a lower response rate at 56% ($P = 0.03$). Similar results were seen in the completers.

Conclusion: This large study did not confirm any benefits from adding mianserin to sertraline or from increasing the daily dose of sertraline to 200 mg. Another implication from the study is that from at least week 4 to week 8, a treatment with 100 mg/day of sertraline should be continued before considering changing strategy, unless of course the patient's condition deteriorates.

NR370 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Mood Stabilizer Effects on Creativity in Bipolar Disorder Patients

Terence A. Ketter, M.D., *Department of Psychiatry, Stanford University School of Medicine, 401 Quarry Road, Room 2124, Stanford, CA 94305-5723*; Claudia M. Santosa, M.A., Po W. Wang, M.D., Bibi Das, Nadia Sachs, M.Eng., Connie M. Strong, M.S., Jenny Mongkolcheep, B.S.C.

Summary:

Objective: To assess medication effects on creativity in 47 euthymic bipolar patients (BP), compared with 47 healthy controls (HC).

Method: Subjects were administered Barron-Welsh Art Scale (BWAS), Adjective Check List Creative Personality Scale, and Verbal and Figural Torrance Tests of Creative Thinking.

Results: A total of 35 medicated patients (MED-BP) had nonsignificantly higher BWAS (30.4) than 12 medication-free patients (MF-BP, 25.8); 22 polytherapy patients (PT-BP) had nonsignificantly higher BWAS (28.7) than 13 monotherapy patients (MT-BP, 23.7); 17 patients on divalproex (DVPX-BP, seven monotherapy) had significantly higher BWAS (32.4) than 30 not on DVPX (No-DVPX-BP, 24.6, p < 0.03); 12 on lithium (LI-BP three monotherapy) had nonsignificantly lower BWAS (23.7) than 35 not on LI

(No-LI-BP, 28.7); eight on olanzapine (OLN-BP, 0 monotherapy) had nonsignificantly higher BWAS (32.3) than 39 not on OLN (No-OLN-BP, 26.4). All BP (BWAS 27.4), MED-BP, PT-BP, DVPX-BP, No-LI-BP, and OLN-BP (but not MF-BP, MT-BP, No-DVPX-BP, LI-BP, No-OLN-BP) had significantly higher BWAS than HC (18.6). Other creativity measure scores did not differ significantly with diagnosis or medications.

Conclusion: Medications in general, polytherapy versus monotherapy, and DVPX, LI, and OLN in particular, did not adversely affect creativity test performance. Indeed, DVPX was associated with higher BWAS scores.

(Supported by NARSAD and Stanley Foundation)

NR371 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Depression, Perceived Health, and Social Support Among End-Stage Renal Disease Patients

Sarah Speranza, B.A., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, Room 786, Philadelphia, PA 19104*; Laraine Winter, Ph.D., Tina L. Harralson, Ph.D., Tiffany A. Purnell, B.A.

Summary:

Objective: The purpose of this study was to examine the relationship between negative physical symptoms reported by end-stage renal disease (ESRD) patients and depression, self-perceived health, and social support.

Method: Participants were 45 elderly, African-American ESRD patients from the University of Pennsylvania hemodialysis Center (mean age = 71.3 years, s.d. = 7.6; 64% women; 18% married; mean education = 11.6 years, s.d. = 2.8) who volunteered to participate in a paid study. Measures included the Center for Epidemiologic Studies Depression Scale (CES-D), self-reported health question (rated "excellent health" = 1 to "poor health" = 5), the seven-item Duke Social Support Index, and a list of 13 negative physical symptoms that are commonly associated with ESRD (each item was rated "not present in the past week" = 1 to "extremely severe in the past week" = 5). The negative physical symptoms (NPS) measured were muscle cramps, nausea, vomiting, headaches, shivering, weakness/fatigue, extremity pain, dry/itchy skin, excessive thirst, lack of appetite, dry mouth, joint pain, and trouble sleeping. Symptom severities were summed for a total score.

Results: NPS were not significantly associated with age, sex, marital status, education, or social support. Poorer self-rated health was correlated with NPS ($r = .34$, $p = .02$) as was depression. The correlation between negative physical symptoms and total CES-D score was $r = .65$ ($p < .001$). To control for the collinearity that exists between the somatic CES-D items and physical, we also examined the relationship between the nonsomatic CES-D items and NPS ($r = .54$; $p < .001$). A linear regression revealed that CES-D non-somatic items predicted NPS even after controlling for self-rated health (Beta = .83, $p = .001$).

Conclusion: Nonsomatic depression plays a role in the severity of the negative physical symptoms experienced by many end-stage renal disease patients.

NR372 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Treatment-Resistant Depression: Retrospective Evaluation of Economic Consequences

Patricia Corey-Lisle, Ph.D., *GEA, Eli Lilly and Company, Lilly Corporate Center, DC 1834, Indianapolis, IN 46285*; Ami J. Claxton, Ph.D., Howard Birnbaum, Ph.D., Maryna Marynchenko, Ph.D., Paul Greenberg, Ph.D.

Summary:

Objective: Major depressive disorder (MDD) is a debilitating condition with significant economic consequences (1). Estimates indicate that up to 30% of individuals with MDD have treatment-resistant depression (TRD) (2). The study objectives were (1) evaluation of studying TRD using claims data and (2) estimation of cost differences between TRD and non-TRD patients.

Methods: Data source was administrative claims data from a Fortune 100 manufacturer. Claims included medical, pharmaceutical, and disability claims for 1996–1998 ($N > 100,000$). The sample was restricted to claims for MDD ($N_{mdd} = 4,186$). Using a treatment algorithm, patients were classified into TRD-likely and TRD-unlikely groups ($N_{TRD} = 487$). Resource utilization was compared between TRD-likely, TRD-unlikely patients, and a sample of the overall population.

Results: The algorithm classified 12% of the MDD sample as having TRD. Average annual costs were $10,954 for TRD-likely patients, $5,025 for TRD-unlikely patients, and $3,006 for average beneficiaries. The average number of health claims among TRD-likely patients were 1.5 times greater than that of TRD-unlikely patients.

Conclusions: Resource utilization by TRD-likely patients is substantial, not only for direct treatment of depression but also for treatment of comorbid medical conditions. Additionally, TRD imposes substantial indirect costs on employers, primarily resulting from high rates of depression-associated disability.

NR373 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Low Activity Level Is Associated with Depression Severity

Grant L. Iverson, Ph.D., *Department of Psychiatry, University of British Columbia, 2255 Wesbrook Mall, Vancouver, BC V6T 2A1, Canada*

Summary:

Objective: To investigate the relationship between activity level and depression in primary care outpatients.

Method: Forty-eight patients with depression and 25 general medical control subjects wore a heart and activity level monitor for 24 hours. Minute-averaged horizontal movement was collected. Patients with depression were sorted into two equal groups based on a median split of their Beck Depression Inventory-II scores.

Results: ANOVAs revealed significant main effects for average movement over the 24-hour interval ($p = 0.013$), average movement between the hours of 12 and 6 p.m. ($p = 0.003$), and a measure of "high activity" level ($p = 0.001$). Patients with more severe depression had lower activity levels than the other two patient groups. The non-depressed and less severely depressed groups were combined and compared to the more severely depressed group by using a standard discriminant function analysis ($p = 0.013$; canonical $r = 0.44$). The overall correct classification rate was 75.3%, with 88% of the combined group and 50% of the more severely depressed group correctly classified. Patients with low activity levels were 7.2 times more likely to fall in the severely depressed group than patients with more normal activity levels.

Conclusion: Activity level appears to be related to depression but only in the more severe cases.

NR374 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Clinical Utility of the British Columbia Major Depression Inventory

Tracey A. Brickell, M.Psy., *Heartlink-Canada, 715-837 West Hastings Street, Vancouver, BC V6C 3N6, Canada*; Grant L. Iverson, Ph.D., Rael T. Lange, Ph.D.

Summary:

Objective: The British Columbia Major Depression Inventory (BC-MDI) was designed to be less sensitive to simple psychological distress and more sensitive to clinically significant symptoms of major depression. Patterned after DSM-IV criteria, respondents rate the severity of each symptom and the degree to which it interferes with daily life but only if it is present nearly every day for the past 2 weeks. This study examined the prevalence of depressive symptoms in individuals free from obvious psychiatric or health-related illnesses.

Method: Participants (N = 148) volunteered to complete the BC-MDI.

Results: Participants rarely reported thoughts of killing themselves (0.7%), weight loss from poor appetite (0.7%), or excessive sleep (2%). Feeling tired and low in energy (14.9%); difficulty falling and staying asleep (14.2%); trouble concentrating, thinking, or solving problems (12.2%); and feeling sad, down in the dumps, and/or blue (10.8%) were the most frequently reported clinically significant symptoms. Eighty-seven percent of the participants scored in the broadly normal range, 7% were classified as having possible major depression, and 6% as having probable major depression.

Conclusion: The BC-MDI appears to be a useful screening measure for major depression and may be less likely to yield false positives than other depression screening tests.

NR375 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Prevalence and Correlates of Depression Symptoms Among the Adolescents in a Korean Urban Area

Hong-Jin Jeon, *Department of Psychiatry, Seoul National University Hospital, Yon-Gyun Dong, Seoul 110-744, Korea*; Seong-Jin Cho, Maeng-Jae Cho, M.D.

Summary:

Objectives: This study aimed to estimate the prevalence and correlates of adolescent depression in Korea as measured by the CES-D. Korean adolescents have a hard time attaining educational achievement because of the need to struggle for supremacy to enter the university. We hypothesical that this severe burden leads to different characteristics of adolescent depression, and if we can show this, we can develop appropriate approach to help adolescents with depressive symptoms in Korea.

Method: We sampled 2,203 adolescents among 35,059 adolescents who live in Puchon City in Korea by a randomized stratified sampling method. Of the 2,203 adolescents, 1,105 adolescents were male, and 1,098 were female. The interview was accomplished in November, 1999. The CES-D (Center for Epidemiologic Studies Depression) which was translated in Korean by Cho et al. (1993), was used to measure the depressive symptoms. 1,972 (89.5%) of all adolescents completed the CES-D.

Result: The rate of depressive symptoms (using a cutoff point of 16) was 34.3% for males and 47.5% for females, and the rate of depression (using a cutoff point of 25) was 17.4% in males and 20.6% in female. We used logistic regression analysis to find the risk factor for adolescent depression in a Korean urban area. Among the variables of sex, age, economic status, family structure, and educational achievement, low educational achievement was the most important risk factor in adolescent depression. The odds ratio was 8.850, and the confidence interval was between 2.921 and 26.801.

Conclusion: Korean adolescents have a high prevalence of depressive symptoms and depression. Educational achievement is an important risk factor in adolescent depression.

NR376 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Health Care Utilization in Patients with Treatment-Resistant Depression

Stan N. Finkelstein, M.D., *Management Department, MIT, 38 Memorial Drive, Cambridge, MA 02139*; William H. Crown, Ph.D., Davina C. Ling, Ph.D., Ernst R. Berndt, Ph.D., Amy S. White, M.S.

Summary:

Objective: Approximately one-half of patients with an episode of major depression will have a recurrent episode, often leading to a chronic course of illness. Recent studies indicate that approximately 20% of depressed patients are resistant to antidepressant treatments. This study utilizes medical and prescription claims data from 1995–1998 to profile the characteristics of patients with treatment-resistant depression.

Methods: Depression-diagnosed patients with adequate antidepressant dosing and treatment duration were selected. Patients were considered treatment-resistant if they switched/augmented initial antidepressant medication with other antidepressants twice or if they switched/augmented their initial medication and had claims for depression-related hospitalizations or suicide attempts. Depression-diagnosed patients meeting initial depression selection criteria but not treatment-resistance were used for comparison.

Results: Patients with treatment-resistant depression were more likely to be diagnosed with bipolar disorder, comorbid anxiety, and substance-related disorders than the comparison group ($p \leq 0.01$). They were at least twice as likely to be hospitalized (for depression- and non-depression-related causes) and have 45% more outpatient visits than the comparison group ($p \leq 0.01$). Treatment resistance was also associated with use of 2–3 times more psychotropic medications (besides antidepressants) ($p \leq 0.01$).

Conclusions: Patients with treatment-resistant depression were higher utilizers of depression-related and general medical services. This finding underscores the importance of early identification and effective treatment for patients with treatment-resistant depression.

Supported by Cyberonics Inc.

NR377 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Recognizing Facial Expressions of Emotion in Euthymic Patients with Bipolar Disorder

Syed O. Ali, B.S., *VSLB, NIH/NIDCD, 9000 Rockville Pike, 10/3C716, Bethesda, MD 20892*; Bryan D. Fantie, Ph.D., Kirk D. Denicoff, M.D., Robert M. Post, M.D.

Summary:

Objective: Euthymic patients with bipolar disorder demonstrate neuropsychological dysfunction in a variety of domains (e.g., verbal learning and memory, executive functioning, and psychomotor performance). Whether deficits in the recognition of facial expressions of emotion are depressive state-dependent, however, remains unclear.

Method: In this study, 34 euthymic patients with bipolar disorder and 26 healthy control subjects completed computer-administered tests (i.e., verbal face-labeling and non-verbal face-matching tasks) that measured both the accuracy and the sensitivity (i.e., reaction time) of recognition of seven basic facial expressions of emotion (i.e., anger, disgust, happiness, sadness, fear, surprise, and neutral).

Results: For the verbal face-labeling task, the patients made significantly fewer correct matches for anger and significantly greater correct matches for fear, compared with the healthy control subjects. In addition, the patients had a significantly lower sensitiv-

ity (i.e., longer reaction time) for recognizing happy faces compared with the healthy control subjects.

Conclusions: This study suggests that some of the alteration in facial affect recognition, observed previously in acutely ill patients with bipolar disorder, persist into the euthymic state and thus may represent a trait marker. This study also highlights the utility of further research using neuroimaging methods to link these abnormalities in patients with bipolar disorder to neuroanatomical structures, such as the amygdala and the prefrontal cortex, which may subserve facial affect recognition.

Supported by the Theodore and Vada Stanley Foundation.

NR378 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Risperidone in Bipolar Depression

Richard C. Shelton, M.D., *Department of Psychiatry, Vanderbilt University, 1500 21st Avenue South, #2200, Nashville, TN 37212*; Stephanie Addington, M.A., Elise J. Augenstein, M.D., Weselyn L. Ball, M.D.

Summary:

Objective: To evaluate the effect of risperidone alone and in combination with paroxetine.

Methods: Outpatients meeting criteria for bipolar disorder, depressed type (N = 22) were randomly assigned to receive blinded risperidone (range 1–6 mg/day; N = 7) (RIS), paroxetine (range 10–40 mg/day; N = 7) (PAR), or the combination of the two (N = 8) (RIS + PAR) added to a mood stabilizer for 12 weeks. Ratings included the Montgomery Ansberg Depression Rating Scale (MADRS, primary outcome variable), Hamilton Rating Scale for Depression (HAM-D), Beck Depression Inventory (BDI), Young Mania Rating Scale (YMRS), the Barnes Akathisia Scale (BAS), the Simpson Angus Rating Scale (SAS), and the abnormal involuntary movement scale (AIMS).

Results: The initial data analysis suggests a more robust early effect (onset week 2) for the RIS and RIS + PAR groups than PAR alone on the MADRS. However, the rapid effect was sustained only in the RIS + PAR groups.

Conclusions: These data suggest that RIS may induce a more rapid change in mood either alone or in combination with PAR than with PAR alone. However, there is not a sustained effect with RIS alone.

Funding Source: Janssen Pharmaceutica.

NR379 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Risperidone Plus Mood Stabilizer Versus Placebo Plus Mood Stabilizer in Patients with Bipolar Disorder: A Combined Efficacy Analysis

Fred Grossman, M.D., *Janssen Research Foundation, 1125 Trenton-Harbourton Road, Titusville, NJ 08560*; Charles L. Bowden, M.D., Akiko Okamato, M.D.

Summary:

Background: The efficacy of risperidone as an adjunctive agent to mood stabilizers in the treatment of acute mania was assessed.

Method: Combined data from two randomized, double-blind, placebo-controlled, three-week studies of 293 bipolar patients with acute mania receiving a mood stabilizer (lithium, divalproex, or carbamazepine) and placebo (placebo/MS group), risperidone (risperidone/MS group), or haloperidol (haloperidol/MS group; active comparator) were assessed. The primary efficacy measure was the Young Mania Rating Scale (YMRS).

Results: Between-group differences in baseline demographic or disease-related characteristics were not significant. Mean modal doses were 3.8 mg/day of risperidone and 6.3 mg/day of haloperidol. Compared with the placebo/MS group, risperidone/MS was associated with greater symptom improvement (mean change in YMRS total score) at week 1 ($p = 0.002$) and endpoint ($p = 0.001$) and greater improvements in the BPRS total score change at week 1 ($p = 0.001$) and endpoint ($p = 0.005$) and in Hamilton Depression Rating Scale total score at week 1 ($p = 0.003$) and endpoint ($p = 0.037$). Clinical Global Impressions scale severity ratings were "very much or much improved" in 38% and 57% of the placebo/MS and risperidone/MS groups, respectively.

Conclusion: Risperidone was effective as an adjunctive agent to mood stabilizers for the rapid control of manic symptoms.

NR380 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Lamotrigine: Evidence for Mood Stabilization in Bipolar I Depression

Charles L. Bowden, M.D., *Department of Psychiatry, University of TX Health Science Center, 7703 Floyd Curl Drive, San Antonio, TX 78284-7792*; John A. Ascher, M.D., Joseph R. Calabrese, M.D., Alan Ginsburg, Paul Greene, Paul Montgomery, Frederick W. Reimherr, M.D.

Summary:

Objective: Lamotrigine (LTG), an established broad-spectrum anticonvulsant drug, is currently under investigation for treatment of bipolar disorder. Previous double-blind studies have demonstrated efficacy in the acute treatment of bipolar depression. This paper reports results from the initial phase of a large, long-term, placebo- and lithium-controlled prophylaxis study in bipolar I depression.

Methods: GW Study #605 enrolled 962 bipolar I patients with recent depression into an initial open-label stabilization phase, during which LTG was added to current treatment. Patients who experienced clinical response were discontinued from medications other than LTG before the randomization phase. Patients achieving stabilization of their depression, defined as four consecutive weeks of Clinical Global Impression (Severity) scores ≤ 3 between the eighth and 16th week of the open phase, were then randomized to monotherapy with LTG, lithium or placebo for up to 18 months.

Results: Of the 962 patients initially enrolled, 462 achieved stabilization and entered the randomized phase. HAM-D results were consistent with this degree of stabilization. These data, combined with previously published placebo-controlled data for LTG in acute bipolar depression and rapid cycling, suggest that LTG possesses a unique spectrum of efficacy that includes both antidepressant and mood stabilizing properties.

NR381 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Comorbidity of DSM-IV MDD in Psychiatric Care

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Summary:

Objective: There are no published reports of overall current comorbidity with axis I and II disorders among psychiatric patients with major depressive disorder (MDD). Furthermore, no earlier study has systematically reported the variations in current comorbidity by sociodemographic and clinical factors.

Method: Psychiatric outpatients and inpatients of Vantaa city, Finland, were prospective screened for an episode of DSM-IV MDD. Altogether 269 patients with a new episode of MDD were enrolled in the Vantaa Depression Study. Axis I and II comorbidity was assessed via SCAN 2.0 and SCID-II-interviews.

Results: The majority of patients with MDD suffered from various current comorbid mental disorders, including anxiety disorder

(57%), alcohol use disorder (28%), and personality disorder (49%). Males had an alcohol use disorder more often than females. Inpatients had an alcohol use disorder, panic disorder, and melancholic or psychotic depression more often than outpatients. The prevalence of personality disorders varied with age, type of residential area, and number of lifetime depressive episodes.

Conclusions: Most (81%) patients with MDD suffered from at least one, and the majority (59%) from multiple, current comorbid disorders. The patterns of comorbidity were associated with age, gender, inpatient vs. outpatient status, type of residential area, and lifetime number of depressive episodes.

NR382 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Depression in Women with Polycystic Ovary Syndrome: Biochemical Correlates

Natalie L. Rasgon, M.D., *Department of Psychiatry, UCLA University, 300 UCLA Medical Plaza, #1544, Los Angeles, CA 90095-7057*; Rekha C. Rao, M.D., Sun Hwang, M.P.H., Lori L. Altshuler, M.D., Joni Zuckerbrow-Miller, Stanley Korenman, M.D.

Summary:

Previous studies report an increased vulnerability to affective disorders (mainly depression) in women with menstrual dysfunction as a symptom of polycystic ovary syndrome (PCOS). This study investigates the relationship between depression and clinical and biochemical markers specific to PCOS. Thirty-two female patients, who presented for evaluation of hyperandrogenic syndromes at the UCLA Endocrinology Clinic, participated in the study. The Center for Epidemiological Studies—Depression Rating Scale (CES-D) was administered to evaluate the severity of depression. A score ≥16 has been associated with clinical depression. A score ≥27 has been used as a more stringent criteria for clinical depression. Sixteen (50%) women scored ≥16, with seven (22%) receiving a score ≥27. In the subgroup of 18 treatment-naive patients, CES-D scores ≥16 positively correlated with greater insulin resistance ($p = .02$) and higher body mass index ($p = .05$). Treatment of PCOS with oral contraceptives had significant negative correlation with depression ($p = .03$). The present findings reveal a higher prevalence of depression in women with PCOS compared with the general population. Data suggest a reciprocal interaction between hypothalamic-pituitary-gonadal axis dysfunction and depression.

NR383 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Olanzapine Is Not Associated with Exacerbation of Bipolar Mania

Robert W. Baker, M.D., *US Medical, Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46285*; Denai R. Milton, M.S., Mauricio F. Tohen, M.D., Virginia L. Stauffer, Pharm.D., Alan F. Breier, M.D.

Summary:

Objectives: To explore whether olanzapine influences mania exacerbation.

Methods: Two inpatient, double-blind, randomized trials investigating the efficacy of olanzapine 5–20 mg daily versus placebo for the treatment of acute mania were combined. Two hundred and fifty-four subjects participated (placebo; N = 129; olanzapine; N = 125) in the two studies. Severity of mania was quantified with the 11-item Young-Mania Rating Scale (Y-MRS). In a post-hoc analysis, after double-blind therapy up to 3 weeks, categorical comparison of olanzapine and placebo groups was made for any worsening and worsening by 10 or 20% from baseline Y-MRS scores (LOCF).

Results: The percentage of placebo and olanzapine subjects with exacerbation at endpoint were as follows: any worsening: 37.7% versus 21.8% respectively ($p = 0.006$); ≥10% worsening: 24.6% versus 14.5% ($p = 0.046$); ≥20% worsening: 15.6% versus 8.1% ($p = 0.068$).

Conclusions: Mania rating scores worsened for some patients during olanzapine therapy. In an uncontrolled setting, such worsening might be misinterpreted as olanzapine *causing* mania exacerbation. However, results from these controlled studies demonstrated that such worsening occurred more often with placebo than with olanzapine. Therefore, the controlled data from up to 3 weeks of treatment in manic patients did not support the clinical speculation that olanzapine may cause mania-like states in patients with pre-existing bipolar disorder.

Funding provided by Eli Lilly and Company

NR384 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Olanzapine Versus Haloperidol: Improvements in Quality of Life and Compliance with Treatment in Patients with Bipolar Disorder

Madhav Namjoshi, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Lizheng Shi, Ph.D., Fan Zhang, Ph.D., Eric T. Edgell, Pharm.D., Mauricio F. Tohen, M.D., Alan F. Breier, M.D.

Summary:

Objective: To compare quality of life outcomes and compliance to treatment associated with olanzapine and haloperidol in patients with bipolar disorder.

Methods: Patients (N = 453) with bipolar I disorder, manic or mixed, were randomly assigned to either olanzapine 5–20 mg/day or haloperidol 3–15 mg/day for 12 weeks. The primary clinical outcome was symptomatic remission rate. Compliance with treatment was assessed using subjective response scores on the Drug Attitude Inventory. Quality of life was assessed using the Psychological Global Well-being (PGWB) and SLICE/LIFE questionnaires.

Results: Olanzapine-treated patients had a higher remission rate compared to those treated with haloperidol during the study (52% versus 44%, $p = 0.08$). While 63% of patients randomly assigned to olanzapine treatment had a positive subjective response at baseline, 88% had a positive subjective response at the end of 12 weeks. Olanzapine-treated patients demonstrated improvements from baseline in PGWB total score compared to a worsening for haloperidol-treated patients (0.95 versus −4.31, $p = 0.08$). Further, olanzapine-treated patients demonstrated statistically significant improvements from baseline compared to haloperidol on the "work activities" ($p < 0.01$) and "household activities" ($p < 0.05$) dimensions of the SLICE/LIFE.

Conclusion: Olanzapine treatment is associated with improvements in clinical and quality of life outcomes that lead to better compliance compared to haloperidol for the treatment of bipolar disorder.

Funding provided by Eli Lilly and Company

NR385 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Impact of Olanzapine Added to Lithium or Valproate on the Quality of Life of Patients with Bipolar Disorder

Madhav Namjoshi, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Richard C. Risser, M.S., Lizheng Shi, Ph.D., Eric T. Edgell, Pharm.D., Mauricio F. Tohen, M.D., Alan F. Breier, M.D.

Summary:

Objective: To compare the quality of life impact of olanzapine and placebo when each is added to mood stabilizers for treatment of bipolar disorder.

Methods: Patients (N = 344) with a diagnosis of bipolar disorder and inadequate response to mood stabilizers before study entry were randomly assigned in a 2:1 ratio to receive either olanzapine or placebo, with each being added to mood stabilizers, for 6 weeks. The Y-MRS and the HAM-D were the clinical outcomes measures, while the Lehman's Brief Quality of Life Interview (QLI) was used to assess changes in humanistic outcomes.

Results: Olanzapine-treated patients had statistically significant improvements from baseline on both the Y-MRS ($p < 0.01$) and the HAM-D ($p < 0.01$) compared to placebo. Response rate (i.e., ≥50% improvement from baseline in the Y-MRS) was also significantly higher for patients treated with olanzapine ($p < 0.01$). Olanzapine-treated patients showed statistically significant improvements from baseline on the Lehman's subjective scales of "Satisfaction with daily activities" ($p < 0.01$), "Satisfaction with family contact" ($p = 0.01$), "Satisfaction with their living situation" ($p < 0.01$), "Satisfaction with social relations" ($p < 0.01$), and "General life satisfaction" ($p = 0.04$) compared to placebo.

Conclusion: The results clearly indicate that the combination of olanzapine added to mood stabilizers had a significant impact on both clinical and humanistic outcomes in the treatment of bipolar disorder.

Funding provided by Eli Lilly and Company

NR386 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Olanzapine Versus Haloperidol: A Prospective Comparison of Clinical and Humanistic Outcomes in Bipolar Disorder

Lizheng Shi, Ph.D., *Eli Lilly, Lilly Corporate Center, Indianapolis, IN 46285*; Madhav Namjoshi, Ph.D., Mauricio F. Tohen, M.D., Fan Zhang, Ph.D., Alan F. Breier, M.D., Eric T. Edgell, Pharm.D.

Summary:

Objective: This study compared the clinical and humanistic outcomes associated with olanzapine and haloperidol treatment in patients with bipolar disorder.

Methods: Patients with bipolar I disorder (manic or mixed episode) were randomly assigned to either olanzapine 5–20 mg/day or haloperidol 3–15 mg/day for 12 weeks. The primary clinical outcome was symptomatic remission rates at 6 weeks and 12 weeks. The humanistic outcomes were changes from baseline to endpoint (week 6 or week 12) in scores on the Medical Outcomes Study Short Form-36 (SF-36).

Results: Olanzapine-treated patients had higher remission rates than those treated with haloperidol at 6 weeks (52% versus 46%, $p = 0.15$) and 12 weeks (52% versus 44%, $p = 0.08$). At week 6, significant changes in five SF-36 domains (general health [$p = 0.010$], physical functioning [$p < 0.001$], role limitations due to physical health problems [$p < 0.001$], social functioning [$p < 0.05$], and vitality [$p < 0.01$] were found in favor of olanzapine-treated patients as compared to haloperidol. At week 12, olanzapine treatment maintained the significantly favorable changes in same domains except social functioning. None of the SF-36 domains favored haloperidol at week 6 or week 12.

Conclusions: Compared to haloperidol, olanzapine treatment was associated with the improvements in the clinical and humanistic outcomes in patients with bipolar disorder.

Funding provided by Eli Lilly and Company

NR387 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Olanzapine Versus Haloperidol Treatment of Acute Mania

Mauricio F. Tohen, M.D., *MC 541, Eli Lilly and Company, One Lilly Corporate Center, Indianapolis, IN 46285*; Fan Zhang, Ph.D., Peter D. Feldman, Ph.D., Angela R. Evans, Ph.D., Alan F. Breier, M.D.

Summary:

Objective: To determine the efficacy and safety of olanzapine versus haloperidol in treating patients with bipolar I disorder.

Methods: Patients with bipolar I disorder (manic/mixed) were randomly assigned to receive olanzapine (5–20 mg/day, N = 234) or haloperidol (3–15 mg/day, N = 219) in a 6-week, double-blind acute study, followed by a 6-week, double-blind continuation study at the same dose.

Results: After 6 weeks, rates of remission (defined a priori as YMRS ≤12 and HAMD-21 ≤8) were not significantly different (52.1% versus 46.1%, $p = 0.152$). MADRS scores improved more among olanzapine-treated patients (–1.97 versus –0.50, $p = 0.028$). Olanzapine was more effective than haloperidol among nonpsychotic patients (56.7% versus 41.6%, $p = 0.043$). Among patients not in remission at 6 weeks, more olanzapine-treated patients were in remission by 12 weeks (68.3% versus 41.0%, $p = 0.014$). Haloperidol-treated patients showed worsening of EPS; olanzapine-treated patients showed improvement. Olanzapine-treated patients showed greater weight gain (6-week: 1.99 kg versus –0.14 kg, $p < 0.001$; 12-week: 3.55 kg versus 0.72 kg, $p < 0.001$).

Conclusion: Olanzapine may be at least as effective as haloperidol in achieving remission of bipolar mania and associated with a more favorable safety profile. Olanzapine appeared to be superior in nonpsychotic patients and in treating depressive symptoms in patients with acute bipolar manic or mixed episodes.

Funding provided by Eli Lilly and Company

NR388 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Continuation Treatment with Nefazodone, Cognitive Behavioral Analysis System of Psychotherapy, and Their Combination for Chronic Major Depression

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Summary:

Objective: Recently, we reported the acute-phase results of a 12-site national collaborative study investigating the therapeutic activity of nefazodone, Cognitive Behavioral Analysis System of Psychotherapy (CBASP), and their combination (COMB) for the treatment of chronic forms of major depression (CMD). Treatment with nefazodone had an earlier onset of effect compared to CBASP. COMB provided the highest response rate ever reported for this difficult-to-treat population. The advantage for continued treatment with COMB is unknown. Here we present the results from the continuation phase of this multiphase study.

Method: 681 patients meeting DSM-IV criteria for chronic depression were randomly assigned to receive 12 weeks of acute-phase treatment with nefazodone, CBASP, or COMB. 399 acute-phase remitters (HAM-D-24 total score ≤8) and responders (HAM-D-24 total score >8 but ≤15 with a 50% decrease from baseline) then received an additional 16 weeks of the same treatment they received in the acute phase (nefazodone up to 600 mg/day in two divided doses; CBASP every 2 weeks for the first 8 weeks and then monthly thereafter; or COMB). The primary efficacy measure was the HAM-D-24 administered by blinded raters.

Results: For patients entering continuation in remission, rates of symptom re-emergence were low (approximately 10%), and did not differ significantly across treatments. For those entering continuation as responders, substantial proportions became fully remitted (CBASP 46%, nefazodone 52%, COMB 53%). Furthermore, combination treatment seemed to protect against symptom re-emergence in this group. All three treatments were weight neutral over 28 weeks. Nefazodone treatment was not associated with any more weight gain than CBASP alone. Discontinuations due to adverse events were rare (<2% in all treatment groups).

Conclusion: Continuation treatment significantly improved remission rates achieved with acute-phase treatment. Combination treatment with nefazodone and CBASP during continuation treatment may prevent the re-emergence of symptoms among responders to acute phase treatment.

The study was supported by a grant from Bristol-Myers Squibb

NR389 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Neonatal Outcome Following Exposure to Lithium: What Happens to Lithium Babies?

Adele C. Viguera, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street/WAC 815, Boston, MA 02114*; Lee S. Cohen, M.D., Christopher J. McCarthy, B.A., Kaaren Bekken, Ph.D., Janet Sherman, Ph.D., Jennifer R. Poitras, B.A.

Cardioteratogenic effects of lithium exposure have been studied extensively, but risk of neurobehavioral sequelae of prenatal exposure to lithium still requires study. Accordingly, we compared neurobehavioral outcomes in preschool children who had or had not been exposed to lithium in utero.

Methods: Children (N = 20) aged 2.5 to 6.0 years (10 prenatally exposed to lithium, 10 not exposed) born to mothers with bipolar disorder were recruited at the Massachusetts General Hospital Perinatal and Reproductive Psychiatry Program. Subjects were evaluated, blind to their lithium exposure status, with age-appropriate standardized neurocognitive assessment instruments—either the Bayley Scales of Infant Development or the Wechsler Preschool and Primary Scale of Intelligence-Revised, and full scale IQ scores were normalized between instruments.

Results: The 10 children exposed to lithium in utero and 10 not exposed did not differ in age, sex, or ethnic distribution, and their mean IQ scores were 106 (SD = 90) versus 110 (SD = 14), respectively. There were also no significant group differences in clinically assessed temperament or distractibility or in risk of parent-reported behavioral/adjustment problems.

Conclusions: These preliminary results of a first systematic neurobehavioral comparison of lithium-exposed and nonexposed preschool children of women with bipolar disorder provide no evidence that lithium might induce lasting adverse effects on cognitive or behavioral development.

[Supported by a NARSAD Young Investigators Award; K23 MH01609]

NR390 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Prevalence of Comorbid Axis I Disorders in Bipolar and Major Depression

Jerrold F. Rosenbaum, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, ACC 812, Boston, MA 02114*; Shamsah B. Sonawalla, M.D., Roy H. Perlis, M.D., Jordan W. Smoller, M.D., Constance Guille, B.A., Gary S. Sachs, M.D., Maurizio Fava, M.D., Leslie J. Yan, B.A.

Summary:

Introduction: Previous studies have reported that comorbid axis I disorders are common among patients with bipolar disorder (BPD) and major depressive disorder (MDD) and may be associated with earlier age of onset.

Methods: We analyzed rates of comorbid axis I disorders among a sample of unipolar (N = 93) and bipolar I and II (N = 112) outpatients administered the SCID-I/P.

Results: We found that patients with BPD had a greater mean number of comorbid axis I diagnoses compared to patients with MDD (2.5 [SD = 2.1] and 1.9 [SD = 1.6], respectively; $t = -2.4$; $p < 0.05$). Specific diagnoses with greater prevalence among the bipolar sample included lifetime substance abuse or dependence (excluding alcohol) (71% BPD versus 29% MDD; $\chi^2 = 8.7$; $p < 0.01$) and lifetime panic disorder (75% of BPD versus 25% of MDD; $\chi^2 = 13.2$; $p < 0.001$); these remained significant after adjusting for age and gender in a logistic regression. Age of onset of affective illness was significantly earlier among BPD patients compared to patients with MDD (18.4 years [SD = 13.8] versus 25.0 years [SD = 2.1], respectively; $t = 2.8$; $p < 0.01$) but was not associated with number of comorbid diagnoses.

Conclusion: Our data suggest that comorbid axis I disorders, particularly panic and substance use disorders, are more common among patients with BPD compared to patients with MDD.

Funding: Millenium Pharmaceuticals, Inc.

NR391 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

GAD in Patients with MDD

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Iwona Chelminski, Ph.D.

Summary:

Objective: In the present report from the Rhode Island Methods to Improve Diagnostic Assessment and Services (MIDAS) project we compared the demographic, clinical, psychosocial, and family history characteristics of three nonoverlapping groups of patients with a principal diagnosis of MDD: 1) those with coexisting DSM-IV GAD; 2) those who met all GAD criteria except for the exclusion criterion that the symptoms were not limited to the time of the mood disorder (modified GAD); and 3) those without DSM-IV GAD or modified GAD.

Methods: Three hundred thirty-two depressed outpatients were evaluated with a comprehensive diagnostic interview (including a family history and psychosocial functioning assessment).

Results: Sixty-four patients had DSM-IV GAD, and 48 were diagnosed with modified GAD. There were no differences between the three groups on demographic variables. The depressed patients with modified GAD were more severely depressed than the no GAD group on both interview and self-report measures of depression severity. Both anxiety disorder groups had higher levels of suicidal ideation. Depressed patients with DSM-IV and modified GAD had poorer current and adolescent social functioning than the no GAD patients. Compared to the no GAD patients, the modified GAD group was more likely to have missed some time from work during the last 5 years, and their GAF scores were significantly lower. Both the DSM-IV and modified GAD groups were diagnosed with significantly more current axis I disorders than the no GAD patients, and both GAD groups were twice as likely to have two or more comorbid disorders. The morbid risk of GAD in patients first-degree relatives was higher in both groups of GAD patients compared to the no GAD group. The two GAD groups did not differ from each other on any variable.

Conclusions: Our findings raise questions about the validity of the DSM-IV hierarchical relationship between MDD and GAD and suggest that the exclusion criterion should be eliminated.

NR392 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Screening for PTSD in a General Outpatient Psychiatric Setting

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Thomas Sheeran, Ph.D.

Summary:

Objective: Findings from this and other sites suggest that PTSD may be underdiagnosed in settings where trauma is not the presenting problem. Thus, a PTSD screening scale might have utility in routine clinical settings. The goals of this report from the Rhode Island Hospital Methods to Improve Diagnostic Assessment and Services (MIDAS) Project was to evaluate the diagnostic performance of the Posttraumatic Diagnostic Scale (PTDS) in a general psychiatric setting. Of particular interest was whether the instrument performed as well in detecting PTSD when it was an additional, comorbid disorder, rather than the principal reason for seeking treatment.

Methods: Participants were psychiatric outpatients (N = 774) presenting for treatment at the Rhode Island Hospital Department of Outpatient Psychiatry. Patients completed a self-report PTSD scale (Foa et al., 1997) and were interviewed with the Structural Clinical Interview for DSM-IV (SCID).

Results: Of the 774 patients in our sample, 87 (11.2%) were diagnosed with current PTSD by SCID interview. Twenty-seven (3.5%) had PTSD as the principal diagnosis, and 60 (7.8%) had PTSD as an additional diagnosis. The scale was almost as sensitive in detecting PTSD cases when it was not the principal diagnosis (88%) as it was in detecting PTSD cases when it was the principal diagnosis (93%).

Conclusion: The primary purpose of screening is to identify patients who may be likely to suffer from symptoms of a given disorder. A screening measure will be particularly useful when the symptoms of the disorder in question are not the main reason the patient is seeking treatment. Our results suggest a screening instrument for PTSD is as good at recognizing PTSD as an additional disorder as it is in identifying patients who have PTSD as their principal diagnosis.

NR393 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Factors Influencing Psychiatrists' Choice of Antidepressants: A Prospective Study

Mark Zimmerman, M.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Michael A. Posternak, M.D., Steven Singer, M.D., Naureen Attiulah, M.D., Rahman Shazad, M.D., Scott E. Baymiller, M.D., Kerstin K. Uy, M.D.

Summary:

Objective: Numerous studies have searched for predictors of preferential antidepressant treatment response with, at best, modest success. With a wide array of antidepressants to choose from, there is thus little empirical data guiding the clinician in choosing an antidepressant. The goal of the present study was to prospectively examine the factors considered by psychiatrists at the time an antidepressant is selected.

Methods: The Factors Associated with Antidepressant Choice Survey (FAACS) lists 43 items that might be considered when selecting an antidepressant. The list includes clinical factors (e.g., symptom profile/target symptoms, depression subtype, comorbid conditions), demographic variables, medication properties (e.g., side effects, half-life, dosing frequency), and insurance considerations (e.g., formulary, co-pay), and other miscellaneous items. The FAACS was completed by psychiatrists immediately after the patient encounter. To date, psychiatrists have completed the FAACS on 121 depressed outpatients presenting for treatment.

Results: The factors most frequently considered by psychiatrists when selecting an antidepressant were symptom profile (73.6%), the presence of a comorbid condition (64.5%), and side effect profile (50.4%). Of the specific vegetative symptoms of depression, the presence of insomnia most frequently influenced antidepressant selection (36.4%). Generalized anxiety disorder and panic disorder were the comorbid disorders that most frequently influenced antidepressant choice (34.7% and 25.6%, respectively). The side effects that psychiatrists most frequently hoped to avoid were sexual dysfunction, weight gain, fatigue, and agitation.

Conclusions: Although antidepressants are generally considered equally effective, and there is little literature identifying patient characteristics associated with preferential response to one AD over another, psychiatrists routinely base their treatment selection on patients' clinical profile.

NR394 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Vagus Nerve Stimulation (VNS) in Outpatients with Treatment-Resistant Depression

Ziad Mahas, M.D., *Department of Psychiatry, MOSC, 171 Ashley Avenue, Charleston, SC 29925*; Harold A. Sackeim, Ph.D., A. John Rush, M.D., Mark S. George, M.D., Lauren B. Marangell, M.D., Sarah H. Lisanby, M.D., Mustafa M. Husain, M.D.

Summary:

We completed an extension of the original open pilot study (N = 30) of VNS in treatment-resistant depression, now with a total sample of 60 subjects. VNS was given for a total of 10 weeks, following a 2–4 week pre-implantation baseline period and a 2-week post-surgical device implantation recovery phase. Subjects were maintained on stable medication regimens, and 2 of the 10 treatment weeks were used for stimulation dose adjustment. All 60 subjects had nonpsychotic major depressive (N = 44) or bipolar I (N = 6) or II (N = 10) disorder in the depressed phase. One patient was a placebo responder and did not receive stimulation during the acute study.

In this treatment-resistant sample (N = 59), response rates were 30.5% (50% reduction in HRSD28 total score); 27% had a partial response (25–49% reduction in HRSD28); and 15.3% had a full response (HRSD28 score ≤10 at study exit). Response rates and partial response rates were similar using the Montgomery-Asberg Depression Rating Scale (MADRS).

Response was not related to the amount of VNS output current. VNS seemed to be particularly effective among patients with moderate treatment resistance. Adverse events were similar to those reported with the use of VNS in treatment-resistant epilepsy. A randomized, blinded, comparative trial of VNS versus sham (delayed) VNS is underway.

NR395 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Early Mood Symptoms in Children of Bipolar Parents Versus Controls: Preliminary Results

Cesar A. Soutullo, M.D., *Department of Psychiatry, University Clinic, A P 4209, University of Navarra, Pamplona 31080, Spain*; Melissa P. DelBello, M.D., Patricia McDonough-Ryan, M.A., Kathleen A. Lake, M.S.W., Teresa Pereda, R.N., Susan L. McElroy, M.D., Stephen M. Strankowski, M.D.

Summary:

Objective: Children of bipolar (BP) parents are at higher risk of developing mood disorders than the general population. Our goal was to evaluate DSM-IV psychiatric symptoms in children of BP parents to identify indicators of early-onset bipolar illness.

Method: We evaluated 24 children of BP parents and 13 controls using the Washington University Kiddie & Young Adult Schedule

for Affective Disorders & Schizophrenia for DSM-IV (WASH-U-KSADS) and 1996-K-SADS-PL given to mothers and children separately. Reliable raters (K > 0.9), trained by Barbara Geller, M.D., were blind to group, and groups were matched for age, sex, and race.

Results: Some WASH-U-KSADS lifetime symptoms were significantly more frequent (Mann-Whitney's U: $p < 0.05$) in high-risk children vs. controls (mean ± SD age: 10.6 ± 3 vs. 10.3 ± 1 years). These symptoms included mania symptoms (elation, irritability, grandiosity, increased activity, and increased speech); depressive symptoms (depressed mood, irritability, withdrawn, decreased energy, insomnia, hipersomnia, and increased appetite); and symptoms of oppositional defiant disorder.

Conclusion: Specific manic or depressive symptoms (especially irritable or depressed mood, grandiosity, low energy and defiance of rules, $p < 0.01$) may appear early in children at risk for BP disorder. Identification of early symptoms of BP illness may help earlier diagnosis and treatment.

Supported by a Grant from the Theodore & Vada Stanley Foundation.

NR396 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Affective Symptoms Across the Menstrual Cycle in Women with Bipolar Disorder

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Summary:

Retrospective assessments suggest that mood symptoms vary across the menstrual cycle in a high percentage of women with bipolar illness. However, the relationship between specific cycle phases and the direction of mood shifts has not been well studied.

Methods: Three women with bipolar disorder were prospectively followed for up to 250 days using the Columbia Daily Bipolar Symptom Scale. Data from multiple menstrual cycles were averaged and repeated measures ANOVA used to evaluate within-subject changes in mood across the menstrual cycle (divided into early and late follicular and luteal phases).

Results: All subjects showed significant effects of menstrual phase on depressed mood, energy level, irritability, anxiety, and functional impairment. Two subjects also demonstrated significant effects of phase on mood elevation. The pattern of change across the cycle for all of the subjects included worsening of depressive (and associated) symptoms in the early follicular phase and worsening of mood elevation and energy level in the late follicular phase. All mood symptoms improved in the luteal phase.

Conclusion: These preliminary data shows that menstrual cycle phase has significant effects on mood in bipolar women and that the pattern of these effects differs strikingly from that seen in PMDD.

NR397 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Reproductive Choices Among Women with Bipolar Disorder

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Summary:

Introduction: Management of bipolar disorder during pregnancy and the postpartum period poses several clinical dilemmas to bipolar women and their clinicians. Historically, concern has focused on known and unknown teratogenic effects of psychiatric medications used to treat this disorder (Cohen 1994) and neonatal outcome following fetal exposure to these medications. More recent studies have also investigated risk for relapse of bipolar illness during pregnancy (Viguera 2000) and attitudes regarding prenatal genetic testing for bipolar disorder (Trippitelli 1998). However, to our knowledge, no studies have investigated the clinical and psychosocial factors that contribute to family planning decisions made by bipolar women.

Methods: A self-report survey was administered to 106 women with bipolar disorder in order to ascertain information regarding decisions about pregnancy and attempts at conception. Subjects had previously been seen through our perinatal consultation service with regard to potential management and course of bipolar illness during pregnancy. Information collected included demographic variables, illness history, reproductive history, reasons for seeking consultation, and ultimate decisions made regarding attempts to conceive.

Results: The majority of the sample reported having been discouraged from becoming pregnant by a physician or family member prior to the consultation. Almost half were pregnant either at the time of the consultation or at post-consultation follow up. Among women who decided not to become pregnant, the most common reasons were concern about risk for relapse during the antenatal or postpartum period and/or fear of the effects of prenatal exposure to mood stabilizers.

Conclusions: Many factors may influence bipolar women in their decisions about whether to pursue pregnancy. Providing accurate information to these women allows for thoughtful treatment decisions that take into account both research data and the individual wishes of patients.

NR398 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Sorting Types of Depression in Cancer Patients

Thomas P. Beresford, M.D., *Department of Psychiatry, VAMC/ University of Colorado, 1055 Clermont Street, Denver, CO 80220*; Leah Widger, B.S., Allyson Miller, B.S., Heather Romero, B.S., Brandon K. Martin, B.A.

Summary:

Objective: Depression is a frequent condition among cancer patients. Sorting neurochemical disorders, amenable to medication, versus adaptive disorders, addressed in psychotherapy, has been perplexing due to symptom overlap. Viewed as an adaptation challenge, we hypothesized that patients using less flexible defense mechanisms would endorse depressive symptoms more often than those who use more mature coping styles.

Method: We interviewed 72 stage III and IV cancer chemotherapy patients using the Defense Style Questionnaire and the Beck Depression Inventory. The mixed gender (37 females, 35 males) group was in middle age (55.7 ± 13.1 years). We then sought statistical associations between defense style endorsement and depressive symptoms.

Results: The 31 patients reporting frequent somatic symptoms of depression demonstrated a positive correlation with immature defense mechanisms ($p < 0.05$) and a negative correlation with mature mechanisms ($p < 0.05$). Conversely, the 17 patients reporting few or no somatic symptoms of depression presented a significant correlation between low BDI scores and the frequencies of both mature and neurotic defense styles ($p < 0.025$, respectively).

Conclusion: These data suggest that adaptive styles play a major role in depression related to cancer. Assessment of this phenomenon may lead to a more focused use of antidepressant medications in this patient group.

NR399 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Assessing Cognitive Deficits in Mood Disorders: Are Self-Reports Valid?

Katherine E. Burdick, M.A., *Department of Psychiatry, New York Presbyterian at Cornell, 525 East 68th Street, New York, NY 10021*; Carrie J. Endick, C.S.W., Joseph F. Goldberg, M.D.

Summary:

Background: Domains of cognitive function are an important aspect of mental status in psychiatric illnesses, particularly since many patients report subjective experiences of attentional and memory dysfunction. However, the lack of easily administered screens for subtle cognitive deficits may limit the extent to which practitioners routinely evaluate this area. We piloted a screening packet of self-reports for cognitive dysfunction, co-administered with a standard, brief neuropsychological battery, in a cohort of affectively ill adults.

Method: Fifty affectively ill outpatients completed three self-administered inventories of cognitive complaints (Cognitive Complaints Questionnaire, Cognitive Deficits Scale, and Patient's Own Assessment of Functioning). Affective symptoms were rated by Young Mania Rating scores (Y-MRS) and 31-item Hamilton Depression scores (HAM-D), along with objective neuropsychological tests (WAIS-III digit span, WAIS-III digit symbol, Stroop, California Verbal Learning Test (CVLT), and Trails A & B). Concurrent validity was assessed between the various self- and clinician-rated assessments of attention, concentration, learning, and memory.

Results: (1) For the cohort (mean HAM-D = 18.6, Mean Y-MRS = 4.3), about 40% had clinically significant impairment in cognitive flexibility by either self-report or objective measures. (2) Stroop interference scores correlated most highly with self-assessment ($r = -.77$, $p < .05$), when controlling for mood state. (3) WAIS-III Digit Symbol and the Recognition measure on the CVLT were also negatively correlated with scores on cognitive self-reports ($r = -.73$, and $r = -.71$ respectively, $p < .05$).

Conclusions: Brief batteries of easily self-administered ratings can help practitioners detect the presence of clinically significant cognitive impairment in affectively ill patients, even while accounting for the presence of current mood symptoms.

NR400 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Safety and Tolerability of Lamotrigine in Controlled Mood Disorder Trials

John A. Ascher, M.D., *GlaxoSmithKline, 5 Moore Drive, Research Triangle, NC 27709*; Stewart Barnett, Sharyn Batey, Ph.D., Terence A. Ketter, M.D., Charles E. Meredith, M.D., Peter D. Londborg, M.D., Scott A. West, M.D.

Summary:

Objective: Substantial use of lamotrigine (LTG) in epilepsy indicates that the drug is well tolerated, but increasing use of the drug for psychiatric indications makes it important to ascertain the safety profile of LTG in the latter population. This paper examines safety data from double-blind, placebo-controlled studies of LTG in the treatment of affective disorders.

Methods: Adverse events reported for 760 patients randomized to monotherapy with lamotrigine for seven to ten weeks in five depression studies (GW 602, 603, 613, 20022, and 20025) and two mania studies (GW609 and GW610) are compared with incidence observed with placebo (PBO, n = 708) or active comparators.

Results: For depression studies, the percentage of patients reporting any adverse event and the incidence of nearly all events was similar for PBO and LTG and higher for desmethylimipramine. For mania studies LTG and PBO safety and tolerability were also similar. Serious adverse events were infrequent with LTG and did not include rash. There were no significant changes in body weight.

Conclusion: These data represent one of the largest safety databases to include placebo-controlled, monotherapy treatment of bipolar disorder, and indicate that lamotrigine at daily doses of 50-400mg is well tolerated in patients with mood disorders.

Research funded by GlaxoSmithKline

NR401 Tuesday, May 8, 2001, 03:00 p.m.-05:00 p.m.

New Data Confirming the Importance of Dosing and Rash with Lamotrigine

John A. Messenheimer, M.D., *GlaxoSmithKline, 5 Moore Drive, Research Triangle, NC 27709*; John A. Ascher, M.D., Nancy L. Earl, M.D.

Summary:

Objective: Due to the large increase in the number of patients enrolled in lamotrigine (LTG) clinical trials over the past three years, a re-examination of the LTG clinical trial database was warranted to better understand the relative risk of serious rash with this new agent for the treatment of bipolar disorder.

Methods: The incidence of serious rash (defined as any skin reaction associated with patient hospitalization and LTG discontinuation, or any case reported as possible Stevens-Johnson syndrome [SJS] or toxic epidermal necrolysis [TEN]) was examined in all controlled clinical trials conducted in adults. The effect of dosing regimen was also examined.

Results: From a datebase including 10,611 adult patients (2,645 of them bipolar patients), 28 (0.26% or 2.6 per 1000 patients) had rash classified as serious and 11 (0.10% or 1/1000) had rash classified as SJS (none as TEN). Of the 5,798 adult patients (2,469 of them bipolar patients) for whom current dosing guidelines were utilized, the corresponding incidence rates for serious rash and SJS were 0.12% (1.2/1000) and 0.05% (0.5/1000), respectively.

Conclusion: These controlled data demonstrate a clear effect of dosing on the incidence of serious rash (including SJS) with LTG.

Research funded by GlaxoSmithKline.

NR402 Tuesday, May 8, 2001, 03:00 p.m.-05:00 p.m.

Bupropion Associated with Less Sexual Dysfunction Than Sertraline or Fluoxetine

R. Taylor Segraves, M.D., *Department of Psychiatry, Case Western Reserve University, 2500 Metro Health Drive, Cleveland, OH 44109-1998*; Charles C. Coleman, M.D., Harry A. Croft, M.D., Sharyn Batey, Ph.D., John A. Ascher, M.D., Carolyn Watson, Ph.D., Benjamin King

Summary:

Objective: To present sexual functioning results from two placebo-controlled studies comparing bupropion sustained-release (SR) with sertraline (Studies 4001 and 4002) and one placebo-controlled study comparing bupropion SR with fluoxetine (Study 4007).

Methods: Outpatients with normal sexual functioning experiencing moderate to severe recurrent major depression were randomized to receive bupropion SR, placebo, or sertraline (Studies 4001 and 4002) or fluoxetine (Study 4007) for eight weeks.

Results: A total of 1,180 patients were randomized to treatment (392 bupropion SR, 237 sertraline, 154 fluoxetine, 397 placebo). Bupropion SR was associated with a lower incidence of orgasm dysfunction ($p<0.001$) from days 7–56 compared with sertraline and days 14–56 compared with fluoxetine. Within each study, active treatments were similarly effective in treating depression. All antidepressants were well tolerated.

Conclusions: Bupropion SR was associated with a significantly lower incidence of orgasm dysfunction than fluoxetine and sertraline in all three placebo-controlled clinical studies. Bupropion SR and the SSRIs had similar efficacy in the treatment of depression.

Research funded by GlaxoSmithKline.

NR403 Tuesday, May 8, 2001, 03:00 p.m.-05:00 p.m.

Lamotrigine Demonstrates Long-Term Mood Stabilization in Manic Patients

Joseph R. Calabrese, M.D., *Department of Psychiatry, University Hospital of Cleveland, 11400 Euclid Avenue, Suite 200, Cleveland, OH 44106*; Charles L. Bowden, M.D., Joseph DeVeaugh-Geiss, M.D., Nancy L. Earl, M.D., Laszlo Gyulai, M.D., Gary S. Sachs, M.D., Paul Montgomery

Summary:

Objective: Lamotrigine, an established anticonvulsant drug, has recently demonstrated efficacy in double-blind, controlled clinical trials in bipolar depression and rapid cycling bipolar disorder. The current study was designed to evaluate the long-term efficacy and safety of lamotrigine as a mood stabilizer in preventing relapse in patients who had recently experienced a DSM-IV manic episode.

Methods: GW Study #606 was a multicenter, double-blind, placebo-controlled, flexible-dose study conducted in bipolar I outpatients. A total of 349 subjects were entered into a preliminary open-label phase during which lamotrigine (100–400 mg/day) was added to current therapy for up to 16 weeks followed by withdrawal to lamotrigine monotherapy. A total of 175 patients achieving stabilization (defined as CGI-S $\leq$ 3 for four consecutive weeks) were randomized to lamotrigine, lithium, or placebo and followed for up to 18 months. Primary efficacy variable was Time (from randomization) to Intervention for a Mood Episode (TIME).

Results: Lamotrigine and lithium demonstrated evidence of long-term mood stabilization indicated by statistically and clinically significant differences from placebo on TIME and other indices of stability and illness relapse. Lamotrigine therapy was well tolerated in this patient population, with low risk of mania exacerbation or weight gain.

Research funded by GlaxoSmithKline.

NR404 Tuesday, May 8, 2001, 03:00 p.m.-05:00 p.m.

Racemic (S,S)-Reboxetine Has Exceptional Selectivity for the Norepinephrine (NE) Transporter

Erik H.F. Wong, Ph.D., *Department of Neurobiology, Pharmacia Upjohn Corporation, 301 Henrietta Street, Kalamazoo, MI 49007*; Paula M. Tinholt, B.A., Patrick R. McFinton, B.S., Luz A. Cortes-Burgos, M.A., Susan G. Amara, Ph.D., Mark S. Sonders, Ph.D.

Summary:

Reboxetine is the first potent, selective, and specific norepinephrine reuptake inhibitor (NRI). It has superior pharmacological selectivity to existing tricyclic antidepressants and selective serotonin reuptake inhibitors when tested in a large number of in vitro and in vivo systems (Wong et al, 2000). We believe this pharmacological profile drives the efficacy and side-effect characteristics of this antidepressant. Reboxetine belongs to a class of compounds known as alpha-aryloxy-morpholines, and is composed of (S,S)-(+) and the (R,R)-(–) enantiomers. Given the fact that previous evaluations of uptake selectivity were based on the racemic mixture, it is important to establish potency and selectivity of these individual enantiomers. Studies were carried out by radioligand binding studies in rat brain membranes and functional studies using Madin-Darby canine kidney (MDCK) cell lines expressing stable human norepinephrine (hNET) or human serotonin transporters (hSERT). In the case of binding studies [^{3}H]nisoxetine and [^{3}H]citalopram were used to label NET and SERT, respectively. (S,S), racemic and (R,R) reboxetine exhibited an affinity of 0.23, 1.6, and 7.0 nM at NET and 2940, 130, and 100 nM at SERT, giving rise to a selectivity ratio of 12770, 80, and 15. The corresponding selectivity values based on the functional studies in human transporters are: 3112, 34, and 40, respectively. These data demonstrate for the first time the superior affinity and selectivity of (S,S)-reboxetine. It also suggests the possibility that (S,S)-reboxetine could be the enantiomer that provides the novel pharmacology of racemic reboxetine. (S,S)-reboxetine constitutes the most potent and selective NRI reported.

NR405 Tuesday, May 8, 2001, 03:00 p.m.-05:00 p.m.

Limitations of Current Antidepressants in Older Patients with Depression

William S. Edell, Ph.D., *Mental Health Outcomes, 1500 Waters Ridge Drive, Lewisville, TX 75057-6011*; Kevin W. Mayo, Ph.D., Roy I. Sandoval, R.Ph., Karen I. Bailey, Pharm.D., Bryan E. Adams, Ph.D., Sarah E. Jensik, M.S.

Summary:

While current antidepressants are reasonably effective in ameliorating depressive symptomatology, less is known about their impact on common areas of deficit, including cognition, maladaptive behaviors, and instrumental activities of daily living (IADLs).

Objective: To examine changes in cognition, maladaptive behaviors, and IADLs of geropsychiatric patients with major depression (ICD-9-CM codes 296.20–296.36) treated with fluoxetine, mirtazapine, sertraline, or venlaxafine.

Method: Data were obtained from the CQI+^{sm} Outcomes Measurement System, an ORYX/JCAHO-accepted performance improvement system, which tracked patients admitted to geropsychiatric inpatient programs in 111 general hospitals across 33 states between 1997–1999. The instruments used to measure cognition, maladaptive behaviors, and IADLs were the Mini-Mental State Examination (MMSE), Psychogeriatric Dependency Rating Scale (PGDRS), and Duke Multidimensional Functional Assessment of Older Adults, respectively. One-way analyses of variance and, if significant, Tukey's pairwise comparisons, compared medication groups on changes across admission, discharge, and three-month follow-up.

Results: At admission, patients exhibited moderate to severe impairment in all three dimensions measured. Measured groups were indistinguishable on change scores with only modest improvement observed, if any.

Conclusions: Antidepressants in this analysis were associated with modest improvement, suggesting the need for new treatment modalities that enhance cognition, behaviors, and functioning along with depressive symptomatology. Further controlled studies are needed.

NR406 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Symptomatic Subsyndromal Depressive Disorders and Quality of Life

Marco De Murtas, M.D., *Department of Psychiatry, University of La Sapienza, Via Panama 68, Rome, IT 00198, Italy*; Paolo Girardi, M.D., Koukopulos Athanasios, M.D., Roberto Tatarelli, M.D.

Summary:

Objective: Epidemiological studies have established that subsyndromal depression is associated with a significant reduction in quality of life. Nevertheless, there are few data to inform how to treat these patients. This pilot study attemps to better define this issue.

Method: Fifty outpatients (36 women, 14 men; mean age 34.6) presenting two or more symptoms of the "alternative research criterion B for dystimic disorder" excluding the 'A' criteria, for a period of over two years, were recruited from primary care settings and were studied in a open-label treatment with sertraline 50–100 mg/day for 16 weeks. The criteria for inclusion in the study were a HAM-17 score of 7 or less and a POMS score of 50 or less. Improvement in quality of life was assessed by Q-LES-Q before starting treatment and at endpoint.

Results: At the end of the treatment patients had shown a significant improvement in the Q-LES-Q score (p<.001).

Conclusion: Since we found a high rate of family history for mood disorder and significant improvement with treatment with SSRI, this study proposes the inclusion of these long-term subsyndromal disorders as a subtype of depressive disorder.

NR407 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Efficacy of Reboxetine Treatment of SSRI-Resistant Panic Disorder

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Summary:

Objective: While selective serotonin reuptake inhibitors (SSRIs) are currently the first-line pharmacotherapy for panic disorder (PD), up to 30% of patients either do not respond to SSRIs or withdraw due to adverse events. Reboxetine, a selective norepinephrine reuptake inhibitor, is effective in treating depression and may alleviate depression-related anxiety. This study aimed to investigate the efficacy of reboxetine in treating patients with PD who fail to respond to SSRIs.

Method: In this six-week, open-label study, 29 adult outpatients with PD who failed to respond to SSRI treatment received reboxetine 2 mg/day, incremented to a maximum of 8 mg/day over the first 10 days. Efficacy was assessed—by a rater blinded to drug treatment—using the Panic Self-Questionnaire (PSQ), the Hamilton Rating Scale for Anxiety (HAM-A), the 17-item Hamilton Rating Scale for Depression (HAM-D), and the Global Assessment of Functioning (GAF) Scale.

Results: The 24 patients (83%) who completed the study responded well to reboxetine treatment. Significant improvements (p<0.001) were observed in the number of panic attacks experienced per day (PSQ), anxiety (HAM-A), depression (HAM-D), and functioning (GAF). Five patients withdrew due to adverse events.

Conclusions: Reboxetine was effective in the treatment of SSRI-resistant PD and warrants further clinical investigation.

NR408 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Augmentation with the Selective Noradrenaline Reuptake Inhibitor (SNRI) Reboxetine in SSRI-Resistant MDD

Christopher J. Hawley, M.D., *Department of Mental Health, QE II Hospital, Howlands, Welwyn Garden City AL7 4HQ, United Kingdom*; Thanusha Sivakumaran, B.S.C., Alison Munns, M.B., Jonathon A. Bevan, M.B., Monicka A. Ochocki, M.B.

Summary:

Objectives: A relatively high proportion of patients (20%–45%) with major depressive disorder (MDD) fail to respond adequately to their initial treatment. In this six-week, open-label study, 24 adult patients who had failed to achieve remission under monotherapy with a selective serotonin reuptake inhibitor (SSRI), at an adequate dose for a minimum of four weeks, received reboxetine 4 mg/day (increased to 8 mg/day at Week 2), plus their previous dose of SSRI.

Methods: SSRI treatment included paroxetine (20–40 mg/day), sertraline (50–100 mg/day), fluoxetine (20 mg/day), or citalopram (20–40 mg/day). Effectiveness was evaluated using the Montgomery–Ansberg Depression Rating Scale (MADRS). Adverse events were recorded contemporaneously.

Results: The mean total MADRS score decreased from 24 (baseline) to 15 (Week 6) points among the 20 patients who completed the study, with nine patients achieving remission (ie MADRS score<10). The most frequently reported adverse events were insomnia (n=13), sweating (n=12) and constipation (n=11). Four patients (17%) completed the study on lower doses of reboxetine (typically 6 mg/day) and four (17%) withdrew due to adverse events.

Conclusions: Coadministration of reboxetine and an SSRI proved effective and well tolerated in SSRI-resistant patients and warrants further clinical investigation.

NR409 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Prevalence of Bipolar Disorder in Women with Polycystic Ovary Syndrome

Kim Gottlieb, M.D., *Department of Psychiatry, New York Presbyterian Hospital, 525 East 68th Street, Box 140, New York, NY 10021*; Joseph F. Goldberg, M.D.

Summary:

Background: To investigate the hypothesis that an intrinsic association may exist between bipolar affective disorder (BAD) and polycystic ovary syndrome (PCOS), we screened lifetime affective symptoms in an outpatient cohort of women with known PCOS. In the literature this link has been attributed to valproate use.

Method: A total of 78 women (mean (SD) age = 33.0 (6.7), range 16–48 years) previously diagnosed with PCOS (at a mean (SD) age of 26.7 (7.5) years) completed the Mood Disorder Questionnaire (MDQ), a new, validated, 13-item self-administered screen for bipolar illness.

Results: (1) 27% of subjects had either a previous diagnosis of bipolar disorder or a MDQ score above the threshold of clinical significance. This represents a 30-fold greater prevalence of BAD than seen in the general population); (2) 29% of subjects had a positive family history of BAD, and 15% had comorbid hypothyroidism; (3) 63% of subjects with above-threshold MDQ ratings had received a previous diagnosis of bipolar disorder (p<.01); modest, significant agreement was observed between MDQ screen-positive ratings and subjects' having previously received a diagnosis of bipolar illness (kappa=.28, 95% CI=0.03–0.53); (4) half of subjects had a prior formal psychiatric diagnosis (79% affective disorder); among subjects scoring above threshold on the MDQ, 92% had no exposure to valproate prior to their PCOS diagnosis.

Conclusions: These findings suggest a higher rate of bipolar spectrum disorders among women with PCOS than would be expected in the general population, independent of an association with valproate use that has been mentioned in the literature. This newly discovered association between an endocrinopathy and bipolar illness, independent of medication use, is suggestive of a possible shared neuroendocrine defect of the HPA axis.

NR410 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Response Rate and Onset of Action of Sertraline Treatment of Outpatients with Major Depressive Episodes (MDE)

Julien D. Guelfi, M.D., *Department of Psychiatry, St. Anne Hospital, 100 Rue De La Sante, Paris 75674, France*; Serge Friedman, Sylvie Lancrenon, Veronique Millet

Summary:

Objectives: As the efficacy of sertraline has been previously confirmed in MDE, the objective of this study was to evaluate response rate, onset of action, and safety of sertraline in naturalistic conditions.

Methods: Patients presenting a MDE according to the DSM-IV criteria with a minimal score of 18 on HAM-D (17 items) entered this eight-week, open study. Patients received sertraline 50 mg/day during at least three weeks; after this period the dose could be increased if necessary, by steps of 50 mg up to 200 mg. Patients were evaluated at W0, W1, W3, W6, and W8, and were classified as responders according to the predefined criteria: much or very much improved on the CGI-improvement scale.

Results: Among the 2,116 included patients, 449 dropped out due to personal decision (46), noncompliance (46), lost of follow-up (100), adverse event (207), and non-efficacy (50); thus, there were 1,656 completers after eight weeks of treatment. At baseline the mean age was 42.6 +/−12.1 years with 65.4% of female. The baseline score on the HAM-D 17 items was 25.3 +/−5.3. On the 1,656 completers patients, 6.3% patients were sustained responders (SR) at W1. After the first three weeks, profile response showed an early CGIi response (i.e 39.2% SR) with 50 mg/day. At W6, 26.8% patients received 100 mg/day, while 73.2% were maintained under 50 mg/day; there were 67.1% SR. At W8, 66.6% of the patients were still under 50 mg/day, while 28.8% received 100 mg/day and 4.5% received 150 mg/day. At the end of the study, 78.1% of patients were SR, 6.8% had a fluctuant response, and 15.1% were resistant. Sertraline was well tolerated: out of 2,116 included patients, 207 (9.8%) dropped out due to adverse events. Among completers, digestive disorders (16.6%), mainly nausea (12.2%) and diarrhea (5.3%), were the most frequently reported adverse event.

Conclusion: At the end of this eight-week trial, 78.1% of the patients were responders and 75% of them were treated by 50 mg/day of sertraline. These results are in line with previous published data.

NR411 Tuesday, May 8, 2001, 03:00 p.m.-05:00 p.m.

Reboxetine Yields Symptomatic and Functional Improvement in Unipolar Depression

Heather V. Krell, M.D., *Department of Psychiatry, UCLA-Neuropsychiatry, 760 Westwood Plaza, 37-426, Los Angeles, CA 90024*; Ian A. Cook, M.D., Michelle Abrams, R.N., Koren Hanson, M.S., Tina Tolbert, B.S., Andrew F. Leuchter, M.D.

Summary:

Objective: To evaluate reboxetine in major depression

Method: Nine-week, single-blind study enrolling 25 adults (ages 18–65).

After a one-week placebo lead-in, subjects meeting DSM-IV criteria for major depressive disorder began reboxetine at 4mg BID. After four weeks, those not responding advanced to 10mg (given in divided doses). Seventeen subjects completed the protocol (two excluded for placebo response; six for side effects). Thirteen subjects underwent the dosage increase, with four subsequently returning to the original dose. The current episode's duration was 10.4 ± 14.2 years, with an average of 5.8 ± 10.7 prior depressions.

Results: Using response criterion of HAM-D ≤ 10, 11 subjects (65%) responded, five subjects at 8mg and six at 10mg. Social functioning improved, with changes in the Social Adaptation Self-Evaluation Scale (SASS) of 22% for responders. Responders also showed improved psychomotor activity, with an average decrease in the Salpetriere Retardation Rating Scale (SRRS) of 52%. On Q-LES-Q quality of life subscales, responders uniquely showed significant improvements in general activities, social relations, leisure activities, feelings, and work.

Conclusion: These data indicate that reboxetine is effective in treating major depressive disorder. Even in these subjects with chronic recurrent illness, improvement was seen in severity of depression, social functioning, and psychomotor activity.

NR412 Tuesday, May 8, 2001, 03:00 p.m.-05:00 p.m.

Psychiatric Morbidity in Chinese Stroke Patients

Wai-Kwong Tang, M.D., *Department of Psychiatry, Chinese University, Prince of Wales Hospital, Shatin, N.T., Hong Kong, SAR, China*; Gabor S. Ungvari, M.D., Helen F.K. Chiu, M.B., Kai-Hoi F. Sze, M.D., Jean Woo, Richard Kay

Summary:

Objective: There is a paucity of data on poststroke psychiatric morbidity in Chinese populations. We examined the prevalence and risk factors of poststroke psychiatric morbidity in Chinese first-ever stroke patients covering depressive and anxiety disorders, mania, and psychosis.

Method: 157 subjects consecutively admitted to a rehabilitation unit participated in this prospective, cross-sectional study. Psychiatric diagnoses were made using the SCID-DSM-III-R. Each subject's cognitive function, neurological status, and level of functioning were also measured.

Results: The prevalence of all depressive disorders was 17.2%. Major depressive episodes, adjustment disorder with depressed mood, dysthymia, and generalized anxiety disorder were diagnosed in 7.6%, 8.2%, 1.3%, and 0.6% of the subjects, respectively. No cases of mania, psychosis, or other anxiety disorders were found. Only the Barthel Index score on admission predicted the development of depression, while age, sex, family, past psychiatric history, and laterality of lesion were not significant predictors. The diagnosis of depression was not a statistically significant predictor of the functional outcome of stroke. Age, degree of neurological deficit, and cognitive status predicted the subjects' level of functioning at discharge.

Conclusions: The low morbidity of affective disorders and their limited impact on functional outcome measures in Chinese first-ever stroke patients warrants further investigation.

NR413 Tuesday, May 8, 2001, 03:00 p.m.-05:00 p.m.

Efficacy and Tolerability of Sertraline in Treating Anxious Depression

Nicholas Demartinis, M.D., *Department of Psychiatry, University of Connecticut, 263 Farmington Avenue, MC 1517, Farmington, CT 06030*; John A. Gillespie, M.D., Cathryn M. Clary, M.D.

Summary:

Objective: Anxiety commonly complicates the clinical presentation of depression and has been associated with poorer medication tolerability and long-term outcome. The efficacy and tolerability of sertraline in anxious depression was evaluated.

Method: Pooled data from two 8-week, double-blind, placebo-controlled sertraline treatment studies were analyzed. Anxious depression was defined as a HAM-D anxiety-somatization score ≥7.

Results: 154 (57%) of 272 outpatients met criteria for the anxious subtype. The ANCOVA found equivalent efficacy at endpoint among both anxious and non-anxious subtypes in improving HAM-D total score (F=1.45; df=1,269; p=0.23). Median time-to-response (in days) on a survival analysis was the same for both groups: 32.5[SD=±1.6] versus 32.6±[SD=1.5] for the anxious versus non-anxious subtypes. At treatment endpoint, anxiety symptoms had responded in 80% of patients with the anxious subtype. A correlational analysis found side effect burden to be correlated more with illness severity than with dose or the presence of anxiety symptoms.

Conclusions: Sertraline was found to have equivalent antidepressant efficacy and tolerability in both anxious and non-anxious depressive subtypes, as well as markedly improving the symptoms of anxiety.

NR414 Tuesday, May 8, 2001, 03:00 p.m.-05:00 p.m.

An Open-Label Trial of Tramadol Treatment of Social Phobia

Nicholas Demartinis, M.D., *Department of Psychiatry, University of Connecticut, 263 Farmington Avenue, MC 1517, Farmington, CT 06030*; Moira A. Rynn, M.D., Laura A. Mandos, Pharm.D.

Summary:

Objective: To assess the efficacy and safety of the mu-opioid agonist tramadol in treatment of social phobia.

Method: 17 patients with social phobia were treated with a flexible dose of tramadol (100–400mg/day) for 12 weeks. Changes in the Liebowitz Social Anxiety Scale and Clinical Global Impression Scale were analyzed with repeated measures ANOVA on a LOCF basis.

Results: Fifteen of 17 patients completed the study. The ANOVA revealed significant improvement in LSAS ($F=3.71$, $df=7$, $p=0.03$) and CGI-Severity ($F=6.32$, $df=6$, $p=0.004$), starting at week 2. Fourteen patients (82%) were judged much or very much improved by week 12. The average dose of tramadol was 254 mg/day. The most common adverse events were nausea, sedation, constipation, and fatigue, resulting in discontinuation in one patient. Ten patients were followed up for 3–24 months with maintenance of clinical effectiveness and good tolerability.

Conclusions: This study presents preliminary evidence for the efficacy and tolerability of tramadol in the treatment of social phobia. These findings suggest that further investigation of interventions utilizing the endogenous opioid system may lead to novel treatment options for social phobia patients.

NR415 Tuesday, May 8, 2001, 03:00 p.m.-05:00 p.m.

Comorbidity, Social Support, and Recovery from Depression

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Summary:

Objective: Research protocols typically exclude patients with a coexisting nonaffective psychiatric and/or medical condition. We purposefully included patients with (or without) a concurrent axis I, axis II, or axis III disorder to see how the kind or number of comorbid illness(es) would impact on the likelihood of recovery. We also examined how perceived social support affects time to recovery.

Method: 53 patients hospitalized with major depression were followed naturalistically for 6 months. Diagnoses were determined through SCID interviews or by an internist completing the Charlson Scale. Social support was measured using the Rand Scale, the Family Assessment Device, and the Social Adjustment Scale.

Results: 34% of completers met criteria for recovery at 6 months. Patients with only an axis I diagnosis were more likely to recover than patients with an additional axis I, II, or III disorder ($X^2(3)= 7.55, p<.0.056$). Perceived positive social support from month 1 through month 5 (but not at baseline) was associated with fewer depressive symptoms (p-values range from <0.0001–0.012). Illness type was correlated with overall family functioning at 6 months ($r=0.533$, $p<0.02$).

Conclusions: Odds of a patient's recovery from depression may depend on the type and number of additional illnesses. Further, a good social support system in the early stages of the illness appears to be strongly associated with a faster diminution of the severity of depressive symptoms.

NR416 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Efficacy of Venlafaxine and Fluoxetine in Individual Depressive Symptoms

Paolo Meoni, Ph.D., *CNS, Wyeth Ayerst, 80 Avenue du General de Gaulle, Paris la Defense 92031, France*; A Richard Entsuah, Ph.D., David Hackett, M.S.C.

Summary:

To characterize depressed patients participating in five randomized clinical studies, HAM-D item scores were used to analyze individual symptom severity before and during treatment with venlafaxine or fluoxetine.

HAM-D items were ranked according to baseline mean score as severe (>2.5 for 4-point items, >1.5 for 2-point items), moderate (>1.5 for 4-point items >0.5 for 2-point items), or mild (>0.5 for 4-point items).

Work and activities, somatic symptoms (general), and depressed mood were ranked as severe. Venlafaxine exhibited significant superiority for all three severe items ($p<0.05$) compared with fluoxetine and showed significant improvement from week 2 and in depressed mood from week 1. Fluoxetine exhibited significant improvement in depressed mood (week 1), work and activities (week 3), and general somatic symptoms (week 4 and 8 only). Feelings of guilt, genital symptoms, psychic anxiety, somatic anxiety, insomnia, diurnal variation, agitation, and gastrointestinal symptoms had moderate status, and suicide, retardation, and hypochondriasis had mild status. Significant treatment effects were observed in nine and four of the 13 "mild" or "moderate" items for venlafaxine and fluoxetine, respectively. Individual HAM-D scores for depression symptoms showed great heterogeneity in their baseline severity. Venlafaxine was significantly more effective than fluoxetine in treating symptoms with the greatest baseline severity.

NR417 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Bupropion Sustained Release, Paroxetine, and Sertraline: Onset and Duration of Adverse Events

Robert Hirscheld, M.D., *301 University Boulevard, Galveston, TX 77555*; Rukmini Rajagopalan, Ph.D., Carolyn Bolden-Watson, Ph.D., Trisha L. Houser, B.A., Brenda Jamerson, Pharm.D., Alan Metz, M.D.

Summary:

Objective: Antidepressant-associated adverse events may result in patient tolerability issues. To help physicians understand the nature of these adverse events, we examined the time course of adverse events associated with bupropion SR, paroxetine, and sertaline from a combined database.

Methods: The time course and duration of commonly experienced adverse events (>5% incidence according to bupropion SR, paroxetine, and sertraline product labeling) were compared across treatments (placebo N=632, bupropion SR N=1398, paroxetine N=52, sertraline N=360). 'Early' onset was defined as occurring within the first 14 days after enrollment; those occurring later were termed 'late' onset. Events resolving within 14 days of occurrence were called "transient"; those that did not were called "persistent."

Results: 2,442 subjects were included in the analysis. For all treatment groups, the majority of adverse events were early onset and transient. Greater than 25% of occurrences of adverse events were persistent across the bupropion SR-, paroxetine-, and sertraline-treated groups.

Conclusion: Data from this analysis demonstrates that most adverse events associated with bupropion SR, paroxetine, and sertraline occur early and are short-lasting. Awareness of specific adverse event profiles may aid the ability of physicians to counsel patients about expected side effects of these medications.

Funding provided by Glaxo Wellcome Inc.

NR418 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Antidepressant Compliance and Side Effects: Results from a Patient Survey

Brenda Jamerson, Pharm.D., *NAMA-CNS, Glaxo SmithKline, P.O. Box 13398, Research Triangle, NC 27709*; Adam K. Ashton, M.D., Trisha L. Houser, B.A., Robert A. Leadbetter, M.D., Christine Wagoner, B.A., Alan Metz, M.D.

Summary:

Objective: Side effects are commonly associated with antidepressant treatment. However, data from clinical trials rarely contain information concerning the impact of side effects on patients' comfort and compliance.

Methods: Patients receiving depression treatment completed a self-administered questionnaire. Questions regarding antidepressant compliance and side effects were asked.

Results: The survey return rate was 53% (350/664). Most patients (78%) indicated that they took their antidepressant exactly as prescribed. Of the top five reasons for noncompliance, 3 were side effects (loss of sexual desire, weight gain, anorgasmia); the other two reasons were "trouble remembering" and "feeling less medication was needed." The same three side effects were in the top five experienced and also described as the most persistent. Nearly one-third and one-quarter of respondents indicated it was "extremely difficult to live with" weight gain and orgasm/erectile dysfunction, respectively.

Conclusions: Patients indicated that it was difficult to live with weight gain and sexual dysfunction. Clinicians should be aware that these side effects appear to be directly associated with lack of medication compliance.

This study was conducted by Market Measures Interactive.

NR419 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Quality of Life in Depressed Geriatric Patients

Zeba M. Khan, Ph.D., *USMA Health Outcomes, Glaxo Wellcome, Five Moore Drive, P O Box 13398, Research Triangle, NC 27709*; P. Murali Doraiswamy, M.D., Rafe M.J. Donahue, Ph.D.

Summary:

Objective: Examine quality of life (QOL) in elderly recurrent major depressive patients before and after antidepressant treatment.

Methods: 100 elderly patients were randomly assigned to either bupropion SR (BUP) or paroxetine (PAR) for 6 weeks. Baseline and end-of-treatment Quality of Life in Depression Scale (QLDS) and SF-36 QOL ratings were examined.

Results: Compared to elderly population norms, depressed subjects showed significant QOL impairments in five of eight baseline SF-36 items ($p<0.05$). At baseline, women had worse ratings on the QLDS ($p<0.05$) and on all eight SF-36 items. Older subjects reported lower QOL on the SF-36 summary physical component ($p<0.05$) and higher QOL on the summary mental component ($p<0.05$). BUP and PAR produced significant changes in QLDS score and on seven of eight SF-36 items ($p<0.05$). Age, gender, baseline depression severity, and anxiety levels did not predict differential response between BUP and PAR. Lower treatment response was associated with lower perceived physical and social functioning at baseline.

Conclusions: Recurrent major depression in elderly women was associated with greater impairments in mental and physical QOL than in men. Older age is not uniformly associated with decreased mental QOL. Both bupropion SR and paroxetine improve a broad range of QOL measures in geriatic depression.

This research was supported by a grant from Glaxo Wellcome Inc.

NR420 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Sexual Functioning Effects of Bupropion Sustained Release and Fluoxetine

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Summary:

Objective: To compare the sexual functioning effects, efficacy, and safety of bupropion SR (BUPSR) and fluoxetine (FLUOX).

Methods: A total of 456 patients with normal sexual functioning diagnosed with moderate to severe recurrent major depression were randomly assigned in a double-blind fashion to BUPSR 150–400 mg/day, FLUOX 20–60 mg/day, or placebo for 8 weeks. Investigator-rated sexual functioning (e.g., orgasm delay/failure), patient-rated satisfaction with sexual functioning, depression (HAM-D), and safety were assessed weekly.

Results: From weeks 2–8, the FLUOX group experienced a significantly ($p<0.001$) higher incidence of orgasm dysfunction (18–32%) than the BUPSR (4–12%) or placebo (5–12%) groups. From weeks 4–8, significantly ($p<0.05$) more FLUOX-treated patients (15–22%) than those treated with BUPSR (3–4%) or placebo (7–9%) who were initially satisfied with their sexual functioning became dissatisfied. BUPSR and FLUOX were similarly effective in treating depression. BUPSR and FLUOX were well tolerated based upon safety assessments.

Conclusion: FLUOX was associated with a greater occurrence of sexual dysfunction than BUPSR or placebo. BUPSR and FLUOX were similarly effective in the treatment of depression and well tolerated. As a first-line antidepressant, BUPSR may be especially appropriate for the treatment of depressed patients who are concerned about sexual functioning.

Funding for this study was provided by Glaxo Wellcome Inc.

NR421 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Bupropion Sustained Release as an Antidote to SSRI-Induced Sexual Dysfunction

Anita L.H. Clayton, M.D., *Department of Psychiatry, University of Virginia, 2955 Ivy Road, Northridge #210, Charlottesville, VA 22908*; Elizabeth L. McGarvey, Ed.D., Julia K. Warnock, M.D., Susan G. Kornstein, M.D., Relana C. Pinkerton, Ph.D.

Summary:

Objective: No placebo-controlled studies have demonstrated the effectiveness of bupropion SR as an antidote to SSRI-induced sexual dysfunction. This study reports a placebo-controlled, double-blind comparison of bupropion SR vs. placebo in 55 patients at three research sites.

Method: Patients with major depression who experienced a therapeutic response to any SSRI and had experienced medication-induced sexual dysfunction as measured by the Changes in Sexual Functioning Questionnaire (CSFQ) total score, desire subscale score, or orgasm subscale score were randomized to receive either bupropion SR 150 mg b.i.d. or placebo for four weeks in addition to the SSRI.

Results: The hypothesis that bupropion SR would be an effective antidote for SSRI-induced sexual dysfunction was confirmed for certain aspects of sexual function. Among the CSFQ subscales, desire/frequency showed a significantly greater improvement among those patients receiving bupropion SR compared with placebo (Wilk's $F(1,38)=7.31$, $p<.05$).

Conclusions: Bupropion SR is an effective antidote to SSRI-induced diminished desire.

NR422 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Antidepressant-Associated Sexual Dysfunction: Risk Factors

Anita L.H. Clayton, M.D., *Department of Psychiatry, University of Virginia, 2955 Ivy Road, Northridge #210, Charlottesville, VA 22908*; Robert A. Leadbetter, M.D., Kristin Bass, B.A., Carolyn Bolden-Watson, Ph.D., Rafe M.J. Donahue, Ph.D., Brenda Jamerson, Pharm.D., Alan Metz, M.D.

Summary:

Antidepressant-associated sexual dysfunction (SD) is highly prevalent and underestimated. Identification of risk factors that increase the odds of SD is important for recognition and prevention.

6,297 primary care outpatients receiving monotherapy with one of eight new-generation antidepressants were enrolled in this cross-sectional, multicenter observational study. SD was measured by the validated Changes in Sexual Functioning Questionnaire-CL (CSFQ).

Among patients free from other probable causes of SD, the odds of developing SD were six times greater with citalopram or venlafaxine XR treatment five times greater with paroxetine or sertraline treatment and four times greater with fluoxetine treatment when compared with bupropion SR.

The odds of having SD were higher for those who were older, married, taking concomitant medications or a higher antidepressant dose, had comorbid illnesses affecting sexual functioning, or experienced SD with a previous antidepressant. Those who were working full time or were college graduates had lower odds of reporting SD. Patients using tobacco 6–20 times/day reported more SD than non-tobacco users. Gender, race, and duration of antidepressant treatment did not predict risk for SD.

Rates of antidepressant-associated SD, and risk factors for SD, should be considered when selecting antidepressant therapy.

Funding for this study was provided by Glaxo Wellcome Inc.

NR423 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Evaluating Sensitivity to Change of the Changes in Sexual Functioning Questionnaire (CSFQ) in Depressed Patients

Anita L.H. Clayton, M.D., *Department of Psychiatry, University of Virginia, 2955 Ivy Road, Northridge #210, Charlottesville, VA 22908*; Fernando Rico-Villademoros, M.D., Margarita Garcia, M.D., Maria P. Gonzalez, Ph.D., Maria T. Bascaran, M.D., Sebastian Banus, M.D., Julio B. Bobes, Ph.D.

Summary:

Sexual dysfunction has been associated with psychiatric illness and psychotropic medications. Accurately evaluating alterations in sexual functioning requires a validated instrument that measures clinically relevant change over time. This study reports the sensitivity to change of the CSFQ. 101 depressed patients from 15 Spanish hospitals completed the CSFQ at baseline and after 6 months of treatment with fluoxetine, nefazodone, paroxetine, or venlafaxine. The only statistically significant sociodemographic variable between the treatment groups involved educational level (higher education level in the fluoxetine and venlafaxine groups), with the only clinical variable being recurrence of major depression (more patients treated with nefazodone). Defining as a substantial floor or ceiling effect when >30% of patients indicated the floor or ceiling score, non-substantial ceiling and floor effects were found for the total and subscale scores in the overall sample. Sexual desire/interest showed a nearly substantial floor effect for women in the nefazodone group at baseline and in the paroxetine group at final visit. By gender, the percentage of dimensions recording change was greater for women (80%) than for men (20%) in the nefazodone group (improving changes), and greater for men (40%) than for women (20%) in the paroxetine group (worsening changes). Highest effect sizes were found on sexual desire/frequency with improvement in women in the nefazodone group (SES=0.49) and on orgasm/ejaculation with worsening in men in the paroxetine group (SES=1.45). In conclusion, the CSFQ is sensitive to bidirectional changes and is appropriate for measuring sexual dysfunction.

Funded by Bristol Myers Squibb, Spain

NR424 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

A Reanalysis of Bupropion Sustained Release Trials Using Subscales of the 31-Item Hamilton Depression Scale

P. Murali Doraiswamy, M.D., *Department of Psychiatry, Duke University Medical Center, Room 3547, South Hospital, Box 3018, Durham, NC 27710*; Hau Lei, Ph.D., Jeremy N. Roberts, M.S.C., Brenda Jamerson, Pharm.D., Alok Krishen, M.S., Rafe M.J. Donahue, Ph.D., Carolyn Bolden-Watson, Ph.D.

Summary:

Objectives: (1) To estimate the odds of response to bupropion SR relative to placebo after controlling for baseline subscale scores of the 31-item HAMD scale, and (2) to examine changes in the subscale scores to determine factors being affected by bupropion SR.

Methods: Data from three 8-week, double-blind, controlled clinical trials with 910 patients were pooled to examine seven subscales identified from a previous post hoc factor anlaysis of the 31-item HAMD scale. Patients were adults with a diagnosis of moderate-to-severe depression. Logistic regression was used to examine the probability of response (at least 50% reduction in HAM-D total score) for each treatment and analysis of covariance was used to compare changes in subscale scores between treatments.

Results: The odds of response for patients treated with bupropion SR were 1.7 times higher than those treated with placebo ($p<0.001$). Bupropion SR demonstrated a significant treatment effect over placebo with respect to down feelings ($p<0.001$), retardation ($p=0.003$), hypersomnia ($p<0.001$), and anxiety ($p=0.002$) subscales.

Conclusions: Bupropion SR showed superiority over placebo when examining overall response and within certain, specific, symptom-related subscales of the HAMD. Bupropion SR may be especially suitable for depressed patients presenting with those symptoms.

These studies were funded by Glaxo Wellcome.

NR425 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Lithium Versus Valproic Acid: A Comparison of the Long-Term Treatment of Bipolar Illness

Caroline M.J. Orsini, B.S., *Department of Psychiatry, Massachusetts General Hospital, 50 Staniford Street, Suite 580, Boston, MA 02114*; William G. Frankle, M.D., Louisa D. Grandin, B.A., Stephen M. Gray, B.A., Leslie J. Yan, B.A., Andrew A. Nierenberg, M.D., Gary S. Sachs, M.D.

Summary:

Objective: To compare the effectiveness of two standard treatments for bipolar illness

Method: We reviewed charts of bipolar patients who were assessed with standard measures used by clinicians during routine, open treatment at the MGH Bipolar Clinic for visits occurring between January 1, 1998 and December 15, 2000. Subjects were then selected for study if they were receiving treatment with either lithium or valproic acid at each visit (those taking both were excluded).

Results: Ninety-four patients (36 taking VPA, 58 taking lithium) were included in the analysis. Demographic characteristics were similar for the two groups (43 years old; 47% male; 75% BPI) Those taking lithium had greater average number of visits (9.6 [SD=8.8] versus 6.1 [SD=5.9], t=–5.3, p<0.0001) but duration of treatment was not statistically different between the groups (235 days for VPA versus 328 for lithium; t=–1.494, p>0.05). No differences were found between the groups for the percentage of time the subjects were well, in elevated mood states, depressed states, and subsyndromally ill states. The number of adjunctive medications were similar for both groups.

Conclusion: Lithium and valproic acid appear equally effective as maintenance treatments for bipolar disorder in a specialty clinic.

NR426 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Seasonality of Mood in African Americans Living in the Washington, D.C., Metropolitan Area

Teodor T. Postolache, M.D., *Department of Psychiatry, Georgetown University, 3800 Reservoir Road, Kogan Hall, Washington, DC 20007*; Charles O. Agumadu, M.D., Samina M. Yousufi, M.D., Irum S. Malik, M.D., Minh-Chau T. Nguyen, M.D., Kambiz Soleymani, M.D., Michael A. Jackson, M.S.

Summary:

Objective: Ethnicity has been recognized as affecting our pattern of mood and behavioral response to seasonal changes (Magnusson, 2000). Asians are different from Caucasians in regard to the prevailing pattern of seasonal changes in mood, having more prevalent summer depression than winter depression (Ozaki et al. 1995, Han et al. 2000). As no previous study on seasonality of mood focused on black populations, this study aimed to estimate, for the first time, the prevalence and pattern of seasonal mood and behavioral changes in African Americans.

Method: We used the seasonal pattern assessment questionnaire (SPAQ) to assess seasonality in 597 African American college students living in the Washington, D.C. metropolitan area. The prevalence of summer SAD (S-SAD) versus winter SAD (W-SAD) was compared using Pearson chi-square tests. The effects of gender, season of administering the questionnaire, and age on the global seasonality score (GSS) were evaluated with ANCOVA.

Results: A significantly (p<0.001) higher proportion of subjects reported a winter type than summer type of SAD. Frequency of winter seasonal affective disorder (SAD) was 5.4%, summer SAD was 0.6%. Mean global seasonality score (GSS) was 8.4 (SD= 5.3) and was not significantly related to age, gender, or season of questionnaire administration.

Conclusion: The prevalent type of seasonal changes in African Americans is similar to that previously reported in Caucasians and different from that previously reported in Asians.

NR427 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

What Causes the Age Effect on Depression?

Eystein Stordal, M.D., *Namdal Hospital, Namsos N-7800, Norway*; Arnstein Mykletun, Ph.D., Alv A. Dahl, Ph.D.

Summary:

Objective: In a health study of a large general population (n= 60,869), we found a close to linear rise in the prevalence of depression in all ten-year age groups from 20 to 89 years, based on self-rating of the depression subscale of the Hospital Anxiety and Depression Scale (HADS-D). The aim of this study was to examine which variables contributed to the increased prevalence of depression with higher age.

Methodology: Covariates were grouped into a multivariate model with five blocks: impairment, socio-demographic and social data, health behavior, somatic health problems, and emotions. Logistic regression was used to model the blocks and single variables with depression defined by a HADS-D score of ≥8 as the dependent variable.

Results: In our model much of the age effect on depression was explained by somatic health problems and impairment. Of the single variables in these blocks, muscular-skeletal problems in the somatic health block, and sight, hearing, and functional disablement in the impairment block explained the age-effect on depression. Also single items in the three other blocks (socio-demografic, health behavior, emotions) did reduce the age effect: Low education (in the socio-demographic block) and low physical activity (in the health behavior block) contributed to explain the age-effect on depression. Controlled for all covariates, the total age effect on depression was more reduced in the higher than in younger age groups. The model did not explain the entire age effect on depression.

Discussion: Due to our large N, we were able to control the age-effect for a high number of covariates. In contrast to most other studies, we still have an increase in prevalence of depression with control for relevant covariates.

NR428 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Escitalopram 10mg/Day: Effective Antidepressants in Primary Care Patients

Stuart A. Montgomery, M.D., *Imperial College, P.O. Box 8757, London w13 8wh, England*; Henrik Loft, Ph.D., Elin H. Reines, M.D.

Summary:

Objective: This study analysis considers whether escitalopram, the active enantiomer of citalopram, reduces depressive symptomatology in the first four weeks of treatment in primary care patients fulfilling the DSM-IV criteria for major depressive disorder.

Method: During this multinational, multi-center, randomized, double-blind, flexible-dose, eight-week study, 310 primary care patients received either 10mg escitalopram or placebo for the first four weeks (with an option for dose escalation after four weeks to 20mg/day). In this analysis, MADRS total scores at baseline (29 for each patient group) and after four weeks were compared, before dose escalation.

Results: A statistically significant difference between escitalopram and placebo emerged as early as after one week. After four weeks, adjusted mean changes from baseline on MADRS were 8.7 and 11.3 in the placebo and escitalopram groups, respectively. The 2.7 difference in MADRS score between the placebo and escitalopram group at week four was statistically significant (p= 0.002). Escitalopram was very well tolerated.

Conclusions: Escitalopram 10mg/day is effective within four weeks in primary care patients suffering from major depressive disorder.

NR429 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Response and Remission as Targets in Long-Term Therapy of GAD

Stuart A. Montgomery, M.D., *Imperial College, P.O. Box 8751, London w13 8wh, England*; Paolo Meoni, Ph.D., Vincent Mahe, David Hackett, M.S.C.

Summary:

The relative importance of response (≥50% reduction from baseline HAM-A score) and remission (absolute HAM-A score ≤7) outcome criteria were examined at different stages of long-term therapy of GAD. Data were pooled and analyzed from two 6-month placebo-controlled trials of venlafaxine XR in generalized anxiety disorder (GAD) patients (intent-to-treat N = 767). Throughout the study and from the first and second week of treatment, response and remission were significantly higher for venlafaxine XR-treated patients compared to placebo. After 24 weeks' treatment, the percentage of responders was 66% in the venlafaxine XR-treated group compared to 39% in the placebo-treated group. Forty-three percent of venlafaxine XR-treated patients achieved remission compared to 19% of placebo-treated patients ($p<0.001$). During the study there was a shift in the balance between the mutually exclusive categories of non-remitting responders and remitters. Non-remitting responders outnumbered remitters in the first few weeks of venlafaxine XR treatment and until the last assessment for placebo. Post 6 weeks' venlafaxine XR treatment, the majority of responders also qualified for remission. These data illustrate that remission follows response during venlafaxine XR treatment and should be the principal goal of long-term treatment.

NR430 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Identifying Subscales of the 31-Item Hamilton Depression Scale

Jeremy N. Roberts, M.S.C., *GlaxoSmithKline, 7333 Mississauga Road, North, Mississauga, ON L5N 6L4, Canada*; Hau Lei, Ph.D., Brenda Jamerson, Pharm.D., Alok Krishen, M.S., Carolyn Bolden-Watson, Ph.D., Rafe M.J. Donahue, Ph.D., Trisha L. Houser, B.A.

Summary:

Objectives: The objective of this analysis was to identify subscales of the 31-item Hamilton Depression Scale (HAM-D). These subscales can be used to assess and understand effects of antidepressant treatments.

Methods: This analysis was based on data from 1,532 depressed outpatients from five randomized, double-blind trials, originally designed to compare the treatment efficacy between bupropion SR and other therapies—either placebo, an active comparator, or both. Patients were men and women ≥18 years of age with a diagnosis of moderate-to-severe depression. Techniques used to identify the subscales were principal component analysis, factor analysis, and clinical judgment.

Results: Based on the scree plot, principal component analysis suggested five sub-scales. However, factor analysis, using Schwarz's Bayesian Criterion, suggested seven subscales. The seven subscales were considered more appropriate based on clinical judgment. The seven subscales identified were: down-feeling, cognitive dysfunction, retardation, hypersomnia, eating disorder, insomnia, and anxiety.

Conclusions: To the best of our knowledge, this is the first analysis to identify factors of the 31-item HAM-D. Applying these subscales to another analysis has led to a better understanding of the effects of bupropion in treating depression.

These studies were funded by Glaxo Wellcome Inc.

NR431 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Escitalopram: Efficacious and Well Tolerated in Depression Management in Primary Care

Ulla M. Lepola, M.D., *Department of Psychiatry, Helsinki University, Helsinki, Finland*; Henrik Loft, Ph.D., Elin H. Reines, M.D.

Summary:

Objective: Escitalopram is the active enantiomer of citalopram. The present study assessed its efficacy and tolerability in major depressive disorder (MDD).

Method: In this double-blind, randomized, eight-week study, patients fulfilling DSM-IV criteria for MDD were enrolled from 69 primary care centers in eight countries. They received either escitalopram 10mg/day or placebo, with an option for dose escalation (escitalopram 20mg/day).

Results: MADRS total score—the primary efficacy outcome—showed a statistically significant improvement for escitalopram versus placebo from week one. The difference in adjusted mean change between the escitalopram and placebo groups at week eight was 2.9 points ($p<0.05$). The proportion of responders at week eight (defined as ≥50% reduction in MADRS total score versus baseline) was 61% with escitalopram and 44% with placebo ($p<0.05$). Escitalopram was very well tolerated: withdrawal due to adverse events was similar in the placebo and escitalopram groups at 2.6%.

Conclusions: To our knowledge, this is the first placebo-controlled study demonstrating an SSRIs efficacy in the treatment of depression in primary care. Escitalopram proved efficacious and well tolerated in moderately to severely depressed patients (MADRS score 22 40). This combination of favorable efficacy and tolerability suggests escitalopram is a potential first-line antidepressant for primary care.

NR432 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Previous Mood State Predicts Response and Switch Rates in Patients with Bipolar Depression

Glenda M. MacQueen, M.D., *Department of Psychiatry, McMaster University, 1200 Main Street, West, 4N774 MUMC, Hamilton, ON L8N 3Z5, Canada*; L. Trevor Young, M.D., Michael Marriott, Ph.D., Helen Begin, R.N., Russell T. Joffe, M.D.

Summary:

Background: The treatment of bipolar depression is a significant clinical problem that remains understudied. The role for antidepressant agents versus mood stabilizers has been particularly problematic to ascertain, as the risk of switch into mania or cycle acceleration must be weighed against efficacy of the agents.

Method: Detailed life charting data from 113 patients with bipolar disorder were reviewed. Mood state preceding onset of depression, treatment modality, and outcome were identified. Response rates and rates of switch into mania were compared based on the preceding mood state and on whether an antidepressant or mood stabilizing agent was added following onset of depression.

Results: Patients who became depressed following a period of euthymia were more likely to respond to treatment (62.5%) than patients who became depressed following a period of mania or hypomania (27.9%). There was a favorable ratio of response to switch for previously euthymic patients that was particularly high (10:1) for patients treated with antidepressants.

Conclusion: Mood state prior to onset of depression in bipolar disorder appears to be an important clinical variable that may guide both choice of treatment administered and expectation of outcome to treatment.

NR433 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Suggestion Influences Airway Tone in Susceptible Asthmatic Subjects

Glenda M. MacQueen, M.D., *Department of Psychiatry, McMaster University, 1200 Main Street, West, 4N774 MUMC, Hamilton, ON L8N 3Z5, Canada*; Richard Leigh, M.D., J. H. Gervais Tougas, M.D., Yin Chen, Ph.D., Patricia Hussack, Fred E. Hargreave, M.D., John Bienenstock, M.D.

Summary:

Background: Although it is recognized that psychological stressors can modulate the immune system, there are only limited data to suggest that psychological stressors can influence the pathogenesis of asthma.

Objective: The purpose of this study was to determine whether suggestion could influence airway tone in a group of suggestible asthmatic subjects.

Methods: Eighty subjects with mild to moderate asthma were screened using the Creative Imagination Scale questionnaire. Nine suggestible and eight nonsuggestible subjects then returned for a second visit. After baseline spirometry had been performed, subjects received two 0.9% saline bronchial challenges (tidal breathing method) 45 minutes apart. It was suggested to the subjects that the first challenge was with a bronchoconstrictor agent, the second with a bronchodilator agent. All subjects then had a true methacholine challenge performed. Power spectral analysis was used to assess vagatone.

Results: Five of six subjects who had a fall in FEV_1 >150ml in response to the sham bronchoconstrictor were in the suggestible group. Similarly, all three subjects in whom the FEV_1 improved > 100 ml following sham bronchodilator were suggestible.

Conclusions: These data indicate that within the asthmatic population there is a subgroup of subjects in whom suggestion can influence airway tone and subjective perception of dyspnea.

NR434 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Persistent Functional Impairment in Bipolar Patients

Glenda M. MacQueen, M.D., *Department of Psychiatry, McMaster University, 1200 Main Street, West, 4N774 MUMC, Hamilton, ON L8N 3Z5, Canada*; Russell T. Joffe, M.D., Michael Marriott, Ph.D., Janine Robb, R.N., Helen Begin, R.N., L. Trevor Young, M.D.

Summary:

Background: Many patients with bipolar disorder (BD) do not regain full function following an acute illness episode, but the extent to which this impairment is the result of persistent symptoms has not been well established. This study examined the effect of subsyndromal symptoms on functional outcome and service utilization in patients with BD who were prospectively followed for a minimum of one year.

Method: Life charting data from 138 patients with BD were reviewed. Patients were categorized into euthymic, subsyndromal, or syndromal groups according to the clinical state during their most recent year of follow up. The three groups were then examined with respect to level of function and service utilization.

Results: Patients with subsyndromal symptom levels had lower GAF scores than euthymic patients, and had as many clinic contacts and medication trials as patients with full episodes of illness. Subsyndromal patients had high rates of comorbid anxiety disorders, and were more likely to have increased rates of eating disorders as well; rates of past substance abuse were predictably low, because patients with current abuse or dependence were excluded.

Conclusions: Persistent subsyndromal symptoms in BD patients are associated with a poor outcome and high service utilization similar to patients experiencing syndromal levels of illness.

NR435 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Long-Term Course of Major Depression: Predictive Value of Sleep (EEG Markers)

Martin Hatzinger, M.D., *Depression Research Unit, Psychiatric University Hospital, Wilhelm Kleinstrasse 27, Basel CH-4025, Switzerland*; Ulrich M. Hemmeter, M.D., Kathrin Baumann, M.D., Barbara Annen, Ph.D., Serge Brand, Ph.D., Edith Holsboer-Trachsler, M.D.

Summary:

In MD sleep disturbances as reflected by sleep EEG measures are well-established findings. Some of them were found to be associated with short-term outcome. However, their predictive value for long-term course is unclear. Thus, the aim of this study was to identify sleep EEG measures that may have predictive value for long-term course of depression.

In 11 patients with MD sleep EEG studies were conducted at baseline (while depressed) (*BL*), after a six-week antidepressive treatment period (trimipramine 200 mg/d) (*W6*), and after long-term course (follow-up after two to ten years) (*FU*). According outcome patients were subdivided into a subgroup with no recurrence (n=6) and a subgroup with recurrence (n=5). *BL* as well as *W6* sleep EEG measures revealed a negative correlation of slow wave sleep (SWS) during the first sleep cycle and a positive correlation of rapid eye movement (REM) density with recurrence rates (RR). Furthermore, the increase of SWS during the first sleep cycle between *BL* and *W6* showed a negative correlation with RR. At *FU* none of the sleep parameters correlated significantly with RR. We conclude that SWS, especially during the first-sleep cycle and REM-density, are of predictive value for the long-term course of MD.

NR436 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Depressive Symptoms During Mania

Ana Gonzalez-Pinto, M.D., *Department of Psychiatry, Hospital Santiago, Olaguibel 29, Vitoria-Gasteiz 01004, Spain*; Blanca Fernandez-Corres, Ph.D., Berta Lalaguna, Ph.D., Fernando Mosquera, M.D.

Summary:

Background: Simultaneous presentation of manic and depressive symptoms has long been recognized. Nevertheless, a variable prevalence of dysphoric mania has been reported. The aim of this study was to estimate the prevalence of dysphoric mania among patients during a manic episode and the factors associated to these symptoms.

Methods: 103 patients who met *DSM-IV* criteria for mania were evaluated at admission with a protocol that included McElroy's criteria for dysphoric mania (McElroy et al, 1992). Sequential assessments were conducted throughout the study (HAM-D 21, YMRS, PANSS, CGI).

Results: 40% of the total sample fulfilled McElroy's criteria for dysphoric mania. Patients with dysphoric mania were more often suicidal ($p<0,05$), had lower scores in manic symptoms ($p<0,05$) and had longer hospitalizations than pure manic patients ($p<0,05$).

Conclusions: Dysphoric symptoms are common in this population of manic patients. The presence of depressive symptoms during mania complicates the clinical picture of manic patients. Although this simultaneous presentation of depressive and manic symptoms in the same patient has been described as a rare phenomenon, there are some data in the literature that indicates that is fairly common. Recently there have been some authors that have proposed that mania has a depressive dimension (Cassidy, 1998).

NR437 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Gender Differences in Patients with Binge Eating Disorder

Declan T. Barry, Ph.D., *Department of Psychiatry, Yale University, P O Box 208098, New Haven, CT 06520-8098*; Carlos M. Grilo, Ph.D., Robin M. Masheb, Ph.D.

Summary:

Objective: This study examined gender differences in patients with binge eating disorder (BED).

Method: Participants were 182 adults (35 male, 147 female) who were consecutively evaluated for outpatient clinical trials and met *DSM-IV* (APA, 1994) criteria for BED. Participants were administered diagnostic interviews and a psychometrically established battery of measures to examine developmental, eating- and weight-related disturbances, and psychological features associated with binge eating disorder.

Results: Men and women did not differ significantly on several developmental variables (age at first overweight, age at first diet, age at onset of regular binge eating, or number of weight cycles). Men had significantly higher current BMI (F (1, 777)=9.42, p= 0.002), highest adult BMI (F(1, 164)=12.69, p=0.000), and were significantly more likely to be classified as obese (85.7% versus 70.7%). Men and women did not differ significantly on measures of current eating disorder features (binge eating, eating concerns, or weight or shape concerns) but women reported significantly greater body image dissatisfaction (F (1, 181)=9.82, p=0.002) and drive for thinness (F (1, 181)=10.33, p=0.002). Men and women did not differ significantly on current depression or self-esteem, but men reported a greater frequency of past drug abuse problems (F (1, 181)=8.76, p=0.004).

Discussion: While men and women who present for treatment for BED show many similarities in current eating disorder features, we observed a number of gender differences on important developmental and physical variables as well as associated psychological features.

NR438 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Assessing Culture via the Internet

Declan T. Barry, Ph.D., *Department of Psychiatry, Yale University, P O Box 208098, New Haven, CT 06520-8098*;

Summary:

Objective: To examine the utility of the internet as a participant recruitment tool in the study of the acculturation experiences of male Arabic immigrants.

Method: Based on in-depth pilot interview data from 10 male Arabic immigrants and items selected from pre-existing measures, the Male Arabic Ethnic Identity Measure (MAEIM) was developed. 115 male Arabic immigrants were solicited through traditional methods (N=45) in addition to the internet (N=70). Participants ranged in age from 18 to 54 years; more than half had lived in the United States for more than 5 years (mean=6.37, SD=5.45).

Results: Satisfactory reliability and validity were reported for the MAEIM. No significant differences emerged between the internet and the locally recruited Midwestern samples (largest t value: t= −1.54, p=0.13).

Discussion: The internet proved to be an effective method for soliciting a relatively large, geographically dispersed sample of male Arabic immigrants. The use of the internet as a research tool is examined in the context of anonymity, networking, low-cost, perceived interactive control, methodological rigor, and external validity. The internet was an effective vehicle for addressing concerns raised by prospective participants. It is suggested that the internet may be an important method to assess culture-relevant variables in further research on Arabic and other immigrant populations.

NR439 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Psychiatric Comorbidity in Patients with Binge Eating Disorder

Leonardo Fontenelle, M.D., *Department of Psychiatry, IPUB-UFRJ, Rua Lopes Trovao 88 1501 A, Niteroi, RJ 24220-071, Brazil*; Gabriela B. De Menezes, M.D., Jose C. Appolinario, M.D., Silvia Freitas, M.D., Marcelo Papelbaum, M.D., Amelio Godoy-Matos, M.D., Walmir Coutinho, M.D.

Summary:

Objective: To investigate whether the diagnosis of binge eating disorder (BED) in a group of patients seeking treatment for obesity is associated with any particular sociodemographic characteristic or further psychiatric diagnosis.

Method: Sixty-five obese patients (body mass index higher than 30 kg/m2 and lower than 45 kg/m2) were evaluated with the Structured Clinical Interview for DSM-IV (SCID), the Binge Eating Scale (BES), and the Beck Depression Inventory (BDI). Patients fullfilling the DSM-IV criteria for BED (n=32) were compared with patients without this diagnosis (n=33) with regard to sociodemographic characteristics and psychiatric status. Chi-square and independent samples t-tests were employed to compare groups.

Results: The groups did not differ in terms of age, gender, race, socioeconomic status, schooling, and body mass index. However, subjects with BED had higher scores in the BES (F=6.86; df=63; p=0.001), the BDI (F=0.37; df=62; p=0.001), and were significantly more likely than those without the disorder to have a current diagnosis (chi=4.47; df=1; p=0.03) and lifetime history of major depressive disorder (chi=5.58; df=1; p=0.02).

Conclusion: Among patients seeking treatment for obesity, BED is associated with high rates of major depressive disorder.

NR440 Tuesday, May 8, 03:00 p.m.-05:00 p.m.

Impaired Set-Shifting Ability and Treatment Response in OCD

Leonardo Fontenelle, M.D., *Department of Psychiatry, IPUB-UFRJ, Rua Lopes Trovao 88 1501 A, Niteroi, RJ 24220-071, Brazil*; Carla Marques, M.D., Engelhardt Eliasz, M.D., Marcio V. Versiani, M.D.

Summary:

Objective: To investigate whether impaired set-shifting ability (SSA) is related to therapeutic response to serotonin reuptake inhibitors (SRI) in patients with obsessive-compulsive disorder (OCD).

Methods: Twenty non-medicated OCD patients were evaluated with the Yale-Brown Obsessive-Compulsive Scale (Y-BOCS), the Clinical Global Impression, the Verbal Fluency Test, the Wisconsin Card Sorting Test (WCST), and the Trail Making Test (TMT). SSA was specifically assessed with the WCST and the TMT B/A time ratio. Vocabulary (WAIS-R) was used as an IQ marker. After these evaluations, patients were treated with a SRI for 10 weeks.

Results: Seventy-five percent of the sample had impairment in two or more neuropsychological tests, while 80% had impairment in at least one WCST subtest. Twenty-five percent had poor verbal fluency, with significantly higher obsessions subscores than unimpaired patients (Z=−2, 47; p=0.01). Among the patients who completed 10 weeks of treatment, 52.9% were responders. A relationship was found between positive treatment response to a SRI and impaired performance in two WCST subtests, namely number of categories completed (chi=4.86; df=1; p=0.01) and perseverative errors (chi=3.90; df=1; p=0.02).

Conclusions: Impaired SSA may be a useful predictor of response to SRI treatment in OCD patients.

NR441 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Obese Binge Eaters, Obese Nonbinge Eaters, and Patients with OCD: Symptom Profile

Gabriela B. De Menezes, M.D., *Department of Psychiatry, IPUB-UFRJ/IEDE, Lopes Trovao 88 1501A ICARAI, Niteroi, RJ 24220-071, Brazil*; Leonardo Fontenelle, M.D., Jose C. Appolinario, M.D., Carla Marques, M.D., Mauro V. Mendlowicz, M.D., Walmir Coutinho, M.D., Marcio V. Versiani, M.D.

Summary:

It has been suggested that anorexia and bulimia nervosa share phenomenological features with obsessive-compulsive disorder (OCD). We investigated whether there are phenomenological similarities between patients with binge eating disorder and patients with OCD. Obese binge eaters (OBE, n=20), obese non-binge eaters (ONBE, n=22), and OCD patients (n=23), diagnosed according to the Structured Clinical Interview for DSM-IV, were compared in terms of presence and severity of psychopathology by means of the Symptom Checklist 90 (SCL-90). To examine differences in psychopathological factors, a MANCOVA model was constructed using diagnostic group as the fixed factor; effects of age and gender were adjusted as covariates. Dependent variables were the nine SCL-90 factors. MANCOVA showed overall group effect on the dependent variables ($F(18, 84)=2.47$, $p=0.005$). Overall effects were not found either for age or for gender. Only the obsessive-compulsive symptoms score showed significant between-group differences. Post-hoc Bonferroni-corrected pairwise comparisons revealed significant effects on this variable. Patients with OCD showed significantly higher scores than ONBE ($F(2,54)= 6.98$, $p=0.005$). No statistically significant difference between OBE and the two other groups emerged. Our results suggest that OBE may share clinical features with OCD patients.

NR442 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Survey of Health Behaviors and Epidemiological Factors Associated with Adolescent Obesity

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Summary:

Background: We have previously examined the relation between obesity and comorbid medical and psychiatric conditions. Preliminary results showed high percentage of both psychological and medical comorbity with similar incidence of some risk behaviors: smoking, alcohol, and drug use. Significant variances were found between obese adolescents and control groups in the areas of sexual activity/pregnancy.

Objective: To further examine gender-specific demographics, self-esteem, locus of control, and health behaviors among obese adolescents, compared with normal weight control subject in an attempt to further elucidate concomitant factors that occur with these varied psychological and medical diagnoses.

Method: Preliminary research conducted on this population consisted of restrospective chart reviews. Current studies involved completion of standardized questionnaires: Perceived Wellness Scale, Norwicki-Strickland Locus of Control Scale, Internal versus External Control of Weight Scale, and the Rosenberg Self-Esteem Scale in addition to demographic and health behaviors surveys. Comparisons were made among intended subjects randomly identified through individuals seeking care at the Cleveland Clinic Foundation, who exhibited a nonpathologic cause for their obesity and had a BMI above the 90th percentile.

Results: Demographic surveys and standardized questionnaires revealed significant variances among the obese and normal weight adolescents as a whole as well as demonstrating gender-specific characteristics. Control female adolescents evidenced increased sexual activity ($p<0.05$), increased cigarette, alcohol, and illicit drug use ($p<0.05$), with reports of increased difficulty managing their eating (ESES) and an overall external LOC (CNSIE). While obese females also reported an external LOC (CNSIE) and weight LOC (ESES) with an expressed increased sense of life meaningfulness compared to other study participants ($p<0.05$), they were noted to exercise significantly more often than other participants ($p<0.05$), despite an increased incidence of asthma ($p<0.05$). Obese males in the study reported decreased self-efficacy relative to eating (ESES) with an internal LOC in general (CNSIE) and relative to weight (IECW) with the lowest self-esteem reported in the study (RSE). As our preliminary research showed, incidence of ADHD was greatest among the control groups per self report ($p<0.05$) while chart review suggested the obese subjects to have a psychiatric diagnosis other than ADHD. Asthma was reported with greater frequency among the obese subjects by chart review and self-report ($p<0.05$). However, there were conflicting results relative to sexual activity: obese females by chart review indicated greater incidence ($p<0.001$), whereas female control subjects indicated increased activity by questionnaire ($p<0.05$).

Conclusion: Although there are methodological restrictions imposed by the small numbers in this study, converging evidence supports the view that children's beliefs relative to the causative factors for their weight may help clarify self-esteem findings. Preliminary results show high percentages of both psychological and medical comorbidity. Incidence of some risk behaviors, including: smoking, alcohol, and drug use, and sexual activity varied relative to LOC, eating self-efficacy, and self-esteem. Future research of clinically overweight children that are balanced for gender are required to further assess for similar correlations relative to learned behaviors, self-concept, or organic gender differences, as well as treatment options in obese adolescents.

NR443 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Validation of the Portuguese Version of the Binge Eating Scale (BES)

Jose C. Appolinario, M.D., *Department of Psychiatry, IPUB/ UFRJ-IEDE, R Visconde de Piraja 550/2002, Rio De Janeiro, RJ 22410-002, Brazil*; Silvia Freitas, M.D., Gabriela B. Menezes, M.D., Claudia S. Lopes, M.D., Leonardo Fontenelle, M.D., Marcelo Papelbaum, M.D.

Summary:

Binge eating is a common problem among obese individuals. The Binge Eating Scale (BES) has been widely used to identify and evaluate obese binge eaters in epidemiological and clinical studies.

Objective: The purpose of this study is to evaluate the validity and reliability of the Portuguese version of the BES in a Brazilian sample.

Methods: A final Portuguese version was obtained after a careful translation and adaptation process.

Validity: Sixty-five consecutive subjects seeking treatment for obesity fulfilled the BES. The Structured Clinical Interview for DSM-IV-patient version (SCID-P) was used as a gold standard for the clinical diagnosis of binge eating disorder (BED).

Reliability: Fifty-one subjects who had fulfilled the BES were re-tested two weeks later.

Results: The BES presented a sensitivity of 78%, a specificity of 84%, a positive predictive value of 84% for the cutoff score of 27. The internal consistency of the instrument measured by Cronbach's alpha was 0.879. The reliability (test-retest) of BES scores was $r=0.8$, $p<0.01$.

Conclusion: These findings suggest that the Portuguese version of BES is a valid and reliable instrument for clinical purposes.

NR444 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

An Open Trial of Sibutramine in Obese Patients with Binge Eating Disorder

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Summary:

Sibutramine, a serotonin and noradrenaline reuptake inhibitor, represents a new class of FDA-approved agents for the treatment of obesity.

Objective: To evaluate the efficacy and tolerability of sibutramine in a group of obese binge eaters.

Method: Ten obese patients with binge eating disorder (BED) (DSM-IV) and no medical comorbidity were consecutively selected from individuals seeking treatment for obesity. Treatment with sibutramine 15 mg/day was administered for 12 weeks. The days with binge episodes per week (DBE), the Binge Eating Scale (BES), the Beck Depression Inventory (BDI), and the bodyweight evaluation were employed for outcome assessment.

Results: Seven patients completed the trial. They showed a complete resolution of BED with no binge eating episodes at the end of the treatment. The mean DBE significantly changed from 5.2 (SD 1.8) at baseline to 0 (SD 0) at the end of the study ($t=6.8$, $df=6$, $p<0.001$), the BES scores fell from 31.5 (SD 6.6) to 12.5 (SD 3.8) ($t=6.0$, $df=6$, $p<0.05$). There was a statistically significant weight loss (mean 2.6 Kg) ($t=2.9$, $df=6$, $p<0.05$). The depressive symptoms did not show significant change, but BDI scores decreased from 25.8 (SD 12.6) to 10.8 (SD 5.9) ($t=2.2$, $df=6$, $p=0.069$). No serious adverse effects were observed.

Conclusion: Sibutramine may be an effective and well-tolerated agent in the treatment of BED in obese patients.

NR445 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Topiramate in Obese Patients with Binge Eating Disorder

Jose C. Appolinario, M.D., *Department of Psychiatry, IPUB/ UFRJ-IEDE, R Visconde de Piraja 550/2002, Rio De Janeiro, RJ 22410-002, Brazil*; Amelio Godoy-Matos, M.D., Luis C. Povoa, M.D., Leonardo Fontenelle, M.D., Joao R. Bueno, M.D., Marcelo Papelbaum, M.D., Walmir Coutinho, M.D.

Summary:

Topiramate is a broad spectrum neurotherapeutic agent that may have utility in treating some psychiatric disorders.

Objective: The aim of this open-label trial was to study the efficacy and tolerability of topiramate in a group of obese binge eaters.

Method: Eight obese patients with binge eating disorder (BED) (DSM-IV) and no medical or psychiatric comorbidity were consecutively selected from individuals seeking treatment for obesity. Treatment with topiramate 150 mg/day (final dose) was administered for 16 weeks. Days with binge episodes per week (DBE), the Binge Eating Scale (BES) score, the Beck Depression Inventory (BDI) score, and the bodyweight evaluation were used as outcome measures.

Results: Six patients completed the trial. All patients showed a binge eating reduction at the end of the treatment. DBE significantly changed from 6.1 (SD=1.8) at baseline to 0.5 (SD=0.84) at the end of the study ($t=6.1$, $df=5$ $p<0.05$). The BES scores fell from 31.6 (SD=8.9) to 13.3 (SD=8.3) ($t=4.2$, $df=5$ $p<0.05$). There was a statistically significant weight loss (mean 5.4 kg) ($t=3.3$, $df=5$ $p<0.05$). The depressive symptoms did not show a significant change, but the BDI scores decreased from 23.8 (SD=11.2) to 11.6 (SD=7.53) ($t=2.3$, $p=0.067$). Paresthesias and somnolence were the side effects observed.

Conclusion: Topiramate may be an effective and well-tolerated agent in the treatment of BED in obese patients.

NR446 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Tryptophan Depletion Test as an Impulsivity Biological Marker

Marina Diaz-Marsa, M.D., *Department of Psychiatry, Fundacion J. Diaz, Av Reyes Catolicos 2, Madrid 28040, Spain*; Carmen Lozano, M.D., Olga Martin, Ph.D., Jose L. Carrasco, M.D.

Summary:

Introduction: Recent literature suggests some relationship between eating disorders and impulsive disorders. Dysfunctions of temperament might not only underlie these relationships and also explain clinical differences among eating disorders. Several biological factors such a serotonergic dysfunction have been described as related to temperament as well as to impulsive disorders.

Objectives: To find serotonergic dysfunctions and their relationship with temperament in patients with eating disorders using a trypthophan depletion test.

Method: This study is designed to get a temporal state of serotonergic brain depletion, which induces a dysphoric response in those patients who present a hypoactivity of serotoninergic systems. In order to reach a temporal state of seronotinergic deficit, patients follow two days of a low trypthophan diet (less than 160 mg/day). In the morning of the third day, patients are given a trypthophan free aminoacid. Trypthophan plasmatic levels (total and free) were measured before the solution intake and three and five hours later. In order to evaluate clinical changes due to depletion, impulsivity scales (Barrat Impulsivity Scale, Columbia University Scale, Karolimska Personality Questionaire, Zuckerman Scale and Brown-Goodwin Scale) were administered as well as analogic visual scales, Hamilton Depression scale, and Hamilton Anxiety scale. Before the study begins a temperament study was performed by the Cloninger TCI and the Eysenck EPQ with the aim of finding possible personality predictors.

Results: Greater dysphoric responses to the test are correlated with the intensity of bulimic symptoms and impulsive personality features. Anorectic patients show a greater anxiety responses to the test. Bulimics have higher scores in novelty seeking and impulsiveness, while anorectics are higher in persistence.

NR447 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Evaluation of Suicide Risk in Individual Psychiatric Patients

Ilan I. Modai, M.D., *Department of Research, Shaar Menashe Mental Health Center, Mobil Post Hefer, Hadera 38814, Israel*; Michael Ritsner, M.D., Olga Rivkin, M.D., Claudia Bernat, M.D., Diana Gelber, M.D., Yael Ratner, M.D., Alexander Ponizovsky, M.D.

Summary:

Background: In practice psychiatrists rely on their own experience and intuition to evaluate suicide potential of individual patients, but the algorithms for the decision-making process remain unclear.

Objectives: 1) To establish models for the decision-making process for evaluating suicide risk and 2) to simulate the impact of information concerning the number of previous suicide attempts on the clinician's ability to detect patients who performed medically serious suicide attempts.

Methods: Four decision models (linear, dichotomized, hyperbolic, and undifferentiated) depicting the influence of the number

of previous suicide attempts on the clinician's recognition of medically serious suicide attempts in 250 major psychiatric inpatients were elicited and tested by a series of discriminant analyses.

Results: The dichotomized model ("all or none") was found to be the most efficient in detecting medically serious suicide attempts.

Conclusion: The 'all or none' paradigm seems to be the most appropriate way to evaluate the weight of previous suicide attempts in the decision-making process identifying medically serious suicide attempt patients.

NR448 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Computerized Lab Alert System for Patient Management in Clinical Care

Ilan I. Modai, M.D., *Department of Research, Shaar Menashe Mental Health Center, Mobil Post Hefer, Hadera 38814, Israel*; Maanit Sigler, M.D., Rena Kurs, B.A.

Summary:

Background: Computers have been introduced into many aspects of health care. Results of laboratory examinations are provided on computer printouts or directly recorded in computerized patient records. But how well do physicians use significant laboratory data that have been so efficiently stored in cyberspace? Do printouts facilitate improvement of patient care or add to the physician's daunting workload and cluttered desktop?

Objectives: To evaluate implementation of the Computerized Lab Alert System (CLAS) a simple, efficient solution for highlighting relevant data that may influence decision making in clinical care.

Methods: CLAS was installed in a psychogeriatric unit to retrieve and register results of routine laboratory tests on daily computer-based medication reports. For 33 days we monitored the total numbers of alerting messages sent, new messages/day, messages indicating physician unawareness, messages already dealth with, and those that initiated a treatment decision or a retest.

Results: The alerting system retrieved a mean of 0.77 ± 0.11 messages per patient per day. 12% - messages and 88% -rotating messages. Three resident psychiatrist-case managers were unaware of half the rotating messages (i.e. 6% of all messages); 7% of the new messages initiated treatment and 15% resulted in laboratory retesting.

Conclusion: The alerting system results in a simple efficient report that contributes substantially to safe patient care.

NR449 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Luteal Phase Treatment of Fluoxetine in PMDD: Effect on Sexual Functioning

Susan G. Kornstein, M.D., *Department of Psychiatry, VCU Mood Disorder I, 700 West Grace Street, Suite 303, Richmond, VA 23220*; Cherri M. Miner, M.D., Eileen Brown, Ph.D., Julia Dillon, Pharm.D.

Summary:

Objective: Sexual dysfunction is commonly reported during treatment with serotonergic antidepressants. Systematic data regarding rates of sexual dysfunction in women treated with SSRIs for PMDD are sparse. We report results from a multicenter, randomized, double-blind, placebo-controlled trial that evaluated sexual functioning in 260 women with PMDD.

Study Design: Following a two-cycle screening and a one-cycle single-blind placebo period, 260 women received fluoxetine, either 10 or 20 mg/day, or placebo (each dosed for 14 days prior to the next expected menses through the first full day of menses) for three cycles. Assessments included the Arizona Sexual Experience Scale (ASEX) (baseline and endpoint) and treatment-emergent adverse event reports (solicited at each visit). ASEX data were analyzed by analysis of variance using last-observation changes from baseline to endpoint.

Results: Data from 222 women were analyzed. Mean changes in ASEX total scores were not significantly different among the three groups (placebo=0.74, fluoxetine 10 mg=0.81, fluoxetine 20 mg=1.21; overall p=0.863). No women discontinued the trial due to sexual adverse events. 'Libido decreased' was reported by more women receiving fluoxetine than placebo (fluoxetine 10 mg= 6%, fluoxetine 20 mg=9%, placebo=0%; overall p=0.007).

Conclusion: Luteal phase dosing of fluoxetine effectively treats PMDD and produces similar changes in sexual functioning, assessed by a scale utilized specifically to measure sexual functioning, to that of placebo.

Research funded by Eli Lilly and Company, Indianapolis, Indiana 46285.

NR450 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Relapse of PMDD After Cessation of Luteal Phase Fluoxetine Treatment

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Summary:

Objective: Several small PMDD trials have identified relapse of symptoms after treatment discontinuation (1,2). We report results from a multicenter, randomized, double-blind, placebo-controlled trial that evaluated PMDD symptoms after discontinuation of luteal phase fluoxetine treatment.

Methods: Following a two-cycle screening and a one-cycle single-blind placebo period, 260 women received fluoxetine, either 10 or 20 mg/day, or placebo. Each women received treatment for 14 days prior to the next expected menses through the first full day of menses for three cycles. All women then received placebo for one cycle (single blind). Assessments of relapse included the Daily Record of Severity of Problems (DRSP), Sheehan Disability Scale, Premenstrual Tension Scale-observer rated (PMTS-O), and Clinical Global Impressions-Severity (CGI-S). Changes from mean treatment scores to post-treatment scores were analyzed using analysis of variance.

Results: Data from 205 women were analyzed. PMDD symptomatology significantly increased after fluoxetine discontinuation, however, resulting scores did not return to baseline but were similar to those of women receiving placebo treatment. Fluoxetine 10 mg versus placebo: p=0.007 (DPRS total), p=0.007 (DPRS mood), p=0.058 (DPRS physical functioning), p=0.003 (DPRS social functioning). Fluoxetine 20 mg versus placebo: p=0.014 (DPRS total), p=0.015 (DPRS mood), p=0.013 (DPRS physical functioning), p=0.01 (DPRS social functioning). PMTS-O total, CGI-S, and Sheehan results were similar.

Conclusion: Luteal phase dosing of fluoxetine effectively treats PMDD; however, symptoms appear to quickly worsen when fluoxetine treatment is discontinued.

Research funded by Eli Lilly and Company, Indianapolis, Indiana 46285.

NR451 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Efficacy of Intermittent Fluoxetine Dosing on the Physical Symptoms of PMDD

Cherri M. Miner, M.D., *Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, DC 2423, Indianapolis, IN 46285*; Eileen Brown, Ph.D., Julia Dillon, Pharm.D.

Summary:

Objective: Treatment with daily fluoxetine has demonstrated efficacy in multiple controlled trials for PMDD. Given findings supporting comparable efficacy of luteal phase dosing and daily dosing fluoxetine in one open-label study, a larger multicenter, randomized, double-blind, placebo-controlled trial was undertaken to evaluate the efficacy of luteal phase dosing of fluoxetine in PMDD.

Methods: Following a two-cycle screening and a one-cycle, single-blind placebo period, 260 women were randomized to fluoxetine 10 or 20 mg/day or placebo (each dosed for 14 days prior to the next expected menses through the first full day of menses) for three cycles. Women recorded PMDD symptoms daily throughout the phases of the trial using Daily Record of Severity of Problems (DRSP). Physical symptoms that were included in the DRSP included breast tenderness, bloating, headache, and joint/muscle pain. The primary analysis was change from mean baseline luteal phase scores to mean treated luteal phase scores over three months of treatment.

Results: Luteal dosing with fluoxetine 20 mg/day significantly improved breast tenderness score ($p<.001$), bloating ($p=.001$), joint/muscle pain ($p=.037$), but not headache ($p=.155$), compared with placebo. Fluoxetine 10 mg/day was not statistically significantly different from placebo for any of the physical symptoms.

Conclusion: Luteal phase dosing of fluoxetine effectively treats the core physical symptoms of PMDD.

Research funded by Eli Lilly and Company, Indianapolis, Indiana 46285.

NR452 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

The National Institute of Mental Health PMDD Prevalence Study: Recent Findings

Shirley A. Hartlage, Ph.D., *Department of Psychiatry, Rush Medical College, 1725 West Harrison Street, Suite 955, Chicago, IL 60612-3864*; Sarah Gehlert, Ph.D., Patricia Meaden, Ph.D.

Summary:

Objective: Scientists and the members of the popular press have debated hotly whether premenstrual dysphoric disorder (PMDD) should be included in the DSM. Some argue that the disorder doesn't exist and others that inclusion will result in labeling normally menstruating females as "pathological." To inform the situation with facts, NIMH sponsored a study of the prevalence of PMDD in a representative sample of 2,600 menstruating females from 13 through 55 years old. Our objective is to present recent study findings regarding PMDD and impaired premenstrual functioning.

Method: Urban and rural Illinois participants (N = 408) rated daily for two menstrual months both DSM-IV PMDD symptoms and functioning. Participants completed psychiatric diagnostic interviews in order to differentiate PMDD from premenstrual exacerbations of other disorders.

Results: Five (1.2%) females met all DSM-IV-TR criteria for PMDD when investigators analyzed symptom severity and daily functioning ratings via the effect size method. All who met symptom criteria were functionally impaired premenstrually. However, at least 56 more females (13.8%) who also were impaired pre- versus post-menstrually did not meet full criteria for PMDD.

Conclusion: The prevalence of PMDD in the normal population may be overestimated in DSM-IV-TR. Concern arises that females who are impaired premenstrually may not receive needed treatment because they do not meet stringent criteria for the disorder.

NR453 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Correlates of Long-Term Satisfaction with ECT

Karen M. Graszer, M.A., *Department of Psychiatry, Mayo Foundation, 200 First Street SW, Rochester, MN 55905*; Julie C. Hathaway, M.S., Teresa A. Rummans, M.D., Glenn E. Smith, Ph.D.

Summary:

Objective: This study examined patient satisfaction with electroconvulsive therapy (ECT) at 6 months following acute treatment and explored satisfaction correlates.

Method: Twenty-five patients completing the multicenter study "Continuation ECT Versus Pharmacotherapy: Efficacy and Safety" (MH #55484) were administered an ECT satisfaction survey, the Hamilton Rating Scale for Depression (HRSD), Mini-Mental State Examination (MMSE), and the Rey Auditory Verbal Learning Test (AVLT). Twelve subjects were randomly assigned to pharmacotherapy and 13 to ECT for continuation therapy. Average pre-ECT HRSD score was 33.4 (SD=6.0); average HRSD score at 6 months was 9.4 (SD=7.9).

Results: Satisfaction scores were not significantly different between subjects randomly assigned to either form of continuation therapy. The 6-month HRSD score was the sole statistically significant correlate of satisfaction ($r = -0.43$; $p = 0.03$). Neither MMSE score ($r = 0.01$; $p = 0.90$) nor AVLT delayed recall score ($r = -0.31$; $p = 0.13$) were significantly correlated with satisfaction scores.

Conclusion: Results suggest that global cognitive measures and specific anterograde memory measures do not correlate with patient satisfaction at 6 months post-acute ECT. Furthermore, satisfaction did not differ across type of continuation therapy. Rather, patient satisfaction was significantly correlated with depression ratings at 6 months post-treatment.

NR454 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Past Year Use of Alcohol and Medications for Sleep

Thomas Roth, Ph.D., *Sleep Disorders Center, Henry Ford Hospital, 2799 West Grand Boulevard, CFP3, Detroit, MI 48202*; Timothy A. Roehrs, Ph.D.

Summary:

Objectives: People with insomnia are not typically treated medically for their insomnia. Studies have reported that approximately 30% of insomniacs self-medicate with alcohol or OTC medications. This study was done to identify determinants of differing insomnia therapeutics.

Methods: A random-digit-dial, computer-assisted survey of a representative sample of adults aged 18–65 yrs was conducted. The survey response rate was 70%. A sample of all respondents over a 1-year period was collected (N=830). Exclusive past-year use of alcohol (Alc) for sleep was reported by 11% (N=89), prescription medications (Rx) by 7% (N=62), and OTCs by 9% (N=79). Six percent used both alcohol and sleep medications. The exclusive substance users formed the three comparison groups of the study.

Results: The Alc group used alcohol for more consecutive nights (χ^2=217.4, $p<0.001$) and more total nights (χ^2=228.7, $p<0.001$) than the Rx and OTC groups used medications. Alc users were predominately male (63%), while 43% of Rx and OTC users were men (χ=8.44, $p<0.01$). Alc users were more likely to be single and never married (48%) (χ^2=30.4, $p<0.001$) than the others. Alc [38.5 yrs] and OTC [39.8 yrs] users were younger than Rx users [46.5 yrs] (F=10.08, $p<0.001$). Rx users had more severe insomnia and reported more frequent episodes of difficulty sleeping lasting more than a month (χ^2=12.9, $p<0.04$), more difficulty falling asleep (χ^2=17.2, $p<0.01$), and more difficulty returning to sleep (χ^2=13.7, $p<0.03$). In contrast, Alc users had more daytime sleepiness, reporting more often falling asleep in conversation (χ^2=16.3, $p<0.01$), falling asleep when sitting (χ^2=15.5, $p<0.05$), and falling asleep in less than 5 min (χ^2=23.0, $p<0.001$) than Rx and OTC users.

NR455 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Efficacy and Safety of Discontinuous Zolpidem Treatment in Primary Insomnia

Goran Hajak, M.D., *Klinik Und Poliklinik fur Psychiatry, Hiatrie Universitatsstrabe 84, Regensberg D-93053, Germany*; Raymond Cluydts, M.D., Christina Soubrane

Summary:

Objective: The primary objective of this study was to compare, in a large primary care insomniac population, the hypnotic efficacy of zolpidem 10 mg five nights/week and placebo two nights/week, taken in random sequence, with nightly zolpidem 10 mg.

Methods: In this multicenter, randomized, double-blind, placebo-controlled, parallel-group study 789 drug-free and otherwise healthy chronic insomniacs (sleep disturbances ≥3 times per week ≥4 weeks) were enrolled by primary care physicians in five European countries. The primary efficacy criterion was investigator-assessed Clinical Global Improvement (CGI-2).

Results: After treatment completion, 58.6% of patients receiving zolpidem discontinuously versus 65.2% of the patients receiving continuous zolpidem were rated as "much" or "very much" improved. Sleep onset latency (SOL), total sleep time, number of nocturnal awakenings, and quality of life (MOS sleep questionnaire and SF36 scale scores) did not differ significantly between treatment groups. Safety was comparable, and no significant rebound phenomena were seen in either group.

Conclusions: Both continuous and discontinuous zolpidem treatment improved sleep and quality of life in insomniac patients. Although statistical equivalence was not achieved for the primary efficacy criterion (Clinical Global Improvement), the small difference was unlikely to be of clinical relevance. Safety was comparable in both treatment groups.

NR456 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Zolpidem "As Needed" Combined with Behavioral Treatment: A Field Study

Goran Hajak, M.D., *Klinik Und Poliklinik fur Psychiatry, Hiatrie Universitatsstrabe 84, Regensberg D-93053, Germany*

Summary:

Objective: The study objective was to validate the feasibility of non-nightly zolpidem treatment with stimulus control under conditions resembling real life.

Methods: This 3-week prospective, open-label trial was conducted on 2,690 otherwise healthy and drug-free chronic insomniac patients enrolled by primary care physicians in over 500 centers in Germany. Patients took 10 mg zolpidem on 3–5 nights per week, "as needed", using stimulus control on drug-free nights. The primary efficacy criterion was Clinical Global Improvement (CGI-2).

Results: At study end, 79.2% of the patients were rated as "much" or "very much improved" (CGI-2), and 91.3% of patients rated treatment efficacy as "good" or "very good". Mean sleep onset latency decreased from 74.4±46.3 min at baseline to 27.0±19.9 min, and mean total sleep time increased from 5.0±1.4 h to 6.8±1.2 h. Tolerance of treatment was rated as "very good" or "good" by 97.1% of the patients. Weekly tablet intake was 3.7 in week 1 and 2.6 in week 3.

Conclusions: Non-nightly use of zolpidem treatment combined with stimulus control was effective and well tolerated by a large chronic insomniac population in primary care. Tablet intake tended to decrease, indicating a low risk of tolerance or dependence.

NR457 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Characteristics of Zaleplon Use in Belgium

Raymond Cluydts, M.D., *Department of Sleep Disorders, University Hospital, Wilrijkstraat 10, Edegem 2650, Belgium*; Annick Mignon, Ph.D., Marc Timmerman, Ph.D., Olivier Van Reeth, M.D.

Summary:

Objective: Given its pharmacological profile, zaleplon permits flexible use by insomniacs. One major issue to be addressed is the dependence potential related to rebound insomnia and withdrawal symptoms.

Method: Drug accountability is used in this study to assess possible escalation in drug intake. In June and July 2000, 43 physicians provided anonymous data on 213 insomniacs who were prescribed zaleplon in April and May. During a face-to-face contact with the doctors interviewers filled out a standardized questionnaire on nature, severity, and duration of the sleep problem as well as intake characteristics of zaleplon (number of pills taken, timing of the intake, and treatment satisfaction).

Results: A scatterplot with polynomial fit revealed that the number of capsules taken by days in the study decreased by time. A MANOVA comparing three groups with different duration of exposure to zaleplon (<2 weeks, 2–4 weeks, >1 month) evidenced, respectively, a mean weekly intake of 6.39; 4.78, and 3.36 pills, respectively.

Conclusion: Flexible use of zaleplon did not lead to intake escalation.

NR458 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Self-Reported Outcome and Satisfaction in Two Acute Partial-Hospital Programs

Eda Ulus, B.S., *Department of Psychiatry, LeHigh Valley Hospital, 406 Rockhill Circle, Bethlehem, PA 18017*; Thomas Miller, M.S.W., Jerome Lee, Ph.D., Ralph A. Primelo, M.D.

Summary:

Objective: Patient outcome and satisfaction were studied in two acute adult partial hospitalization programs within the same hospital system.

Methods: In a repeated-measures design, 101 patients completed the 32-item Behavior and Symptom Identification Scale (BASIS-32), which assesses self-reported patient outcome, at admission and discharge. The 18-item Perceptions of Care Scale, a measure of patient satisfaction, was completed at discharge. Overall and subscale scores were analyzed by diagnostic group, including dual diagnosis with substance abuse. The two programs were compared to assess if improvement and satisfaction were consistent regardless of program location. In addition, the relationship between outcome and satisfaction was studied.

Results: Patients improved significantly overall and on many specific subscales equally well, regardless of program location. Several differences by diagnostic group and dual diagnosis were observed with regard to outcome and satisfaction. Significant relationships were illustrated between outcome and satisfaction.

Conclusions: The results indicate that both partial programs are similarly effective for treating patients with a variety of acute illnesses and past diagnoses. Studying specific components of outcome and satisfaction, as well as the relationship between outcome and satisfaction, are areas essential for future exploration to enhance program development and ensure the efficacy of partial programs within the psychiatric continuum of care, particularly in the era of managed care.

NR459 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Anxiety Symptoms in Depressed Patients With and Without Comorbid Anxiety Disorders: Implications for Generalizability of Antidepressant Efficacy Studies

Diane D. Young, Ph.D., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Mark Zimmerman, M.D.

Summary:

Objective: Antidepressant efficacy studies often exclude patients with comorbid anxiety disorders. In such studies, the prognostic significance of anxiety symptoms and the impact of medications on anxiety symptoms have been examined. This study investigated the impact of the anxiety disorder exclusion criterion on the representativeness of study samples regarding their level of anxiety symptoms.

Method: Of 422 psychiatric outpatients with a principal diagnosis of major depressive disorder as determined by the Structured Clinical Interview for DSM-IV (SCID), 235 (55.7%) patients also met criteria for a comorbid anxiety disorder. Anxiety symptoms were compared in patients with and without comorbid anxiety disorders, using the agitation, psychic, and somatic anxiety items from the Hamilton Rating Scale for Depression (HAM-D).

Results: By excluding patients with comorbid anxiety disorders, over one-half of potential participants would not have qualified for an antidepressant trial. Patients with comorbid anxiety disorders had significantly higher scores on all anxiety items evaluated when compared to depressed patients without anxiety disorders.

Conclusions: This analysis suggests that the level of anxiety severity experienced by patients included in efficacy trials is not representative of the level of anxiety severity experienced by all depressed patients, especially at the upper end of the severity dimension. This raises questions about studies of the prognostic significance of anxiety severity and the efficacy of antidepressants in reducing anxiety levels in depressed patients.

NR460 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Venlafaxine Versus SSRIs: Effect Size Comparison for the Hamilton Depression Scale Total and Subscale

A. Richard Entsuah, Ph.D., *Clinical Research and Development, Wyeth-Ayerst Research, 145 King of Prussia Road, Radnor, PA 19087*

Summary:

Objective: HAM-D_{17} subscales may be more sensitive to therapeutic change than HAM-D_{17} total. Sensitivity and power were compared.

Method: In a meta-analysis of data from 2,045 depressed patients receiving venlafaxine/venlafaxine XR (ven/ven XR), an SSRI, or placebo for ≤8 weeks, HAM-D_{17} subscale scores were recorded. Effect sizes for subscales and HAM-D_{17} total were compared.

Results: In SSRIs versus placebo, subscales yielded effect sizes 60%–100% larger than HAM-D_{17} total (0.24–0.30 versus .15). In ven/ven XR versus placebo, subscales yielded effect sizes 21%–32% larger (0.41–0.45 versus 0.34). In ven/ven XR versus SSRIs, subscales and HAM-D_{17} total yielded similar, positive effect sizes (0.19–0.20). Compared to placebo, SSRIs and ven/ven XR led to larger, positive effect sizes on psychic rather than somatic HAM-D items. SSRIs yielded net negative effect size for somatic HAM-D items (–0.28); ven/ven XR generated net positive effect size (+0.05) for somatic items.

Conclusions: Compared to HAM-D_{17} total, HAM-D subscales appear more sensitive to therapeutic change on active agent-placebo comparison and equally sensitive in a comparison of ven/ven XR and SSRIs. Findings further suggest that ven/ven XR exert greater therapeutic effect than SSRIs. Accordingly, prudent use of subscales may be appropriate, cost-effective, and informative.

NR461 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Remission Rates with Different Venlafaxine Dosages Versus SSRIs in MDD

A. Richard Entsuah, Ph.D., *Clinical Research and Development, Wyeth-Ayerst Research, 145 King of Prussia Road, Radnor, PA 19087*

Summary:

Objective: To evaluate various dosages of venlafaxine, selective serotonin reuptake inhibitors (SSRIs), and placebo in the treatment and remission of major depressive disorder (MDD).

Methods: Data from over 2,000 patients with moderate to severe MDD were pooled for analysis. Patients received venlafaxine (≤75 mg, 76–150 mg, 151–225 mg, or >225 mg), an SSRI (fluoxetine, paroxetine, or fluvoxamine), or placebo for ≤8 weeks. Remission (HAM-D_{17} total ≤7), absence of depressed mood (ADM; HAM-D Item 1=0), and response to treatment (≥50% reduction from baseline on HAM-D_{21}) were assessed.

Results: Remission rates for all venlafaxine dosages (43%–45%) were significantly higher than those for the SSRIs (35%; $p<0.001$) or placebo (25%; $p<0.001$). ADM rates were 33%–43% for venlafaxine ($p<0.001$ versus placebo), 31% for the SSRIs, and 20% for placebo; venlafaxine ≤75 mg was significantly better than the SSRIs. Response rates ranged from 61%–66% for venlafaxine, compared with 57% for the SSRIs and 42% for placebo; the high dosage of venlafaxine was significantly better than placebo ($p<0.05$).

Conclusions: At established safe dosages, venlafaxine was superior to the SSRIs and placebo in achieving remission of MDD as well as in rates of ADM and response to treatment.

NR462 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Double-Blind Comparison of Lamotrigine Versus Valproate on Mood and Body Weight

Nancy L. Earl, M.D., *GlaxoSmithkline, 5 Moore Drive, Research Triangle, NC 27709*; Victor Biton, Keith R. Edwards, M.D., Wagar Mirza, Dalma Sackellares, Pamela Barrett, Alain Vuong

Summary:

Objective: Lamotrigine (LTG) and valproate (VPA) are two anticonvulsant drugs commonly used in the treatment of bipolar disorder. This study was designed to compare effects on mood and body weight in epilepsy patients.

Methods: A total of 133 patients with any seizure type were randomized to double-blind treatment with VPA or LTG, which were titrated according to manufacturer's recommendations over an eight-week period followed by 24 weeks of maintenance treatment. Mood (assessed by Profile of Mood States, Beck Depression Inventory, and Cornell Dysthymia Rating Scale) and vital signs were assessed periodically throughout the study.

Results: Overall completion rates were 71% for LTG and 56% for VPA (p=0.05). Mean weight increase was significantly greater for VPA from week 10 onwards, with total increases of 12 pounds for VPA vs. one pound for LTG. Mood ratings were consistently higher in the LTG group compared with VPA, despite similar scores at baseline. Adverse event profiles for both drugs were consistent with previous experience. The rate of drug-related rash was 6% for LTG and 4% for VPA.

Conclusion: Although both drugs appear to be useful agents in the treatment of this patient population, there were important differences in their effects on mood and body weight.

Research funded by GlaxoSmithKline

NR463 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Replication of Chromosome 15 Linkage to Schizophrenia: A Veterans Administration Cooperative Study

Debby W. Tsuang, M.D., *MIRECC 166, VAPSHCS, 1660 South Columbian Way, Seattle, WA 98108*

Summary:

Objective: To replicate previous findings of positive linkage on chromosome 15 in a large VA sample using affected sibling pair analysis.

Methods: One-hundred and sixty-six families with two or more affected individuals with schizophrenia were ascertained. These families contained a total of 216 affected sibling pairs, comprising the largest North American sample of schizophrenia sibling pairs. In addition, this is the largest sample of African-American families collected to date (n=74; 45%). Overall, 307 probands (92.5%) met DSM-III-R criteria for schizophrenia, and 25 (7.5%) met DSM-III-R criteria for schizoaffective disorder, depressed. Probands were 76% male and relatives were 42% male. DNA samples were genotyped with genetic markers on chromosome 15 spaced 10 cM apart, followed by genotyping of additional high density markers spaced approximately 5 cM apart. Nonparametric affected-only multi-point analysis was used for linkage.

Results: The most significant findings were in African-American families, with markers on chromosome 15 yielding a maximum lod score of 2.23. Higher density markers spaced at 2–5 cM increased the maximum lod score to 2.46 for the markers D15S1040 and D15S118. These markers are 7cM from the α-7 nicotinic cholinergic receptor subunit (CHRNA-7) gene, previously implicated by Freedman et al.

Conclusion: These findings are consistent with previous reports of linkage to the CHRNA-7 region. Additional studies are necessary to evaluate the involvement of the CHRNA-7 and other susceptibility genes in schizophrenia.

NR464 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

OCD in the Afrikaner Population: An Association Study with Polymorphisms in the Dopamine and 5HT Transporter Genes

Dana J.H. Niehaus, M.B., *Department of Psychiatry, University of Stellenbauch Medical School, P.O. Box 19090, Tygerberg 7505, South Africa*; Sian Hemmings, Craig Kinnear, Jeanine Van Kradenburg, Johanna Moolman-Smook, Valerie Corfield, Paul Brink, Annamarie Potgieter, Robin A. Emsley, M.D., Dan J. Stein, M.D.

Summary:

There is increasing evidence that the etiology of obsessive-compulsive disorder (OCD) has a marked genetic component, although the precise mechanism of inheritance is unknown. Biological markers for subsets of OCD may allow more specific treatment and permit early detection of subclinical OCD. Clinical studies have implicated a dysfunction in the catecholaminergic and serotonergic systems in the pathogenesis of OCD. The serotonin transporter (5HTT) and the dopamine transporter (DAT) are central to the fine tuning of brain catecholaminergic and serotonergic neurotransmission, since they mediate the synaptic inactivation and the subsequent reuptake of dopamine and serotonin, respectively. 5HTT has also been found to be a major site of action for serotonin specific reuptake inhibitors (SSRI's). The actions of the 5HTT and DAT protein pumps, and their localisation to specific dopaminergic and serotonergic neurons, make the genes encoding them promising candidates for detecting genetic susceptibility to OCD.

Consequently, the association with OCD of a polymorphism (5HTTLPR) in the 5HTT gene (SCL6A4), reported to have functional significance and a polymorphism in the DAT gene (SCL6A3) were investigated in the genetically homogeneous Afrikaner population.

Patients and ethnically matched controls underwent a structural interview (SCID, MinI) and were diagnosed according to DSM-IV criteria. Allelic variation was assessed by a polymerase chain reaction (PCR) - based method, and patients and controls were genotyped accordingly (54 OCD patients and 60 controls were genotyped using the SCL6A4 polymorphism, 47 OCD patients and 48 controls were genotyped using the SCL6A4 polymorphism, 47 OCD patients and 48 controls were genotyped using the SCL6A3 polymorphism.).

A comparison of genotypic and allelic distribution of polymorphisms in both genes yielded no statistically significant differences between patients and controls. These data therefore do not support an association between the allelic variants in either the SCL6A4 or SCL6A3 genes and OCD. It can thus be assumed that neither of the genes plays a major role in the pathogenesis of OCD in the study population.

NR465 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

5HT-1B Polymorphism and Weight Regulation in Bulimia Nervosa

Allan S. Kaplan, M.D., *Department of Psychiatry, Toronto General Hospital, 200 Elizabeth Street, EN8-231, Toronto, ON M5G 2C4, Canada*; Robert D. Levitan, M.D., Mario Masellis, B.S.C., Vincenzo S. Basile, B.S.C., Gabrielle Siegel, B.A., Nancy Lipson, B.S.C., James L. Kennedy, M.D.

Summary:

Background: It is well established that some patients with bulimia nervosa (BN) achieve a very low body mass index (BMI) in response to dieting, whereas others appear to have a high minimum set point of weight that prevents weight loss beyond a certain point. The biological basis for this clinical finding remains unknown. We are currently exploring a possible connection between serotonin genetic variation and weight regulation in a sample of women with BN.

Methods: 106 women with BN were genotyped based on the G8GIC polymorphism of the serotonin-IB receptor gene (HTRIB). Lifetime BMI measures were compared across the genotypic groups using ANOVA.

Results: There were significant differences in minimum lifetime BMI across the three genotypic groups (G/G: mean=19.4, SD=3.2; G/C: mean=17.4, SD=2.0; C/C: mean=16.6, SD=2.4) ($F=7.95$, df=2,103, $p=0.001$). Post-hoc testing revealed that the G/G genotype of HTRIB was associated with significantly higher minimum lifetime BMI than the other two genotypes.

Conclusions: These preliminary findings suggest a possible association between HTRIB genetic polymorphism and weight regulation in women with BN. Pending replication in a larger sample, these findings point to a possible genetic factor of fundamental importance to the eating disorder population.

For clinicians and investigators who are interested in the relationship between serotonergic system genes, weight regulation and eating behaviour.

Research supported by the Ontario Mental Health Foundation.

NR466 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

DRD4 Receptor Gene in OCD

Fariba Sam, B.S.C., *Department of Neurogenetics, CAMH-Clarke Division, 250 College Street, Toronto, ON M5T 1R8, Canada*; Emanuela Mundo, M.D., Margaret A. Richter, M.D., James L. Kennedy, M.D.

Summary:

Objective: Family and twin studies have shown the involvement of genetic factors in the pathogenesis of obsessive-compulsive disorder (OCD). Serotonin dysregulation seems to be the leading pathogenetic hypothesis for OCD; however, there is also good evidence implicating dopaminergic mechanisms based on the relationship between OCD and tic disorders. The aim of this study was to investigate the presence of linkage disequilibrium between the dopamine D4 receptor (DRD4) gene and OCD.

Methods: One hundred twenty OCD probands with their living parents gave their informed consent to participate in the study. Patients were diagnosed using the structured interview for DSM-IV (SCID-I). The 48-bp repeat polymorphism in the third exon of the DRD4 gene was genotyped, and the Transmission Disequilibrium Test (TDT) was applied to the genotyping data.

Results: Fifty-six families were informative for the analysis that showed no biases in the transmission of the alleles from the heterozygous parents to the affected subjects.

Conclusions: These results do not appear to show a major involvement of the DRD4 gene in the pathogenesis of OCD. However, further investigations on larger samples and on OCD patients with comorbid tic disorders are warranted.

NR467 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Specificity of 5HT Transporter Gene in Predicting Antidepressant-Induced Mania in Bipolar Disorder

Emanuela Mundo, M.D., *Neurogenetics Department, University of Toronto-CAMH, 250 College Street, Toronto, ON M5T 1R8, Canada*; Melissa Walker, B.S.C., Xingqun Ni, M.D., Gwyneth Zai, Tasha Cate, B.A., Fabio Macciardi, M.D., James L. Kennedy, M.D.

Summary:

Objective: The occurrence of antidepressant-induced mania is an important problem in the clinical management of bipolar disorder (BP). Given the involvement of serotonin mechanisms in the response to antidepressants, the serotonin receptor genes are considered good candidates for the prediction of antidepressant response. Recently, we found a strong association between the short (and less functional) variant of the promoter polymorphism of the serotonin transporter (5HTT) gene and antidepressant-induced mania in a sample of BP patients treated with pro-serotonergic compounds. The aim of this study was to investigate, in the same sample, the 5HT1Dβ and the 5HT2A genes as complementary predictors of the development of antidepressant-induced mania.

Methods: Two groups of DSM-IV BP I or BP II patients, matched for age, gender, and ethnicity, with at least one depressive episode treated with pro-serotonergic antidepressants, gave their informed consent and were studied. The first group (N=27) included patients with at least one DSM-IV manic/hypomanic episode developed during the antidepressant treatment; the second (N=29) included patients with no antidepressant-induced switches. The 5HT1Dβ (G861C) and the 5HT2A (T102C) polymorphisms were genotyped blindly with respect to the 5HTT genotype and to the presence of induced mania and were compared between the two groups.

Results: No association between antidepressant-induced mania and either the 5HT1Dβ (χ^2=1.331, df=2, p=0.514) or the 5HT2A (χ^2=0.115, df=2, p=0.925) variants was found.

Conclusions: These results appear to confer specificity to the role of the 5HTT gene as a risk factor for the development of antidepressant-induced mania in BP. Further investigations on larger samples and on additional genes are warranted.

NR468 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

N-Methyl-D-Aspartate Receptor (NMDAR1) Gene Is Associated with Bipolar Disorder

Emanuela Mundo, M.D., *Neurogenetics Department, University of Toronto-CAMH, 250 College Street, Toronto, ON M5T 1R8, Canada*; Subi Tharmalingham, B.S.C., Sagar V. Parikh, M.D., Anusha Bolonna, M.S.C., Maria Arranz, Ph.D., Robert W. Kerwin, M.D., James L. Kennedy, M.D.

Summary:

Objective: Bipolar disorder (BP) has a strong genetic component. The glutamate system and the N-methyl-D-aspartate receptor (NMDAR) have been implicated in the pathogenesis of psychoses, and there is good evidence that lithium and valproate act via the NMDAR. These findings suggest a role for the NMDAR genes as candidates for BP. The key sub-unit of the NMDAR (NMDAR1) is coded by a gene located on chromosome 9q34.3. The aim of this study was to determine whether there is linkage disequilibrium between the NMDAR1 gene and BP.

Methods: Two hundred eighty-three subjects with a DSM-IV diagnosis of BP I, BP II, or schizoaffective disorder, bipolar type, and their living parents comprised the sample. All gave their written informed consent to participate in the study. The Transmission Disequilibrium Test compares the number of transmissions and non-transmissions of the alleles possibly associated with the disease from the parents to the affected offspring to detect any deviation from what would be expected by chance. It was applied to the genotyping data of the 1,001 G/C, the 1,970 A/G, and the 6,608 A/G polymorphisms of the NMDAR1.

Results: A significant association between both the 1,001 G/C ($\chi^2$4.765, df=1, p=0.030) and the 6,608 A/G (χ^2=8.395, df=1, p=0.004) polymorphisms and BP was found.

Conclusions: These findings may have important implications. Replication on independent samples and the study of the NMDAR1 gene variants as potential predictors of the response to mood stabilizers in BP are warranted.

NR469 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

5HT Gene Polymorphisms and Schizophrenia

Pilar A. Saiz, Ph.D., *Department of Psychiatry, University of Oviedo, Julian Claveria No 6-30, Oviedo 33006, Spain*; Blanca Morales, M.D., Victoria Alvarez, Ph.D., Eliecer Coto, Ph.D., Juan M. Fernandez, M.D., Manuel V. Bousono, Ph.D., Julio B. Bobes, Ph.D.

Summary:

Objective: To investigate the potential association between four serotonin gene polymorphisms [T102C, A-1438G, VNTR (5-HTT), 5-HTTLPR] and schizophrenia.

Patients and Methods: We genotyped 106 schizophrenic outpatients (Sc) (DSM-IV) [mean age: 35.12 (10.25), 55.6% males] and 119 healthy volunteers (blood donors) [mean age: 43.29 (11.28), 75.8% males] from Asturias (Northern Spain). Polymorphisms were determined after PCR amplification followed by digestion with restriction enzymes and electrophoresis on an agarose gel.

Results: 5-HT_{2A} polymorphisms.- both 5-HT_{2A} polymorphisms (T102C and A-1438G) are in complete linkage desequilibrium in our population. T102C or A-1438G (Sc vs Controls): TT or AA: 26.4%, 19.5%; TC or AG: 53.8%, 52.5%; CC or GG: 19.8%, 28.0% (p=.255). Serotonin transporter polymorphisms.- VNRT (5-HTT) (Sc vs Controls): 12rep12rep: 37.1%, 39.1%; 12rep10rep: 41.9%,

31.3%; 12rep9rep: 0%, 0.9%; 10rep10rep: 20.0%, 27.8%; 10rep9rep: 1%, 0.9% (p=.397). 5HTTLPR (Sc vs Controls): LL: 21.4%, 30.3%; Ls: 43.7%, 47.9%; ss: 35.0%, 21.8% (p=.071). However, the additive presence of alleles T or A plus 12rep plus s confers a risk for schizophrenia (Sc vs Controls): 52.4%, 35.1% [OR: 2.03; 95%CI=1.18 – 3.52; p=.013].

Conclusions: Multiple serotonin genes, having small additive effects, in combination with environmental influences, could contribute to the development of schizophrenia.

NR470 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

5HT Gene Polymorphisms and Suicidal Behavior

Blanca Morales, M.D., *Department of Psychiatry, Oviedo University, Julian Claveria 6, #3, Oviedo 33006, Spain*; Pilar A. Saiz, Ph.D., Victoria Alvarez, Ph.D., Eliecer Coto, Ph.D., Juan M. Fernandez, M.D., Manuel V. Bousono, Ph.D., Julio B. Bobes, Ph.D.

Summary:

Objective: To investigate the potential association between four serotonin gene polymorphisms [T102C, A-1438G, VNTR (5-HTT), 5-HTTLPR] and suicidal behavior.

Patients/Methods: We genotyped 41 parasuicidal patients (PP) [mean age: 32.44 (9.48), 39.0% males] and 119 healthy blood donors [mean age: 43.29 (11.28), 75.8% males] from Spain.

Polymorphisms were determined after PCR amplification followed by digestion with restriction enzymes and electrophoresis on an agarose gel.

Results: 5-HT_{2A} polymorphisms.- both 5-HT_{2A} polymorphisms (T102C and A-1438G) are in complete linkage desequilibrium in our population. T102C or A-1438G (PP vs Controls): TT or AA: 17.1%, 19.5%; TC or AG: 51.2%, 52.5%; CC or GG: 31.7%, 28.0% (p=.882). Serotonin transporter polymorphims.- VNRT (5-HTT) (PP vs Controls): 12rep12rep: 48.8%, 39.1%; 12rep10rep: 39.0%, 31.3%; 12rep9rep: 0%, 0.9%; 10rep10rep: 12.2%, 27.8%; 10rep9rep: 0%, 0.9% (p=.283). 5HTTLPR (PP vs Controls): LL: 25.0%, 30.3%; Ls: 45.0%, 47.9%; ss: 30.0%, 21.8% (p=.557). The additive presence of alleles C or G plus 12rep plus s does not confer a risk for parasuicidal behaviour (PP vs Controls): 55.0%, 41.4% [OR: 1.73; 95%CI=0.83 – 3.58; p=.194].

Conclusions: Polymorphic variations at several serotonin genes were not associated with an increased risk of parasuicidal behavior, nor did they have an additive effect.

NR471 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Adolescent Suicide Attempts in Spain: Risk Factors

Juan C. Gonzalez-Seijo, M.D., *Salud Mental, S. E. S. P. A., Uria 34, #4, Gijon 33202, Spain*; Yolanda M. Ramos, M.D., Jose L. De Dios, M.D., Ismael Lastra, M.D., Carlos Carbonell

Summary:

Objective: Suicide rates in young people have increased in Spain the past three decades. The San Carlos Study has been designed to identify the risk factors for suicide attempts.

Method: Subjects were 54 adolescents aged 13 to 18 referred to San Carlos Hospital after a suicide attempt, and 108 normal comparison adolescents from the same socioeconomic status. A case-control study design has been used and they have been matched by age and sex.

Results: The risk factors that contribute to suicidal behavior include previous mental disorder (OR = 6.54), alcohol abuse (OR = 4.50), depressive symptomatology (OR = 6.40), parental psychopathology (OR = 8.67), parental discord (OR = 3.00), parental losses (OR = 19.00), unsatisfactory social adjustment (OR = 2.60), three or more live events (OR = 8.20), and a pleasant concept of death (OR = 39.32).

Conclusions: Such factors belong to the following four areas of suicidal vulnerability: psychopathological, cognitive, familial, and psychosocial.

NR472 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Managing Suicide Risk in Late Life: Access to Fire Arms

David W. Oslin, M.D., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, Room 790, Philadelphia, PA 19104*; Cynthia Zubritsky, Ph.D., Anthony Puliafico, Gregory Brown, Ph.D., Trevor Hadley, Ph.D., Marian Mullahy, Ira R. Katz, M.D.

Summary:

According to the National Center for Health Statistics, people over 65 made up 12.5% of the population but committed 20% of all suicides. The purpose of this study was to assess the public health risk of firearm availability as a risk factor for suicide. Data are presented from two urban sites that are participating in a SAMHSA- and VA-sponsored multisite study (PRISMe Study) comparing referral care to a collaborative care model for mental health services. A random sample of older adults from primary care is being screened using the General Health Questionnaire and questions about suicidality, alcohol use, and availability of firearms. Of 447 patients screened, 126 (25%) report having any type of firearm in the home and 90 (20%) report having a handgun in the home. In 76% of the homes with a firearm, there is ammunition available and the majority of the firearms are stored unlocked. Patients with suicidal ideation or high levels of distress or depression were as likely to have a gun in the home as those without these emotional stressors. These preliminary data suggest that a significant proportion of the elderly have firearms available to them and that most do not exhibit safe firearm practices. These data strongly suggest the need for screening for firearm availability and the safe storage of those firearms among patients suffering from emotional distress or suicidal ideation.

NR473 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Risk Factors of Suicide Attempts: A Cross-Section Survey of Army Recruits

Tsung-Tsair Yang, Ph.D., *Military Psychiatric Center, No. 60 Hsin-Ming Road, Taipei, Taiwan*; Yueh-Ming Tai, M.D., Ming Chang, M.D.

Summary:

Objective: Suicide attempt (incomplete suicide) has been an essential factor for predicting suicide behavior. This study tried to clarify the relationship between history of previous suicide attempts and depression, anxiety, and suicide ideation of young men.

Method: Previous suicide attempt history, demographic data, Zung's self-administrated Anxiety scale (SAS), and Zung's self-administrated Depression scale (SDS) were collected from 1,039 Taiwanese army recruits during the first week of their entry. A psychiatrist interviewed all the recruits who were suspected by their squad leaders as having a psychiatric problem.

Results: 11.6% of recruits admitted a previous suicide attempt (SH group); about 60% of the SH group reported only one previous suicide attempt (SH1 group), and 10% reported more than one suicide attempt (SH2+ group). The comparison between the SH group and the rest of our sample, who had no history of suicide attempts (NSH group), showed that the SH group had a higher percentage of unemployment status, separated parents, non-drug crime records, family history of psychosis, family history of suicide, and higher mean SAS scores. SDS score, as well as lower mean scores for general satisfaction and mastery about economic,

health, emotion, and social situations, and family relationships. The comparison between SH1 group and SH2+ group showed higher SDS scores, higher SAS scores, and lower satisfaction scores of the SH2+ group that were significantly different from those of the SH1 group. The study population with higher frequency of previous suicide attempts were positively associated with past psychiatric history, with attempting to see a psychiatrist, with probable psychiatric disorder suspected by the investigator, and suicidal ideation.

Conclusion: In Taiwanese army recruitment population, suicide attempt, psychiatric disorder, and suicidal ideation were highly related. Early psychiatric consulting of this group (SH group) would be meaningful.

NR474 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Risk Factors for Suicide Behavior in the Canadian Arctic

John M. Haggarty, M.D., *Department of Psychiatry, University of Western Ontario, 580 North Algoma Street, Thunder Bay, ON P7B 5G4, Canada*; Michel Bedard, Ph.D., Mariwan Husni, M.D., Zachias Cernovsky, Ph.D., Harold Merskey, M.D.

Summary:

Introduction and method: Rates of completed suicide in the circumpolar region rank as some of the highest in the world. We undertook a random household survey in a Canadian Arctic Inuit community (N = 111) using a four-item self-report questionnaire (in English or in Inuktitut) dealing with thoughts of killing oneself in the past week, suicide attempts, plans to kill oneself, and wish to die within the last 6 months. The respondents were also administered the Hospital Anxiety and Depression Scale (HAD).

Results: Thirty percent of those responding attempted suicide within the last 6 months, 52.9% reported a wish to die in the past 6 months, 30.3% reported having a plan to die in the last 6 months, and 43.6% have thought of committing suicide in the past week. Our present analysis combined data from these four items in composite measure to identify respondents who fell in the top quartile (high suicide ideation). We used a multivariate logistic regression model to determine the independent contribution of age, gender, language, anxiety, and depression to increased suicidal behavior. Age less than 35 (OR = 6.12, 95% CI = 1.30–28.77) and high anxiety (OR = 3.68, 95% CI = 1.04–10.07) were strongly associated with high suicidal ideation and behavior. Gender, language, and depression were not.

Conclusion: Suicidal behavior in the Arctic is a frequent event and the relationship between high anxiety in young Inuit and suicide behavior must be examined further to ascertain causality.

Funding sources: University of Western Ontario. Baffin Regional Health Board.

NR475 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Lack of Association Between 102T/C Polymorphism and Suicidal Behavior

Humberto Correa, M.S.C., *Department of Pharmacology, UFMG-ICB, Antonio Carlos 6627, Belo Horizonte, MG 31270-901, Brazil*; Wolfanga Bonson, Ph.D., Melissa Machado, Julio Noronha, Mauro Carvalho, Luis A. De Marco, Ph.D., Marco A. Romano-Silva, Ph.D.

Summary:

Central serotonergic dysfunction and genetic factors are associated with suidical behavior in psychiatric patients. The objective of this study was to examine the association between the 5HT2A gene polymorphism (102T/C) and suicide in a sample of Brazilian psychiatric inpatients. Subjects were 48 schizophrenic I (age: 41.3 ± 8.8; 17 with a life-time history of suicide attempt (35.4%) I, 41 major depressed I (age: 43.6 ± 9.5; 17 with a life-time history of suicide attempt (41.1%) I and 38 healthy controls (age: 45 ± 9.2). Diagnosis were based on a structured interview (MINI-PLUS), according DSM-IV criteria. Comparisons of genotypic frequences between the groups were performed using the Fisher's exact test (2 x 2). No differences were found in genotypic frequencies across schizophrenic, depressed or healthy controls groups: TT I12 (25%), 11 (26.8%), 9 (23.65%) I; TC I26 (54.2%), 20 (48.9%), 20 (52.6%) I; CC I10 (20.8%), 10 (24.3%), 9 (23.7%) I. No differences were found between patients with a suicide attempt (n = 34) and without (n = 55): TT I9 (26.6%) I, TC I18 (52.9%), 30 (54.5%) I, CC I7 (20.6%), 12 (21.8%). These preliminary results, of a large epidemiological-molecular investigation of serotonin-related genes in a Brazilian population, suggest this polymorphism seems not involved in the genetic susceptibility to suicidal behavior.

NR476 Tuesday, May 8, 3:00 p.m.-5:00 p.m.

Fluoxetine Reduces Food Cravings During the Luteal Phase in Women with PMDD

Meir Steiner, M.D., *Department of Psychiatry, St. Joseph's Hospital, 301 James Street, South, Room 639, Hamilton, ON L8P 3B6, Canada*; Eileen Brown, Ph.D., Julia Dillon, Pharm.D.

Summary:

Introduction: A previously reported, placebo-controlled, multisite trial found fluoxetine effective in mediating PMDD mood symptoms; these data are now used to determine fluoxetine's effectiveness on eating habits during the luteal phase in women with PMDD. Although cyclical mood disturbance is the pathognomonic feature of PMDD, a marked change in appetite, overeating, or specific food cravings is one of the 11 DSM-IV criteria for PMDD.

Method: Eating habits were assessed in 320 women who were randomly assigned to fluoxetine 20 mg/day, fluoxetine 60 mg/day, or placebo. Symptoms were measured by two questions on the self-rated and one question on the observer-rated Premenstrual Tension Syndrome Scale (PMTS-SR, PMTS-O). Both scales assessed increase in food intake and specific food cravings. Outcome measure for each woman was her frequency of increased food intake/cravings during the luteal phase of the 6 months of treatment.

Results: Fluoxetine treatment (20 and 60 mg/day) significantly reduced the frequency of increased food intake/cravings compared with placebo treatment when measured on the PMTS-SR ($p<0.01$). A statistically significant reduction was detected for fluoxetine 20 mg/day versus placebo using PMTS-O ($p<0.01$).

Conclusion: Fluoxetine treatment was significantly superior to placebo in reducing the frequency of reported food cravings in women suffering from PMDD as measured by the PMTS-SR and PMTS-O.

Research funded by Eli Lilly and Company, Indianapolis, Indiana 46285.

NR477 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Psychophysiological Measures of DSM-IV Personality Disorders

Jose L. Besteiro, Ph.D., *Department of Psychiatry, Oviedo University, Julian Claveria 6, #3, Oviedo 33006, Spain*; Serafin Lemos, Ph.D., Angel Garcia-Prieto, Ph.D., Jose Muniz, Ph.D., Maria P. Gonzalez, Ph.D., Pilar A. Saiz, Ph.D., Julio Bobes, Ph.D.

Summary:

Objectives: Discover whether the triple cluster DSM-IV classification of personality disorder categories could be based on psychometric empirical evidence, using some personality and physiological measures.

Subjects/Method: The MCMI-II and BFQ Scale were administered to 138 subjects (mean age: 32.5; SD: 11.85; 47.8% males] who met DSM-IV criteria for a personality disorder (30.4% Cluster A, 55.8% Cluster B, 13.8% Cluster C). The psychophysiological measures were obtained from patients in response to experimental stress: heart rate, skin conductance response, and their correspondent speed of recovery to baseline responses (slope measures).

Results: The Cluster B individuals showed higer speed of recovery to baseline of heart rate [mean: .0921 (SD: .0239); (p = .020)]. The Cluster B patients showed higher mean rate on BFQ scales/subscales: openess: ideas [76.30 (SD: 11.15); p = .091], extraversion: activity [36.52 (SD: 9.33); p = .060], extraversion [70.30 (SD: 15.64); p = .096]. The Cluster C patients showed higher mean rate on agreeableness: trust [39.22(SD: 10.89); p = .019].

Conclusions: There were significant group differences between DSM-IV Cluster groups on openess, extraversion, agreeableness, and speed of recovery to baseline of heart rate. There is a slight tendency to lower impulse control in Cluster B subjects.

NR478 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Mirtazapine Versus Paroxetine in Elderly Depressed Patients

Alan F. Schatzberg, M.D., *School of Medicine, Stanford University, 401 Quarry Road, Room 3215, Stanford, CA 94305*; Charlotte Kremer, M.D., Heidi Rodrigues

Summary:

Objective: This multicenter, double-blind, eight-week study was performed to evaluate the antidepressant efficacy and safety of mirtazapine (15–45 mg/day) compared with paroxetine (20–40 mg/day) in patients aged 65 or older.

Methods: A total of 255 outpatients ≥65 years old who met DSM-IV criteria for major depression were included if they had a baseline HAM-D 17 score of ≥18 and an age-adjusted Mini Mental State Examination (MMSE) above the lowest 25th percentile. Assessments for efficacy and cognitive performance were obtained. Blood samples were obtained for determining genetic polymorphisms.

Results: Mirtazapine-treated patients (n = 126; mean daily dose of 25.6 ± 6.7 mg) demonstrated comparable baseline demographics to patients receiving paroxetine (n = 120; mean daily dose of 26.5 ± 5.5 mg). Dropouts due to adverse events occurred at rates of 14.8% (mirtazapine) and 26.2% (paroxetine), p = 0.030. Based on LOCF analysis, percent responders (decrease in HAM-D 17 score of at least 50% compared with baseline) were 27.8% and 13.3% (p < 0.05) at Day 14 for mirtazapine and paroxetine, respectively, and 57.9% and 50.0% at Day 56 (p = 0.239). A significant difference (p < 0.05, change from baseline) in mean HAM-D 17 scores between the two groups was demonstrated at Days 7, 14, 21 and 42 in favor of mirtazapine-treated patients.

Conclusions: Both mirtazapine and paroxetine were shown to be effective and well-tolerated, although dropouts due to adverse events were significantly greater with paroxetine. Based on response rates and weekly HAM-D scores, mirtazapine appears to exert an earlier onset of action compared with paroxetine.

This research was supported by a grant from Organon Inc., West Orange, NJ.

NR479 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Relapse Prevention During Long-Term Gepirone Therapy for Major Depression

Jay D. Amsterdam, M.D., *Department of Psychiatry, University of Pennsylvania School of Medicine, 3600 Market Street, Room 850, Philadelphia, PA 19104*

Summary:

Gepirone is a partial 5-HT_{1A} receptor agonist that has been shown in preliminary studies to be safe and effective in major depressive disorder (MDD). This multicenter study evaluated gepirone immediate release (Gep-IR) vs placebo in patients with a baseline HAMD-17 score ≥20 (later modified to ≥20 on the HAMD-25). Eligible patients initially received Gep-IR at a dose of 20 to 90 mg daily for six weeks on an open-label (OL) basis. Responders who completed the OL phase with a HAMD-17 score ≤12 (or a ≥50% reduction in HAMD-17 score *plus* a CGI score of at least "moderately improved") were randomized to receive Gep-IR or placebo for an additional six weeks. This double-blind (DB) phase allowed comparison of relapse rates between subjects who continued on Gep-IR compared with those switched to placebo. Relapse during the DB phase was defined as a return to ≥75% of pretreatment HAMD-17 score, or a CGI score of "no change" or "worse than pretreatment." A total of 134 patients entered the OL phase, and 70 enrolled into the DB phase. In the DB phase, subjects receiving Gep-IR demonstrated a significantly lower relapse rate at endpoint compared with placebo (26% vs 55%; $p < 0.03$). Overall, Gep-IR was well tolerated: 36 patients discontinued OL treatment, and four Gep-IR patients discontinued DB treatment due to side effects. In conclusion, Gep-IR was effective in preventing relapse in outpatients with MDD who initially responded to short-term Gep-IR therapy. These data provide additional evidence that gepirone has good therapeutic efficacy and a favorable safety profile.

NR480 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Insight in Patients with Schizophrenia and Schizoaffective Disorder

Martha Sajatovic, M.D., *Department of Psychiatry, Case Western Reserve, 345 Timberidge Trail, Gates Mills, OH 44040*; Debra A. Rosch, Ph.D., Harry J. Sivec, Ph.D., Dilara Sultana, M.D., Douglas A. Smith, M.D., Peter F. Buckley, M.D., C. Raymond Bingham, Ph.D.

Summary:

Objective: This study is an evaluation of symptoms, illness severity, attitudes toward medication treatment, and insight into illness in newly admitted state psychiatric patients.

Methods: Subjects were evaluated before and after treatment with atypical, typical, or mixed (atypical plus typical) antipsychotic medications. Measures used were the Brief Psychiatric Rating Scale (BPRS), Clinical Global Impression (CGI), Global Assessment of Functioning (GAF), Drug Attitude Inventory (DAI), and Scale to Assess Unawareness of Mental Disorder (SUMD). Hospital length of stay (LOS) was also evaluated.

Results: 45 patients were enrolled. Overall, subjects had significant improvement in symptoms, illness severity, insight, and functional level during course of hospitalization. Attitudes towards medication treatment changed minimally during treatment. Patients treated with either atypical antipsychotic alone or typical antipsychotic alone had greater improvements in insight, overall illness severity, and endpoint functional level compared to individuals receiving mixed medication treatment. LOS was shortest with atypical medications (12.0 days) and longest with mixed treatment (34.2 days).

Conclusion: Both atypical and typical antipsychotic medications are associated with improvements in psychiatric symptoms and insight into illness, but attitudes towards medication treatment may not be changed in spite of objective symptom reduction. This may be a potential factor in future medication compliance. Hospital use is lowest with atypical medication, and highest with combination treatment.

Funded in part by a grant from Janssen Research Foundation

NR481 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Lamotrigine in Rapid-Cycling Bipolar Disorder: Predictors of Response

Patricia Suppes, M.D., *Department of Psychiatry, Univ. of Texas Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX 75080*; John A. Ascher, M.D., Charles L. Bowden, M.D., Joseph R. Calabrese, M.D., Nancy L. Earl, M.D., Paul Greene

Summary:

Objective: Lamotrigine (LTG) has demonstrated efficacy as a mood stabilizer in patients with rapid cycling bipolar disorder in a double-blind, placebo-controlled study (GW#614). This paper analyzes predictors of response to drug and placebo.

Methods: A total of 324 rapid cycling patients entered an open-label stabilization phase, in which LTG was added in any phase of the illness. From this group, 177 patients achieved mood stabilization and were tapered to LTG monotherapy prior to entering the double-blind, six-month maintenance phase. For hypothesized groups of variables, multiple regression analysis was conducted to identify variables best predicting response. Survival analysis methods were employed to examine groups of variables best predicting survival time.

Results: LTG 41% vs. PBO 26% ($p < 0.05$) patients completed six months of randomized treatment without additional clinical intervention. Survival analysis based on time from randomization to time of intervention suggested a six-week difference in median survival in favor of LTG. Bipolar disorder type (BPI/BPII) and number of episodes in the preceding year were factors that differentiated survival in this study. Other variables are also discussed.

Conclusion: Analysis of this study has identified patient attributes that may predict response to LTG of patients with rapid cycling and thus assist in the design of future studies.

Research funded by GlaxoSmithKline.

NR482 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Lack of Weight Gain During Long-Term Therapy with the Novel Antidepressant Reboxetine

Michael E. Thase, M.D., *Department of Adult Psychiatry, University of Pittsburgh-WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213-2593*; Cynthia Bartlett, M.D.

Summary:

Objectives: Weight gain is a common problem during longer term therapy with some antidepressants and an infrequent, but severe problem for patients treated with SSRIs. The aim of the current study was to investigate the effect of long-term treatment with reboxetine on patients' weight.

Methods: Patients with major depressive disorder (MDD) received reboxetine 4 mg bid for six weeks. Patients who responded to treatment (≥50% reduction in HAM-D) entered the long-term phase and were randomized (double-blind) to reboxetine 4 mg bid or placebo for up to 46 weeks. Weight was measured every two weeks.

Results: A total of 283 patients entered the long-term phase (reboxetine n = 143; placebo n = 141). There were no spontaneous reports of weight change as an adverse event and no patient discontinued due to weight change. No statistically significant change in body mass index (BMI) or weight was observed in either the six-week, open-label phase vs baseline (mean decrease in BMI 0.06 kg/m^2; weight −0.16 kg) or the double-blind, long-term phase (mean decrease in BMI 0.02 kg/m^2; weight −0.10 kg) vs placebo.

Conclusions: Up to one year of reboxetine therapy was associated with no more weight gain than placebo.

NR483 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Mirtazapine Versus Sertraline after SSRI Nonresponse

Michael E. Thase, M.D., *Department of Adult Psychiatry, University of Pittsburgh-WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213-2593*; Charlotte Kremer, M.D., Heidi Rodrigues

Summary:

Objective: To evaluate the efficacy and safety of mirtazapine and sertraline in patients with major depression who had failed to respond to fluoxetine, paroxetine or citalopram.

Methods: Two hundred fifty outpatients with major depression according to DSM-IV criteria and lack of response to an adequate trial of fluoxetine, paroxetine, or citalopram were randomized to treatment with mirtazapine (15–45 mg per day) or sertraline (50–200 mg per day) for a maximum of eight weeks.

Results: A total of 119 patients took mirtazapine (mean daily dose 30.4 mg) while 124 patients received sertraline (mean daily dose 120.2 mg); both groups were matched for baseline demographics. Discontinuation due to adverse events was 18.5% (mirtazapine) and 9.5%, (sertraline) $p = 0.26$. Response (at least 50% decrease in HAM-D 17) rates for mirtazapine and sertraline were, respectively, 36.1% and 24.2% at Day 21 ($p = 0.018$); 40.3% and 27.4% at Day 28 ($p = 0.024$); and 51.3% and 50.8% at Day 56 ($p = 0.891$). Remission (HAM-D 17 ≤ 7) rates for mirtazapine and sertraline were, respectively, 12.6% and 4.8% at Day 14 ($p = 0.033$) and 37.8% and 28.2% at Day 56 ($p = 0.79$).

Conclusion: Mirtazapine and sertraline are effective and well tolerated for SSRI non-responders. Response rates at Day 21 and 28 and remission rates at Day 14 are consistent with an earlier onset of action for mirtazapine.

This study was supported by a grant from Organon Inc., West Orange, NJ.

NR484 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Fully Sustained Remission Rates Among Citalopram-Treated Patients

Michael E. Thase, M.D., *Department of Adult Psychiatry, University of Pittsburgh-WPIC, 3811 O'Hara Street, Pittsburgh, PA 15213-2593*

Summary:

Studies of acute-phase antidepressant therapy usually define response as ≥50% reduction in symptoms. However, several lines of evidence support use of the stricter goal of remission, defined as a virtual absence of residual symptoms, as the optimal therapeutic outcome. During continuation phase antidepressant therapy, the comparable goal is full-sustained remission, which is defined by DSM-IV as a period of at least two months in which there are no significant symptoms of depression. There is some evidence that antidepressants are not equally likely to produce remission and, in particular, it has been suggested that antidepressants with effects on multiple neurotransmitter systems may have advantages over SSRIs. To gauge the impact of longer-term antidepressant therapy with the SSRI citalopram, a retrospective analysis was conducted. Data from four studies of at least 20 weeks in duration, evaluating more than 800 patients, were examined. Sustained remission rates ranged from 53% to 72% among patients entered in the long-term studies. These results indicate that the majority of citalopram-treated patients will achieve DSM-IV-defined sustained remission. Prospective studies using such rigorous criteria for sustained remission criterion are needed to assess relative remission rates among various antidepressant therapies.

NR485 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Effects of Bupropion Sustained Release and Sertraline on Anxiety in Depressed Patients

Madhukar H. Trivedi, M.D., *Department of Psychiatry, University of TX Southwestern Medical Center, 5959 Harry Hines Boulevard, #600, Dallas, TX 75235-9101*; A. John Rush, M.D., Thomas Carmody, Ph.D., Rafe M.J. Donahue, Ph.D., Carolyn Bolden-Watson, Ph.D., Trisha L. Houser, B.A., Alan Metz, M.D.

Summary:

Objective: As previously reported, baseline anxiety levels did not predict antidepressant response to either bupropion sustained release (BUPSR) or sertraline (SERT). The current analysis was performed on the same dataset to examine the effects of these antidepressants on symptoms of anxiety in patients with recurrent major depression regardless of baseline anxiety status.

Methods: This retrospective analysis used pooled data from two identical 8-week, double-blind, placebo-controlled, parallel group trials of BUPSR (N = 234), SERT (N = 225), and placebo (N = 233). Anxiety and depression were measured by the 14-item Hamilton Anxiety Scale (HAM-A) and the 21-item Hamilton Depression Scale (HAM-D_{21}), respectively. CNS adverse events were tabulated.

Results: Both agents were statistically superior to placebo in treating depression. Antidepressant responders (≥50% reduction in baseline HAM-D_{21} score) in both groups showed marked and comparable reductions in HAM-A scores (baseline to exit). BUPSR and SERT responders had the same time (4 weeks) to clinically significant anxiolysis (≥50% reduction in baseline HAM-A score). CNS adverse events were comparable for BUPSR and SERT except for somnolence (more common in SERT-treated patients).

Conclusion: BUPSR and SERT had comparable antidepressant and anxiolytic effects. Selection between these agents cannot be based on anticipation of differential anxiolytic effects.

Funding provided by Glaxo Wellcome Inc.

NR486 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Prevalence and Predictors of PMDD in Older Premenopausal Women

Lee S. Cohen, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 815, Boston, MA 02114*; Claudio N. Soares, M.D., Michael W. Otto, Ph.D., Bernard L. Harlow, Ph.D.

Summary:

Objective: To examine the prevalence and predictors of PMDD in a community-based sample.

Methods: Premenstrual symptoms of 4,164 premenopausal women (aged 36 to 44 years) were retrospectively assessed by the Moos Premenstrual Inventory. From this sample, 976 subjects were further interviewed, at which time demographic and lifestyle characteristics, gynecologic history, and medical conditions were examined. The Structured Clinical Interview for DSM-IV (SCID) was used to assess past and current psychiatric morbidity. Additionally, 513 women completed a prospective evaluation of premenstrual symptoms by using the Daily Rating of Severity of Problems Form (DRSP).

Results: The diagnosis of PMDD was confirmed in 33 of 513 women (6.4%) who completed the prospective evaluation with daily records. Fourteen subjects (2.7%) met criteria for PMDD *and* had no history of depression. PMDD was associated with lower education (odds ratio [OR] = 2.3, confidence interval [CI] = 1.1–4.9), a history of major depression (OR = 3.6, CI = 1.7–7.4), and current cigarette smoking (OR = 4.1, CI = 1.5–11.1). In addition, women not working outside the home were significantly less likely to meet criteria for PMDD.

Conclusions: This study indicates a significant prevalence of PMDD in a large community-based sample. Given the associated impairment in social and occupational functioning seen in PMDD, these prevalence data provide a strong rationale for enhanced recognition and treatment of the disorder.

NR487 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Efficacy of Intermittent Fluoxetine Dosing in PMDD

Lee S. Cohen, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 815, Boston, MA 02114*; Cherri M. Miner, M.D., Eileen Brown, Ph.D., Julia Dillon, Pharm.D.

Summary:

Objective: Treatment with daily fluoxetine has demonstrated efficacy in multiple controlled trials for PMDD. Given findings supporting comparable efficacy of luteal phase dosing and daily dosing of fluoxetine in one open-label study, a larger multicenter, randomized, double-blind, placebo-controlled trial was undertaken to evaluate the efficacy of luteal phase dosing of fluoxetine in patients with PMDD.

Methods: Following a two-cycle screening and a one-cycle single-blind placebo period, 260 women were randomly assigned to receive fluoxetine, either 10 or 20 mg/day, or placebo. Each woman received treatment for 14 days prior to the next expected menses through the first full day of menses) for three cycles. Women recorded PMDD symptoms daily throughout the phases of the trial using Daily Record of Severity of Problems (DRSP). The primary outcome variable was change from mean baseline luteal phase scores to mean treated luteal phase scores over 3 months of treatment.

Results: Luteal dosing with fluoxetine 20 mg/day significantly improved DRSP total scores, as well as DRSP mood, physical, and social functioning subtotal scores compared with placebo ($p < 0.05$ for all measures). Fluoxetine 10 mg/day significantly improved the DRSP mood and social functioning subtotals compared with placebo ($p < 0.05$ for both measures). Both dosages significantly improved DRSP total scores by the first treatment cycle (repeated-measures analysis of variance $p < 0.05$ for each comparison); however, fluoxetine 20 mg/day demonstrated statistically significant improvement throughout the trial, while fluoxetine 10 mg/day did not. Treatment was well tolerated; discontinuations from the trial due to adverse events did not differ among the three groups ($p = 0.316$).

Conclusion: Luteal phase dosing of fluoxetine effectively treats PMDD. Fluoxetine 20 mg/day appears to provide advantages over fluoxetine 10 mg/day with regard to physical symptoms and an overall measure of PMDD.

Research funded by Eli Lilly and Company

NR488 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Quality of Life in PMDD Patients After Daily Versus Luteal-Phase Sertraline Treatment

Kimberly A. Yonkers, M.D., *Department of Psychiatry, Yale University School of Medicine, 142 Temple Street, Suite 301, New Haven, CT 06510*; Teri B. Pearlstein, M.D., Anna Stout, Ph.D., Wilma M. Harrison, M.D., John A. Gillespie, M.D.

Summary:

Objective: The current study was designed to compare the effect of daily versus intermittent luteal phase treatment with sertraline on quality of life (QOL) in women with PMDD. Given the high rate of past MDD among PMDD women, the influence of past MDD on QOL improvement was also evaluated.

Methods: Data from the active treatment cells were analyzed from two placebo-controlled studies, one using sertraline as a

daily treatment and the second limiting medication administration to the luteal phase.

Results: QOL was significantly impaired pretreatment, with mean baseline Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q) summary scale scores of 68.0 (SD = 12.6) for the daily dosing study (N = 62) and 62.3 (SD = 11.9) for the luteal dosing study (N = 119). Both continuous and intermittent treatment led to improvement (Q-LES-Q increase of 13.9 and 16.5, respectively), changes that were unaffected by prior history of MDD. The difference between the two modalities of drug administration was not significant. Sertraline was well-tolerated; adverse events were not found to reduce QOL improvement.

Conclusion: Luteal phase and daily sertraline treatment were equivalent in improving QOL among PMDD patients. For both modalities, significant and rapid improvements occurred and were not affected by history of depression.

NR489 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Clozapine Levels Upon Smoking Cessation: Results and a Predictive Model

Jonathan M. Meyer, M.D., *Mental Health and Development, Oregon State Hospital, 2600 Center Street NE, 35C, Salem, OR 97301-2682*

Summary:

Background: Published reports have documented 20%–40% lower mean serum clozapine concentrations in smokers compared with nonsmokers due to enzyme induction. Despite the increase in nonsmoking psychiatric facilities in the United States, previous studies have not tracked individual changes in serum clozapine levels after smoking cessation.

Methods: Clozapine level changes in 11 patients at Oregon State Hospital, on stable clozapine doses, before and after implementation of a hospital-wide nonsmoking policy were analyzed.

Results: A mean increase in clozapine levels of 71.9% (442.4 ng/ml ± 598.8 ng/ml) occurred upon smoking cessation ($p < 0.034$) from a baseline level of 550.2 ng/ml (±160.18 ng/ml). One serious adverse event, aspiration pneumonia, was associated with a nonsmoking serum clozapine level of 3066 ng/ml. Elimination of statistically extreme results generated a mean increase of 57.4% or 284.1 ng/ml (±105.2 ng/ml) for the remaining cases ($p < 0.001$), and permitted construction of a linear model that explained 80.9% of changes in clozapine levels upon smoking cessation ($F = 34.9$; $p = .001$): *clozapine level as nonsmoker* = 45.3 + 1.474 (*clozapine level as smoker*).

Conclusions: Significant increases in clozapine levels upon smoking cessation may be predicted by use of a model. Those with high baseline levels should be monitored for serious adverse events.

NR490 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

One-Year Comparison of Lipids, Glucose, and Weight with Olanzapine or Risperidone

Jonathan M. Meyer, M.D., *Mental Health and Development, Oregon State Hospital, 2600 Center Street NE, 35C, Salem, OR 97301-2682*

Summary:

Background: Metabolic side effects have been increasingly noted during therapy with novel antipsychotics, but there is a dearth of comprehensive comparative data in this area about risperidone (ris) and olanzapine (olz).

Methods: Retrospective study at Oregon State Hospital of changes in fasting triglycerides, glucose, cholesterol, and weight during the first year of therapy with risperidone or olanzapine.

Results: Among those <60 years old, olanzapine cohort (N = 37) experienced significantly greater increases in all parameters than the risperidone group (N = 39), except for weight variables: fasting triglycerides: +104.8 mg/dl [olz] versus +31.7 mg/dl [ris] ($p = 0.037$); cholesterol: +30.7 mg/dl [olz] versus +7.18 mg/dl [ris] ($p = 0.004$); glucose: +10.78 mg/dl [olz] versus +0.743 mg/dl [ris] ($p = 0.030$). Age <60 and concurrent use of lithium or valproate were associated with greater weight gain in both drug groups, but this was statistically significant only for the olanzapine group. Neither weight change nor use of lithium or valproate were associated with increases in glucose or lipids among those <60 years old for either drug.

Conclusions: Compared to treatment with risperidone, olanzapine therapy is associated with significantly greater increases in fasting glucose, triglycerides, and cholesterol after 1 year of treatment for nongeriatric adult patients.

NR491 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

The Lack of Drug Interactions Between Zaleplon and Venlafaxine Extended Release

Mona Darwish, Ph.D., *Department of Research, Wyeth-Ayerst, 145 King of Prussia Road, Philadelphia, PA 19087*; V. Parker, Ph.D., D. Harper, B.A., C. Leister, M.S., D. Raible, M.D., R. Fruncillo, Ph.D.

Summary:

Objective: Patients with depression and anxiety frequently experience insomnia and may receive both antidepressant and hypnotic medications. Therefore, extended-release venlafaxine and zaleplon coadministration was evaluated for interactions.

Methods: This randomized, double-blind, placebo-controlled, two-period crossover study was conducted in 24 healthy adult subjects who received venlafaxine, 75 mg/day or placebo-matching-venlafaxine (PMV) on days 1–3, followed by venlafaxine 150 mg/day or PMV on days 4–9. On study days 7 and 9, subjects received zaleplon 10 mg or placebo-matching-zaleplon. A two-period crossover ANOVA compared pharmacokinetics (PK) of each agent (and the venlafaxine metabolite, O-desmethylvenlafaxine [ODV]) with and without the other medication. Digit Symbol Substitution Test, word recall test, and Stanford Sleepiness Scale (SSS) evaluated pharmacodynamic (PD) effects on psychomotor performance, memory, and sedation. A four-period crossover ANCOVA compared results across the four treatment conditions.

Results: No statistically significant differences occurred in PK of zaleplon with or without venlafaxine. Zaleplon C_{max} and AUC were approximately 4% and 6% lower, respectively, with venlafaxine. No statistically significant differences occurred in PK of venlafaxine or ODV with or without zaleplon. Venlafaxine C_{max} and AUC did not differ by treatment. ODVC_{max} and AUC increased 15% and 6%, respectively, with zaleplon. No statistically significant differences occurred in PD effects, except for slightly significant results ($p = 0.04$) at two time points for SSS score.

Conclusion: Venlafaxine did not significantly affect PK of zaleplon, nor did zaleplon change PK of venlafaxine or ODV. No PD effect resulted from addition of zaleplon to venlafaxine. Therefore, zaleplon and extended-release venlafaxine can be safely coadministered.

"There were no differences between the brand and the generic products in WBC values (3-year data: p = 0.9992; 1-year data: p = 0.9991) or in dosage comparison at 3 years and 1 year (p = 0.9999 and p = 0.9993, respectively)."

NR492 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Converting Patients from Brand Name Clozapine to Generic

Terrie A. Sajbel, Pharm.D., *Department of Pharmacy, Colorado Mental Health Institute, 1600 West 24th Street, Pueblo, CO 81003*; Gary W. Carter, R.Ph., Roy B. Wiley, M.S.

Summary:

Objective: Evaluation of the safety and dosage requirements when converting from brand to generic clozapine.

Methods: In November of 1999, patients at Colorado Mental Health Institute at Pueblo (CMHIP) taking brand name clozapine were changed to generic clozapine. Seventeen patients taking brand name clozapine for 3 years were included in the study. Dosage, white blood cell (WBC) values, and adverse drug reaction reports were compared. Brand name patient data were evaluated retrospectively for the months of November, December, January, and February during 1996/97, 1997/98, and 1998/99. The same patients were evaluated while taking generic clozapine for the same months in 1999/2000. Also a 1-year comparison of brand 1998/99 data to generic 1999/2000 data was performed. Statistical analysis included a standard t test comparing WBC values and a Brown-Forsythe test for comparing dosages.

Results: There were no differences between the brand and the generic products in WBC values (3-year data: $p = 0.9992$; 1-year data: $p = 0.9991$ or in dosage comparison at 3 years and 1 year ($p = 0.9999$ and $p = 0.9993$, respectively).

Conclusions: No differences were found between the brand and the generic groups with regard to WBC, dosage, and adverse events. The conversion to generic is projected to save the pharmacy $90,000 annually.

NR493 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Acute Dystonic Reactions in Patients Treated with Atypical Antipsychotics

Michele Raja, M.D., *Department of Mental Health, Santo Spirito Hospital, Prisciano 26, Rome, IT 00136, Italy*; Antonella Azzoni, M.D.

Summary:

Background: The growing use of atypical antipsychotics has led to a decrease of acute dystonic reactions (ADR).

Objective and Methods: To evaluate the prevalence of ADR among patients admitted to a psychiatric intensive care unit between 1997 and October 2000, we prospectively recorded all ADR.

Results: Among 1310 cases treated with antipsychotics, we observed 41 cases (3.1%) affected by ADR. At discharge, mean chlorpromazine-equivalent daily dose was 465.8 (±421.5) mg, while 39 cases (3.0%) (all treated with typical neuroleptics) received anticholinergics. During hospitalization, 15 cases received quetiapine, 19 sertindole, 95 olanzapine, 142 clozapine, 495 risperidone, and 561 typical neuroleptics. Risperidone caused three ADR. We observed four ADR after emergency treatment with typical neuroleptics in patients receiving risperidone. Typical neuroleptics caused 32 ADR cases (the difference between typical and atypical neuroleptics was significant: $p = 0.000$). One patient treated with olanzapine (20 mg) presented with a long-lasting dystonia of the neck. One patient presented with a long-lasting dystonia of the trunk after treatment with risperidone (3mg) and after treatment with 600 mg of quetiapine. Both patients immediately recovered after withdrawal of the offending drugs.

Conclusion: Atypical antipsychotics carry a minimal risk of ADR. However, since the novel antipsychotics are currently not available in injectable form, many patients treated with neuroleptics will continue to experience ADR.

NR494 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Sertraline Decreases Reaction Times as Compared with Imipramine in Depression

Mauro Garcia-Toro, M.D., *Department of Psychiatry, Complex Hospital, Jesus No. 40, Palma de Mallorca 07003, Spain*; Juan A. Talavera, Ph.D., Jeronimo Saiz-Ruiz, M.D., Alicia Gonzalez, M.D., Cesar Azpeleta, M.D., Miguel Lazaro, M.D.

Summary:

Objective: To establish the effect of antidepressants upon vocal reaction times.

Methods: 26 patients meeting DSM-IV criteria for dysthymia ($N = 9$) or major depression without melancholy ($N = 17$) volunteered to participate in a tape-recorded test in which they were instructed to repeat out loud the vowel "a" immediately after hearing it in the earphones. This test served to instrumentally measure vocal reaction time using computer software. The test was repeated twice: under baseline conditions and 2 months later, and the patients were randomly assigned to receive imipramine or sertraline during this period. The control group consisted of 20 healthy volunteers.

Results: The reaction times were reduced to a greater extent in the sertraline group than in the control group (−125.5 vs −48.6 ms; $p = 0.037$), unlike the imipramine group, where the reaction time actually increased (19.82 ms). The difference between the two patient groups was significant ($F = 7.357$; $p = 0.027$), after controlling in the analysis of variance for other potentials factors involved, such as differences in group composition or in the decreases in anxiety and depression scale scores.

Conclusions: Patients treated with sertraline improved their reaction times compared to patients treated with imipramine.

NR495 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Olanzapine-Induced Weight Gain in Patients with First-Episode Schizophrenia

Michael Poyurovsky, M.D., *Research Unit, Tirat Carmel Mental Health Center, 3 Eshkol Street, Tirat Carmel 30200, Israel*; Artashas Pashnian, M.D., Camil Fuchs, Ph.D., Iris Gilad, Ph.D., Rachel Maayan, Ph.D., Abraham Weizman, M.D.

Summary:

Objective: Olanzapine-induced weight gain is a major cause of noncompliance and is associated with increased morbidity. Antagonistic activity at the serotonin 5-HT2C receptor may be an underlying mechanism of weight gain, and fluoxetine may counteract olanzapine-induced weight gain.

Method: Thirty inpatients with first-episode DSM-IV schizophrenia were enrolled. They were randomly assigned in a double-blind design to receive olanzapine (10 mg/day) coadministered with either fluoxetine (20 mg/day; $N = 15$) or placebo ($N = 15$) for 8 weeks.

Results: Sixteen (66.6%) of the 24 study completers demonstrated "much" or "very much" improvement on the CGI scale that was associated with a more significant decrease in the positive and disorganized symptoms for the olanzapine-placebo group ($F = 5.23$, $p < 0.01$ and $F = 3.43$, $p < 0.01$, respectively) as assessed by the SANS and the SAPS. Both groups demonstrated gradual increase in body weight: mean weight gain was 7.91 ± 46 kg in the olanzapine + fluoxetine group and 6.51 ± 4.19 kg in the olanzapine + placebo group ($t = 0.78$; $p = 0.44$). No correlation between weight change and clinical response for either group was found. Somnolence and transient akathisia were the only side effects observed.

Conclusions: Results confirm a high efficacy of olanzapine in patients with first-episode schizophrenia and their high vulnerability for weight gain. Fluoxetine coadministration appears to be

clinically ineffective and cannot attenuate olanzapine-induced weight gain.

NR496 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Probenecid Effects on the Disposition of Olanzapine and Risperidone

John S. Markowitz, Ph.D., *Department of Psychiatry, Medical University of South Carolina, 67 President Street, P. O. Box 250861, Charleston, SC 29425*; C. Lindsay DeVane, Ph.D., Heidi L. Liston, Ph.D., Dave W. Boulton, Ph.D., Craig Risch, M.D.

Summary:

The metabolic pathways of the majority of xenobiotics and endogenous compounds can be divided into Phase I (oxidative, reductive, and hydrolytic) and Phase II (glucuronidation, sulfate conjugation, glycine and glutathione conjugation, acetylation and methylation) processes. Oxidative metabolism by the cytochrome P450 (CYP) system has been intensively investigated compared with glucuronidation and other conjugation pathways. The primary aim was to evaluate the disposition of olanzapine (OLZ) or risperidone (RIS) in normal volunteers with and without coadministration the UDP-glucurononyl transferase (UDPGT) inhibitor, probenecid (PB). We hypothesized OLZ disposition would be altered due to decreased glucuronidation, while RIS disposition would be relatively unaffected. Twelve healthy volunteers, aged 22–42 years, participated in a single-dose, randomized, four-period, double-blind, crossover study receiving a single dose of either 5 mg of OLZ or 1 mg of RIS with and without PB 500 mg (eight doses over four days). Multiple blood samples were analyzed by LC-MS or HPLC to assess the 48-hour time course of RISP and OLZ. Urine was assayed for free and glucuronidated drugs. Statistically significant differences were observed between plasma pharmacokinetic parameters (C_{max} [$p < 0.05$)]; AUC_{0-24} [$p < 0.01$]; $T1/2\alpha$ [<0.001]) for OLZ administered alone and with PB. RIS pharmacokinetic parameters were not significantly different (all parameters $p > 0.05$). Inhibition of UDPGT appeared to influence the disposition of OLZ but not RISP. The implications for clinical use of OLZ and RISP are unclear.

NR497 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Reversal of Weight Gain Associated with Antipsychotic Treatment

Christopher O'Keefe, M.A., *Department of Research, MHC-CM, 1555 Elm Street, Manchester, NH 03101*; Douglas Noordsy, M.D., Thomas Liss, B.S.

Summary:

Objective: To describe a population of patients who demonstrated a reversal of weight gained subsequent to treatment with an antipsychotic medication, and to describe the course of the weight loss and methods used.

Method: This report presents a retrospective chart analysis of 35 patients who gained ≥20 lbs associated with antipsychotic treatment and subsequently lost >10 lbs.

Results: The study group gained an average of 29.36 ± 13.70 kg over a mean period of 33.09 ± 27.92 mos. Patients demonstrated a mean weight reduction of 18.61 ± 15.12 kg over 22.31 ± 17.82 months. All patients received antipsychotic medication during this period. The most frequent interventions during the weight loss period were monthly meetings with a nutritionist for at least one year (42.8%), irregular nutritionist meetings (20.1%), and diet (18.6%). The least frequent interventions were no intervention (5.7%), surgical intervention (2.9%), and psychiatrist intervention (2.9%). Most recent weight was significantly higher than lowest weight achieved (mean 3.84 kg ± 11.26).

Conclusions: Some patients who experience weight gain associated with antipsychotic treatment are able to stop gaining and then lose the weight over time. While patient's weight may fluctuate, this group sustained a loss of approximately half of their initial weight gain. Dietary interventions were most commonly used by this group and should be incorporated into weight management plans for this population.

NR498 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Flexible Dose Study of Olanzapine Treatment of Trichotillomania

Rege S. Stewart, M.D., *Department of Psychiatry, UT Southwestern Medical Center, 5323 Harry Hines Boulevard, Dallas, TX 75235-9070*; Vicki A. Nejtek, Ph.D., Joseph Gilbert, R.N., Humera Chowdhary, M.D.

Summary:

Twenty-one patients were screened for a 12-week, open-label study of olanzapine for TTM. Patients with comorbid psychiatric disorders were excluded. With the exception of one patient, none of them were on any psychoactive medication. Sixteen patients were treated with olanzapine, which was titrated from the initial dose of 2.5 mg. to 10 mg. by week 8 of the study.

Patients were assessed at baseline, week 1, 2, 4, 6, 8, and 12, using the Hamilton Depression Scale (HamD) and Hamilton Anxiety Scale (HamA), the Simpson Angus Scale (SAS), the Clinician rated Global Improvement Scale (CGI-S), and Massachusetts General Hospital Hair Pulling Scale (MGH-HPS). Patients were also required to keep a daily hair pulling diary.

Data analysis of the 16 patients indicates significant decrease in MHG-HPS and CGI-S $p < 0.001$ using Wilcoxon signed rank test. MHG-HPS dropped from initial mean score of 17.2 at baseline to 5.76 at completion of the study. CGI-S initial mean was 4.4 at baseline and 2.2 at completion. HamA improvement was significant to $p < 0.05$. Change in HamD was not significant. Two patients developed major depressive disorder at the end of the study even though their TTM was in complete remission. Of the 16 patients entered, eight completely recovered from TTM.

NR499 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

S-Adenosyl-Methionine (SAMe) in Major Depression: Two Multicenter Trials Versus Imipramine

Roberto Delle Chiaie, M.D., *III Clinical Psychiatry, University of Roma, Via Cicerone 44, Roma 00193, Italy*; Paolo Pancheri, M.D., Pier L. Scapicchio, M.D.

Summary:

Objective: Intravenous administration of SAMe, a natural substance, proved to be effective against major depression in recent international multicenter studies. Aim of this study was to investigate the antidepressant efficacy of oral (MC3) and intramuscular SAMe (MC4).

Methods: MC3, a six-week study, was carried-out on 295 patients with major depression in 33 centers to compare 1,600 mg/day oral SAMe double-blind *vs* 150 mg/day oral imipramine (IMI).

MC4, a four-week study, was carried out on 281 patients with major depression in 31 centers to compare 400 mg/day i.m. SAMe double-blind, double-dummy *vs* 150 mg/day oral IMI.

Results: According to intention to treat analysis of data, in both studies SAMe and IMI did not differ significantly on any efficacy measure, either main (endpoint HAM-D score and percentage of responders at end-point) or secondary (final MADRS scores and response rate). On the other hand, adverse events were fewer in patients treated with SAMe.

Conclusion: These data show 1,600 mg/day oral, or 400 mg/day i.m. SAMe to be comparable to 150 mg/day oral IMI in terms

of antidepressive efficacy, but to be significantly better tolerated. These data suggest interesting perspectives for the use of SAMe, especially when depression coexists with any type of somatic comorbidity.

This research was funded by Knoll-Italia, Liscate, Italy.

NR500 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

S-Adenosyl-Methionine (SAMe) in Major Depression: Clinical Profile of Treatment Responders

Roberto Delle Chiaie, M.D., *III Clinical Psychiatry, University of Roma, Via Cicerone 44, Roma 00193, Italy;* Paolo Pancheri, M.D., Pier L. Scapicchio, M.D.

Summary:

Objective: Orally (MC3) and intramuscular (MC4) SAMe, a natural substance, were found to be effective in major depression in two recent multicenter studies. Aim of this study was to identify any responder characteristics.

Methods: In MC3 and MC4, 576 patients (281 + 295) with major depression were studied. When using as response criterion an at least 50% drop of end-point total HAM-D scores from baseline, of the 289 patients who received SAMe, 154 (53.3%) could be classified as nonresponders and 135 (46.7%) as responders, whereas, using as a criterion a final CGI score ≤2, 123 (42.6%) could be classified as nonresponders and 166 (57.4%) as responders. The whole sample was then stratified according to the following anchor-points: gender, age, severity, presence of chronic course, melancholia, atypical features, seasonal course, rapid cycling. Subgroups thus obtained were compared for positive response frequency.

Results: Frequency of positive response to SAMe was higher among female patients, among nonmelancholic patients with nonchronic course, and among those with severe symptoms or atypical features.

Conclusion: These data show that some clinical features of patients with major depression may be considered predictive of a better response to SAMe.

This research was funded by Knoll-Italia, Liscate, Italy.

NR501 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Atypical Antipsychotics Are Associated with Lower Mortality Than Haloperidol in Geriatric Patients

Henry A. Nasrallah, M.D., *Department of Psychiatry, University of Mississippi, 1500 East Woodrow Wilson Drive, Jackson, MS 39216;* Thantween White, M.P.A., Amelia Nasrallah, M.A.

Summary:

Introduction: Antipsychotic medications (AP) are commonly used in geriatric patients for psychotic symptoms associated with dementia, delirium, or chronic schizophrenia. Over the past decade, the use of atypical antipsychotics in geriatric psychosis and/or behavioral agitation has steadily increased due to their lower risk of extrapyramidal side effects (EPS). However, conventional antipsychotics, especially haloperidol, continue to be used in a substantial proportion of patients. Based on recent reports of possible neurotoxicity of conventional AP (Mahadik et al, 2000), we hypothesized that geriatric patients (>65 years) receiving haloperidol may have higher mortality rates than those receiving novel antipsychotics.

Methods: Using our computerized medical records database at the VA Medical Center, we recorded the deaths of all patients in the two calendar years 1998 and 1999 who were receiving haloperidol or the new atypical AP. We tabulate the entire pool of patients over age 65 who were receiving those drugs and calculated the death rate for those receiving haloperidol vs. atypical AP at the time of their death.

Results: A total of 61/1284 patients receiving atypical AP died during the two-year study period (4.75) compared-with 64/299 patients who were receiving haloperidol (21.4%). The difference was highly significant ($X^2 = 6.524$ $P < .00001$).

Discussion: These data suggest that mortality rates in older patients are substantially lower with novel AP than with haloperidol. If replicated, these findings may have important implications for using novel antipsychotics in geriatric patients with psychosis or behavioral agitation of dementia, rather than using the older generation neuroleptics. Further studies are also needed to determine how haloperidol increases mortality risk in the elderly. We postulate that tardive dyskinesia as well as depression, both of which are much higher in the elderly with conventional AP, and both of which are associated with higher mortality, may be some of the factors underlying our findings.

NR502 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Effects of Bupropion Sustained Release on Dimensions of Mood

Gabriel Dichter, B.A., *Department of Psychology, Vanderbilt University, 111 21st Avenue, South, Nashville, TN 37240;* Catherine Freid, B.A., Andrew J. Tomarken, Stephanie Addington, M.A., Richard C. Shelton, M.D.

Summary:

Objective: To assess the impact of sustained-release bupropion (BUP) on dimensions of mood.

Methods: Nineteen outpatients with major depression were randomily assigned to receive either BUP (max. 300 mg/day) or placebo for 6 weeks (phase 1). During a second 6-week period (phase 2), dosages were increased for participants in the BUP group (max. 400 mg/day) while participants formerly in the placebo condition received active BUP (max. 300 mg/day). Assessments included the Hamilton Rating Scale for Depression (HAM-D), the Beck Depression Inventory (BDI), and the Mood and Anxiety Symptom Questionnaire (MASQ).

Results: Random regression analyses revealed that 1) BUP produced robust effects on all dimensions of mood and elicited greater declines than placebo on all measures except those that assessed anxiety; 2) across 12 weeks, the measures that most strongly differentiated BUP from placebo were the BDI, the HAM-D, and the anhedonic depression subscale of the MASQ; 3) placebo induced declines on all measures except anhedonic depression; and 4) greater improvement was seen in subjects who received BUP in phase 1 than in those who initially received placebo and were subsequently treated with BUP in phase 2.

Conclusions: BUP may have its most pronounced effects on symptoms of anhedonia. In addition, anhedonia may be less susceptible to placebo effects than anxiety-related symptoms.

Funding Source: Glaxo/Wellcome

NR503 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Behavioral Effects of Escitalopram Predict Rapid Antidepressant Activity

Paul J. Mitchell, Ph.D., *Department of Pharmacy, University of Bath, 5 West-3.4 Claverton Down, Bath BA2 7AY, England;* Sandy Hogg

Summary:

Objective: The common ability of chronic antidepressant treatment (including SSRIs) to increase the aggressive behavior of resident rats is highly predictive of antidepressant activity and reflects increased assertiveness observed during the recovery process from depressive illness. Recent studies (1) suggest that the antidepressant effect of citalopram resides in the S-(+)-enanti-

omer escitalopram. Here we report the effects of chronic escitalopram treatment in the resident-intruder paradigm.

Methods: Resident rats were subjected to daily encounters with unfamiliar drug-free intruder rats over 8 successive days. Osmotic minipumps containing drug-vehicle or escitalopram (0.5 mg/kg/day) were implanted subcutaneously after the first (baseline) encounter. Encounters with intruders were then performed at 24-hour intervals thereafter.

Results: Significant treatment x time interactions were identified for aggressive and flight escape behaviors only (all F values ≥4.036, d7 = 7.98, all p values < 0.01). Post hoc analysis revealed that escitalopram-treated resident rats exhibited elevated aggression from treatment day 1 and reduced flight escape behavior from day 4 compared to vehicle-treated control subject: (all F values ≥23.494, d7 = 1, 14, all p values < 0.001). In comparison, previous studies have shown that venlafaxine and fluoxetine only increase aggression from treatment days 2 and 5, respectively (2).

Conclusion: The ability of escitalopram to increase aggression from treatment day 1 predicts rapid onset of antidepressant activity of this agent.

NR504 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

A Prospective Study of Obsessive-Compulsive Symptoms During Clozapine Therapy

Lakshmi N.P. Voruganti, M.D., *University of Western Ontario, 850 Highbury Avenue, London, ON N6G 2K4, Canada;* Chris Tremblay, R.N., A. George Awad, M.D.

Summary:

Objective: To examine the incidence and course of comorbid obsessive compulsive symptoms (OCS) during clozapine therapy for treatment-refractory schizophrenia.

Methods: Using a prospective, naturalistic study design, we evaluated a group of subjects with treatment-refractory schizophrenia initiated on clozapine (n = 52), and a matched group of subjects who were continued on other antipsychotic drugs (n = 43). Evaluations were carried out at the baseline, and at three monthly intervals with Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and Leyton Obsessional Inventory (LOI); symptom severity, comorbid depression, serum clozapine levels, and quality of life were also simultaneously evaluated.

Results: At 24 weeks follow-up, 4 (7.7%) subjects receiving clozapine developed new obsessive compulsive symptoms, and 8 (15%) experienced an exacerbation of pre-existing symptoms, compared to the controls (0% & 11.5%). On the otherhand, some subjects (3.8%) reported an improvement in the comobid OCS in the clozapine group during follow-up, while none improved among the controls. The presence and severity of obsessive compulsive symptoms were independent of subjects' mood status or serum clozapine levels.

Conclusions: Comorbid obsessive compulsive symptoms were common among people with treatment-refractory schizophrenia, and may likely to be an integral part of the illness. The effects of clozapine on obsessive compulsive symptoms varied, with evidence of improvement in some, and worsening among others.

NR505 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

A Double-Blind, Placebo-Controlled Study of Antidepressant Augmentation with Mirtazapine

Linda L. Carpenter, M.D., *Department of Psychiatry, Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI 02906;* Sarah Yasmin, M.D., Lawrence H. Price, M.D.

Summary:

Objective: Pharmacotherapeutic strategies that target specific actions at multiple neuronal receptors or cellular components may offer a superior approach for treatment of refractory depression. A pilot study of open-label mirtazapine augmentation in 20 patients with persistent MDD yielded a 55% response rate at week 4.

Methods: 26 adult outpatients with persistent MDD despite adequate antidepressant monotherapy were randomly assigned to receive mirtazapine or placebo augmentation in a double-blind fashion. Mirtazapine or matching placebo was begun at 15 mg p.o. q.h.s. with possible titration to 30 mg p.o. q.h.s. per physician's discretion during the remainder of the augmentation trial. The majority of patients (N = 22; 84%) had study drug added to ongoing regimens of SSRI therapy.

Results: The early discontinuation rate did not differ statistically between the active mirtazapine (9.1%) and placebo (13.3%) groups. Both definitions utilized for categorical response at endpoint (CGI Improvement score criteria and 50% reduction in HRSD-17) yielded a 64% response rate for the active drug and a 20% response rate for placebo (p = 0.043). Mirtazapine demonstrated statistically significant superiority to placebo on all of the other major outcome measures: HRSD-17 total (p = 0.017), IDS-SR (p = 0.050), and PRAS (p = .028). Additionally, active mirtazapine augmentation was associated with improvement in overall functioning as reflected by GAF scores (p = 0.038) and with enhanced quality of life in several domains as measured by the Q-LES-Q (physical health, general activities, and leisure activities). There were no significant group differences with regard to emergent side effects, weight change, or serum concentrations of primary antidepressant drugs.

Conclusions: Results from this double-blind, placebo-controlled study of 26 patients suggest mirtazapine is an effective, well-tolerated agent for acute augmentation of the newer antidepressant medications. Sponsored by an unrestricted educational grant from Organon, Inc.

NR506 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Association of Diabetes Mellitus with Atypical Neuroleptics

Michael J. Sernyak, M.D., *Department of Psychiatry, VACT HCS, 950 Campbell Avenue, # 116A, West Haven, CT 06516;* Robert A. Rosenheck, M.D., Douglas Leslie, Ph.D.

Summary:

Introduction: There have been reports of the development of both type I and type II diabetes following initiation of some of the atypical neuroleptics. These studies have consisted primarily of small series of patients.

Methods: All VA neuroleptic-treated outpatients with schizophrenia in the last quarter of fiscal year 1999 were included in this study. Patients who received clozapine, olanzapine, risperidone, or quetiapine comprised the atypical group. The frequency of diabetes mellitus across age groups and different atypical neuroleptics was examined using a multiple logistic regression analysis.

Results: 30,819 veterans were studied: 12,695 received typical neuroleptics (T), and 18,124 received atypical neuroleptics (A) (clozapine: 935 [5.2%]; olanzapine: 8,772 [48.4%]; quetiapine: 773 [4.3%]; or risperidone: 7,944 [43.8%]). A higher percentage of the A group compared with the T group in the under 40 (8.74% versus 6.21%, p = 0.007), 40–49 (15.89% versus 13.93%, p = 0.002), and 50–59 (22.73% versus 20.56%, p = 0.003) age groups were diagnosed with diabetes. By medication prescribed, risk of diabetes was also increased for clozapine (odds ratio [OR] = 1.251, 95% confidence interval [CI] = 1.070–1.462), olanzapine (OR = 1.107, CI = 1.038–1.180), and quetiapine (OR = 1.313,

CI = 1.113–1.547) but not risperidone (OR = 1.049, CI = 0.982–1.120).

Conclusions: In this large group of patients with schizophrenia, atypical neuroleptic prescription was significantly more often associated with diabetes mellitus than typical neuroleptic prescription.

NR507 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Cardiac Arrest Risk Appears to Vary Little by Choice of Antipsychotic Drug

Sean Hennessy, Pharm.D., *Department of Epidemiology, University of Pennslyvania, 423 Guardian Drive, 803 Blockley Hall, Philadelphia, PA 19104-6021;* Warren B. Bilker, Ph.D., Jill C. Santanna, M.S., David J. Margolis, M.D., Dale Glasser, Ph.D., Stephen E. Kimmel, M.D., Robert F. Reynolds, D.Sc., Mary F. Morrison, M.D., Brian L. Strom, M.D.

Summary:

Objective: To compare the risk of cardiac arrest and ventricular arrhythmia among schizophrenic patients taking clozapine, risperidone, thioridazine, and haloperidol.

Method: We used data from three U.S. Medicaid programs from 1993–96 to perform a cohort study. The outcome was a diagnosis of ventricular arrhythmia or cardiac arrest. We calculated rate ratios and 95% confidence intervals (CIs) that adjusted for sex, age, state, dose, and number of previous prescriptions for a study drug and evaluated potential confounders.

Results: 100,301 individuals experienced 101 events during 78,077 person-years of follow-up, for a rate of 1.3 per 1,000 person-years. The adjusted rate ratios, using haloperidol as the reference drug, were as follows: thioridazine: 1.0 (CI = 0.5–1.9); risperidone: 0.7 (CI = 0.3–1.8); and clozapine: 0.6 (CI = 0.2–2.0). The results were similar in the subgroup using ≥100 mg thioridazine or its equivalent.

Conclusions: There were no discernible differences in the risk of cardiac arrest and ventricular arrhythmia, with confidence intervals ruling out more than a doubling of risk for any drug when compared to haloperidol. These findings suggest that a drug's ability to prolong the electrocardiographic QT interval may not necessarily connote a marked increase in the risk of cardiac arrest and ventricular arrhythmia.

NR508 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Quetiapine Does Not Produce Sustained Elevations of Prolactin Levels

Mark B. Hamner, M.D., *VA Medical Center, Medical University of South Carolina, 109 Bee Street, #116A, Charleston, SC 29403*; Brian J. McConville, M.D.

Summary:

Objective: Hyperprolactinemia associated with typical antipsychotics may result in side effects such as galactorrhea, sexual dysfunction, and amenorrhea. The effects of the atypical antipsychotic quetiapine on plasma prolactin concentrations were examined in adults and adolescents.

Methods: For adults, the data from Phase II/III trials that comprised over 2,000 patients were reviewed, including pooled analyses. For adolescents, data came from a study where 10 patients, mean age = 13.1 years, received quetiapine doses rising from 50 to 800 mg/day over 21–27 days.

Results: For adults, pooled analyses of controlled data for 2,185 quetiapine-treated patients found a 1.0% incidence of adverse events due to hyperprolactinemia. Plasma prolactin levels of quetiapine were no different from those of placebo across the dose range studied (75 to 750 mg/day). Plasma prolactin was consistently below baseline in quetiapine-treated patients (range: –10.01 to –29.65 μg/l), irrespective of the length of therapy (up to 52 weeks). In adolescents, plasma prolactin changes decreased from baseline for girls (–12.6 μg/l), and the prolactin level remained unchanged for boys.

Conclusion: Quetiapine does not produce sustained elevations of prolactin levels in adults or adolescents with psychotic disorders.

NR509 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Literature Review of Hyperglycemia and Diabetic Ketoacidosis (DKA) with Atypical Neuroleptics

Melanie E. Schwarz, M.D., *Department of Psychiatry, New York University-Bellevue Hospital, 225 East 95th Street, Apt. 22E, New York, NY 10128-4007*; Asher D. Aladjem, M.D.

Summary:

There has been little research published on an association of atypical neuroleptics with diabetes and diabetic ketoacidosis (DKA). This abstract reviews 26 case reports of new-onset diabetes after antipsychotic treatment initiation. Although the number of case reports is few, these reports are worrisome, since the use of atypical antipsychotics has become the first line of treatment for schizophrenia.

There have been 14 case reports of diabetes, DKA, or worsening diabetic blood glucose control after initiation of olanzapine. Five (36%) of these patients developed DKA, and 79% required discontinuation of their antipsychotic. Of those who discontinued treatment, 18% required long-term insulin, and 18% required long-term oral hyperglycemia treatment. There also have been 12 case reports of diabetes, DKA, or worsening glucose control after the initiation of clozapine. Six (50%) of the patients developed DKA, and 42% required discontinuation of their antipsychotic. Of those who discontinued treatment, one patient required long-term insulin, and two required long-term oral hyperglycemic treatment.

Further review of the literature found one report each of associated increases in blood glucose with thioridazine, loxapine, and quetiapine. In each case, blood glucose levels normalized after medication discontinuation. No cases of diabetes associated with risperidone were found.

These cases of diabetes and DKA should be significant enough to stimulate further research into an association of secondary diabetes with atypical neuroleptics, specifically olanzapine and clozapine. Clinicians should keep this in mind when starting these neuroleptics, since diabetes and DKA can involve serious morbidity and mortality.

NR510 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Prospective Naturalistic Study of Weight Change with Mirtazapine

Kenneth A. Kobak, Ph.D., *Health Care Technology Systems, 7617 Mineral Point Road, #300, Madison, WI 53717*; Charlotte Kremer, M.D., John H. Greist, M.D., James W. Jefferson, M.D., Diane M. Burroughs, B.A.

Summary:

Objective: Antidepressants, such as TCAs, mirtazapine, or SSRIs may be associated with weight change over time. It has been reported that paroxetine-treated patients show a significant weight increase after 10 to 16 weeks of treatment. In 6-week U.S. trials, mirtazapine has been reported to produce a mean weight increase of 4.4 lbs, while studies over 40 weeks suggest that the long-term effects on weight are comparable to placebo. The purpose of this study was to examine this issue in a naturalistic, clinical setting.

Method: Participating community physicians recruited depressed outpatients who were starting mirtazapine treatment. Data were gathered directly from patients over the telephone by

computer using Interactive Voice Response (IVR) technology. Patients were instructed to phone in for evaluation at baseline and at the end of weeks 1, 2, 4, 8, 12, 16, 20, and 24. The data reported here are from the first 102 mirtazapine patients. Final data will be presented at poster.

Results: The mean change (in pounds) from baseline with mirtazapine treatment was 1.17, 1.93, 1.95, 3.94, 3.88, 4.19, 2.23, and 4.48 respectively, at weeks 1, 2, 4, 8, 12, 16, 20, and 24. The mean dose was 34.2 mg. Patients with <4% gain by week 4 were 39 times less likely to have ≥7% gain at week 12 and 9 times less likely at week 24, compared with patients with ≥4% weight gain.

Conclusion: Weight gain associated with mirtazapine treatment in naturalistic settings was modest, and plateaued between weeks 8 and 24. It appears that if there is no weight gain by week 4, it is unlikely that weight gain will occur in the long term.

NR511 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Brief, Abrupt Treatment Interruption in Fluoxetine- or Paroxetine-Treated Patients

Jennie G. Jacobson, Ph.D., *Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, DC 2032, Indianapolis, IN 46285;* Mark Parry, M.D., Deborah Quail

Summary:

Objective: This study sought to elucidate the symptoms that result when patients miss a few doses of antidepressant therapy. The effects of an abrupt 3–5 day treatment interruption on remitted depressed patients receiving fluoxetine or paroxetine treatment were examined.

Methods: Patients who had been successfully treated for depression and were stable on regimens of fluoxetine or paroxetine underwent a double-blind 3–5 day treatment interruption. New signs and symptoms were assessed using the Discontinuation-Emergent Signs and Symptoms checklist. Changes in depressive symptoms were assessed using the MADRS and CGI-Severity scales.

Results: One hundred and fifty patients (fluoxetine: N = 75, paroxetine: N = 75) at six sites in Europe completed the study and had data available for analysis. Mean treatment interruption period was 4.1 days for both treatment groups. The mean number of treatment interruption-emergent signs and symptoms was statistically significantly greater for paroxetine-treated patients than for fluoxetine-treated patients ($p = 0.001$). Paroxetine-treated patients showed statistically significantly greater mean increases in depressive symptoms following treatment interruption than fluoxetine-treated patients did as assessed by changes in MADRS ($p = 0.021$) and CGI-Severity ($p = 0.034$) scores.

Conclusion: Brief, abrupt interruption of paroxetine treatment, but not fluoxetine treatment, is associated with emergence of physical and psychological symptoms detrimental to patient well-being.

Research funded by Eli Lilly and Company, Indianapolis, Indiana 46285.

NR512 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Enhanced Tolerability and Efficacy in Switch to Divalproex Extended Release

Robert L. Horne, M.D., *University of Nevada School of Medicine, 2915 West Charleston, Suite 4, Las Vegas, NV 89102*

Summary:

Successful medication treatment requires good patient compliance. Prior studies showed compliance increased from 60% to 80% with change from twice-a-day to once-a-day dosing. The FDA recently approved extended-release divalproex for once-a-day use to prevent migraines.

Method: Psychiatric patients (N = 55) were taking divalproex b.i.d. (mean = 1827 mg, range 500–5000). DSM-IV diagnoses were mood disorders (63%), schizophrenia (27%), other (10%). 25% were inpatient and 75% were outpatients. On day 1, a baseline VPA blood level was drawn. Patients then received their usual morning dose of delayed-release divalproex bedtime. At bedtime of day 1 and every night thereafter they received extended-release divalproex at a dose equivalent to their delayed-release dose. Blood levels were drawn at 36, 84, and 132 hours post first dose. Efficacy was measured by the PANSS and side effects by the UKU scale at baseline and day 7.

Results: Mean VPA blood levels (mcg/ml) were as follows: baseline (day 1) = 81.5; day 3 = 87.4; day 5 = 88.7; and day 7 = 88.5. Efficacy was seen in terms of improvement in positive symptoms (mean PANSS 17.8 to 16.3, $p < 0.01$), general symptoms (38.0 to 35.9, $p < 0.02$) and total score (71.6 to 67.3, $p < 0.02$). Side effects decreased both in number (mean 7.7 to 6.2, $p < 0.0001$) and severity (12.5 to 9.7, $p < 0.0001$). Implications will be discussed.

Research grant provided by Abbott Laboratories.

NR513 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Depressive Symptoms in GAD and Outcome of Treatment with Venlafaxine Extended Release

Alan Lenox-Smith, *Wyeth Laboratories, Huntercombe Lane South, Berks SL6 OPH, United Kingdom*; Peter Shaw, Alan Reynolds

Summary:

Objective: Venlafaxine extended-release (XR) is effective in the treatment of generalized anxiety disorder (GAD) (1,2). The current study was designed to assess the efficacy of venlafaxine XR in primary care patients with GAD without excluding comorbid moderate depression.

Method: Patients enrolled in the study were >18 years who met DSM-IV criteria for GAD and had a HAM-A score ≥20. A MADRS score ≥23 excluded patients. Eligible patients were randomly assigned to either venlafaxine XR 75 mg/day or placebo. After 4 weeks, the venlafaxine XR dose could be increased to 150 mg/day. The duration of treatment was 24 weeks.

Results: 244 patients were enrolled. Baseline characteristics of the two groups were similar. The mean change from baseline in HAM-A total was greater in the venlafaxine XR group ($p = 0.05$). When patients were stratified to those with baseline MADRS above and below the mean (15.8), neither group showed significant differences from placebo for total HAM-A. In the high MADRS group, however, significant differences were seen for the HAM-A psychic anxiety factor and anxious mood item ($p = 0.029$ and 0.038, respectively).

Conclusions: These results suggest that the presence of depressive symptoms in patients with GAD may affect response to treatment with venlafaxine XR.

NR514 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Effects of Venlafaxine Extended Release on Psychic and Somatic Anxiety Symptoms in GAD

Alan Reynolds, *Wyeth Laboratories, Huntercombe Lane South, Berks SL6 OPH, United Kingdom*; Alan Lenox-Smith, Peter Shaw

Summary:

Objective: Venlafaxine extended-release (XR) is effective in the treatment of generalized anxiety disorder (GAD) (1,2). The current study was designed to assess the efficacy of venlafaxine in primary

care patients with GAD without excluding comorbid moderate depression.

Method: Patients enrolled in the study were >18 years who met DSM-IV criteria for GAD and had a HAM-A score ≥20. A MADRS score ≥23 excluded patients. Eligible patients were randomly assigned to either venlafaxine 75 mg/day or placebo. After 4 weeks, the venlafaxine dose could be increased to 150 mg/day. The duration of treatment was 24 weeks.

Results: 244 patients were enrolled. The baseline characteristics of the two groups were similar.

The results are tabulated below.

Scale	Mean Score Change from Baseline		p value
	Venlafaxine XR	Placebo	
HAM-A Total	14.2	11.9	0.05
Psychic Anxiety	7.3	5.7	0.007
Anxious Mood	1.3	0.7	0.016
Somatic Anxiety	6.8	6.2	NS

Conclusions: Venlafaxine XR is an effective treatment for patients having GAD and possible comorbid mild-to-moderate depression. Drug-placebo differences are more pronounced on psychic anxiety than on somatic symptoms.

NR515 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Comparative Remission Analysis Between Venlafaxine and Paroxetine

A. Richard Entsuah, Ph.D., *Clinical Research and Development, Wyeth-Ayerst Research, 145 King of Prussia Road, Radnor, PA 19087*; John M. Zajecka, M.D., Andrew A. Nierenberg, M.D., Marc Cantillon, M.D., Holly Huang

Summary:

Objective: Compare response rates and absence of depressed mood (ADM) among venlafaxine- and paroxetine-treated patients.

Method: Pooled data from 1,108 depressed patients receiving venlafaxine, paroxetine, and placebo during 8-week studies were used. HAM-D_{17} and MADRS total, HAM-D_{17} depressed mood item, CGI-S, and CGI-I scores were included in efficacy analysis. ADM was defined as HAM-D_{17} depressed mood item score = 0; response defined as ≥50% decrease in HAM-D_{17} from baseline; remission defined as HAM-D_{17} ≤7.

Results: Venlafaxine-treated patients showed numerically higher rate of ADM at all time points; however, this was statistically significant at week 8 only ($p < 0.01$ versus paroxetine, 39% versus 30%). Venlafaxine-treated patients also showed significantly greater remission rate at weeks 6 and 8 (p values <0.05 versus paroxetine, 45% versus 38%). Overall, venlafaxine-treated patients showed a trend toward greater improvement in all efficacy measures except MADRS total score.

Conclusions: Pooled data analysis indicates that venlafaxine-treated patients experience greater improvement and a higher rate of ADM compared with paroxetine-treated patients. Venlafaxine-treated patients consistently showed greater response rate across time than patients in the paroxetine treatment group.

NR516 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Global Benefit-Risk Comparison of Venlafaxine, SSRIs, and Placebo

A. Richard Entsuah, Ph.D., *Clinical Research and Development, Wyeth-Ayerst Research, 145 King of Prussia Road, Radnor, PA 19087;* Bo Gao, Ph.D.

Summary:

Objective: To compare differences in benefit-risk of venlafaxine, SSRIs, and placebo.

Method: Efficacy/safety data were obtained from >2,000 depressed outpatients who received venlafaxine/venlafaxine XR, SSRIs, and placebo. Primary response variable was HAM-D_{17} remission (final score ≤7). Patients were considered "at risk" if they reported adverse experiences (AEs) or discontinued due to AEs or lack of efficacy. A ratio global benefit-risk (GBR) analysis was used to compare groups.

Results: Relative gain (ratio of benefit-risk between groups) was 1.6 ($p < 0.001$) for venlafaxine versus SSRIs, 2.3 ($p < 0.001$) for venlafaxine versus placebo, and 1.5 ($p < 0.001$) for SSRIs versus placebo. Remission benefit was greater than risk for 44% of venlafaxine/venlafaxine XR patients, 32% of SSRI patients, and 23% of placebo patients ($p < 0.001$ venlafaxine versus SSRIs and venlafaxine versus placebo). Odds ratio that patients would be in the benefit > risk category was 1.65 for venlafaxine versus SSRIs and 2.6 for venlafaxine versus placebo; odds ratio for SSRIs versus placebo was 1.58.

Conclusions: GBR analysis provides clinically meaningful results when relative gain of one treatment to another is >1. Pooled data analysis indicates that venlafaxine and SSRI treatment results in a significantly higher benefit-risk ratio than placebo; venlafaxine/venlafaxine XR patients have a 1.6 relative gain compared with SSRI patients.

NR517 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Depression-Free Days and CGI-S: A Venlafaxine, SSRI, and Placebo Comparison

Rajiv Mallick, Ph.D., *Wyeth Ayerst, 145 King of Prussia Road, Radnor, PA 19087*; A. Richard Entsuah, Ph.D., Jieling Chen

Summary:

Objective: To estimate depression-free days (DFDs) and sustained low clinical global severity of illness among venlafaxine-, SSRI-, and placebo-treated patients.

Method: Pooled data from 2,046 depressed patients who received venlafaxine (75–375 mg/day), SSRI, or placebo were used. Adapting previously reported methods (1,2), DFDs were estimated using weekly HAM-D_{17} scores and compared across patients classified by duration of low clinical global severity (sustained CGI-S score of 1 or 2).

Results: For all groups combined, longer sustained low clinical global severity of illness was associated with more median DFDs. Treatment groups differed as well: venlafaxine group: median = 18.8 DFDs; SSRIs: median = 13.6 DFDs; placebo: median = 7.4 DFDs ($p < 0.0001$, venlafaxine versus placebo; $p = 0.0015$, venlafaxine versus SSRIs; $p = 0.0007$, SSRIs versus placebo). Similar treatment-related differences emerged in distribution of patients by duration of sustained low clinical global severity ($p = 1.001$). The venlafaxine group was associated with greatest proportion of patients having sustained low clinical global severity for ≥6 weeks.

Conclusions: Overall, DFDs were highly associated with sustained low clinical global severity. Across treatment groups, venlafaxine was associated with more DFDs than SSRIs, which were associated with more DFDs than placebo, consistent with treatment-related trends in distribution of patients by duration of sustained low clinical global severity.

NR518 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Fixed-Dose Study of Escitalopram Treatment of Depression

William J. Burke, M.D., *Department of Psychiatry, University of Nebraska, PO Box 985575 Nebraska Medical Center, Omaha, NE 68198-5580*

Summary:

Escitalopram, the S-enantiomer of the selective serotonin reuptake inhibitor (SSRI) antidepressant citalopram, is responsible for the serotonin reuptake inhibition produced by racemic citalopram. The present randomized, double-blind, placebo-controlled, fixed-dose multicenter trial was designed to evaluate the safety and efficacy of escitalopram in the treatment of major depressive disorder. Outpatients with an ongoing major depressive episode (N = 491) were assigned to placebo, escitalopram 10 mg/day, escitalopram 20 mg/day, or citalopram 40 mg/day. Subjects entered the 8-week double-blind treatment period following a 1-week single-blind placebo lead-in. Severity of depressive symptomatology was evaluated with the Montgomery-Asberg Depression Rating Scale (MADRS), the 24-item Hamilton Depression Rating Scale (HAMD), and the Clinical Global Impression severity and improvement scales. At endpoint, all active treatment groups were significantly superior to placebo: $p \leq 0.01$ for both escitalopram doses and $p \leq 0.05$ for citalopram. The effects of both escitalopram doses were numerically superior to that of citalopram at endpoint. Escitalopram was well tolerated: the incidence of discontinuation for adverse events was similar for placebo and the 10 mg dose (2.5% versus 4.2%). In summary, escitalopram showed a highly significant and consistent anti-depressive effect at 10 mg/day.

NR519 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Glucose Intolerance with Atypical Antipsychotics

Daniel Wilson, M.D., *Department of Psychiatry, Creighton University, 3528 Dodge Street, Omaha, NE 68131*; Leo DeSouza, M.D., Widar Sarkar, M.D., Michael A. Newton, M.D., Connie Hammond, R.Ph.

Summary:

Objective: To evaluate the risk of new-onset diabetes and ketoacidosis in patients treated with atypical antipsychotics.

Method: Our initial case series is augmented by an interim analysis of statewide data maintained by the Ohio Department of Mental Health (ODMH). Records of patients treated with an atypical antipsychotic and also evaluated or treated for diabetes mellitus are being systematically examined.

Results: The case series was obtained by a collation of blood glucose levels, glucose tolerance, or other evaluations of diabetes conducted in 14 of the 126 patients treated with atypical antipsychotics at the state hospital in Cincinnati. In 11 of the 14 patients, new-onset, acute, and marked glucose intolerance developed after treatment with clozapine, olanzapine, or quetiapine. Of these, six patients required insulin therapy (four only transiently) and five patients developed diabetic ketoacidosis. Additional interim data are accruing from analysis of similar information for patients treated with any atypical antipsychotic at ODMH inpatient facilities from 1994.

Conclusion: Certain atypical antipsychotics are associated with new-onset glucose intolerance that can result in ketoacidosis. Monitoring patients taking atypical antipsychotics for changes in blood glucose levels may be indicated. Preliminary analysis of a larger database appears to confirm these risks. More systematic study data are needed.

NR520 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Serum Prolactin Levels in Schizophrenia

Sally A. Berry, M.D., *Janssen Pharmaceutica, 1125 Trenton-Harbourton Road, Titusville, NJ 08560*; Rick A. Martinez, M.D., Gary A. Gudelsky, Ph.D., Joyce E. Myers, M.D., Ramy A. Mahmoud, M.D.

Summary:

Introduction: Serum prolactin levels increase in response to some antipsychotics, including risperidone. Prolactin level elevation has not been shown to be correlated with an increase in side effects, but the condition itself bears careful study.

Methods: Data from a multicenter, eight-week, randomized, double-blind, prospective comparative trial of risperidone and olanzapine in schizophrenia were analyzed to test the correlation between serum prolactin and potentially related symptoms.

Results: Endpoint serum prolactin values did not differ significantly between male patients who reported sexual dysfunction and those who did not ($p = 0.73$). Endpoint serum prolactin values did not differ significantly between female patients who reported menstrual changes and those who did not ($p = 0.40$). Moreover, the percentage of women reporting menstrual changes with normal versus elevated prolactin did not differ significantly ($p = 0.59$). Likewise, the percentage of men reporting sexual dysfunction with normal versus elevated prolactin did not differ significantly ($p = 0.62$).

Conclusion: Serum prolactin was not correlated with menstrual changes or male sexual dysfunction in this patient population.

NR521 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Comparison of Efficacy in Placebo-Controlled Trials of Escitalopram

Jack M. Gorman, M.D., *Columbia Presbyterian Medical Center, 722 West 168th Street, New York, NY 10032*

Summary:

Very few double-blind, placebo-controlled studies have been published from which definitive comparisons of efficacy can be made between available SSRI antidepressants. Attempts to combine comparator trials of SSRI antidepressants (placebo controlled or not) for the purpose of creating larger datasets for analysis are often complicated by differences in study design, lack of common assessment measures of efficacy and safety, diverse patient populations, or the different time frames during which the studies were conducted. Three comparative studies of escitalopram (the active enantiomer of the SSRI antidepressant citalopram) versus racemic citalopram were recently concurrently initiated and completed, all of which were similar in design, with common patient entry criteria, and an identical primary efficacy endpoint, the MADRS. Over 500 patients were randomized to receive escitalopram in these studies. All three placebo-controlled, randomized, double-blind trials were eight weeks in duration and employed parallel, fixed- or flexible-dose arms of escitalopram (10–20 mg/day), citalopram (20–40 mg/day), or placebo in patients with moderately severe to severe major depressive disorder (MADRS ≥22). Both escitalopram and citalopram were effective in reducing depressive symptoms and were well tolerated, with trends for greater efficacy observed with escitalopram. The results of the combined efficacy analyses across all three studies will be presented.

NR522 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Association of New-Onset Diabetes and Antipsychotics: Findings from a Large Health Plan Database

Frank Gianfrancesco, M.D., *Hecon Associates, 15717 Crebs Braud Way, Suite 202B, Rockville, MD 20855*; Amy L. Grogg, Ph.D., Ramy A. Mahmoud, M.D., Henry A. Nasrallah, M.D.

Summary:

Background: Case series suggest that some antipsychotics may induce diabetes. This study measured the association of antipsychotic treatments with diabetes at a population level.

Methods: Claims data for psychosis patients (n = 7,933) within health plans encompassing 2.5 million lives were analyzed. Patients reporting pre-existing diabetes, either with diagnosis or claim for antidiabetic medication, up to eight months prior to observation were excluded. The frequency of newly reported diabetes in untreated patients and among patients treated with risperidone, olanzapine, clozapine, and high-and low-potency conventionals was compared. Logistic regression models compared the odds of diabetes based on exposure to each of the antipsychotic categories and other explanatory variables.

Results: The odds of diabetes for risperidone patients was not significantly different from untreated patients (OR = 0.88, 95% CI = 0.37-2.07). Other antipsychotics had significantly higher odds of diabetes than untreated patients: olanzapine (OR = 3.10, 1.62-5.93); clozapine (OR = 7.44, 1.60-34.75); high-potency conventionals (OR = 2.13, 1.10-4.13); and low-potency conventionals (OR = 3.46, 1.52-7.79). The odds of developing diabetes with olanzapine, clozapine, and high-potency conventionals differed significantly from risperidone ($p < 0.05$).

Conclusions: These data support case findings that some antipsychotics may increase the risk of developing diabetes. Risperidone was not associated with a higher risk of developing diabetes.

NR523 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Differential SSRI Responses of Early-Onset and Late-Onset Alcoholics with Depressive Disorders

Simon S. Chiu, M.D., *Addiction Rehabilitation Unit, St Thomas Psychiatric Hospital, 467 Sunset Drive, St. Thomas, ON N5P 3V9, Canada*; M. Ausni, M.D., G. Sidhu, M.B., Jane Ammons, M.D.

Summary:

Introduction: Model of serotonergic dysregulation has been proposed for alcohol dependence and depression; however, findings of SSRI (selective serotonin reuptake inhibitors) treatment among depressed alcoholics have been inconclusive.

Objective: to evaluate the differential treatment responses of SSRI among early-onset (<25 yrs, EOS) and late-onset (>25 yrs, LOS) alcoholics with unipolar depression.

Method: The study was open-label and naturalistic. Outpatients with DSM-IV diagnosis of alcohol dependence and depressive disorders entered into the study upon withdrawal from alcohol for at least four weeks. Dosage of SSRI (paroxetine, fluoxetine, and nefazodone) was adjusted to the optimal level for the 12-week period. Efficacy measures included CGH (Clinical Global Impression Scale-improvement), GAF (Global Assessment Functional Scale) and HAM-D (Hamilton Depression Scale), self-report craving and relapse, and random urine toxicology screen, at baseline, 6-wk, and 12-wk. Tolerability was monitored with treatment-emergent adverse events.

Results: Of the 50 patients (EOS: 35, LOS: 15), comorbid cocaine and marijuana abuse tended to cluster more frequently among the EOS; both groups had high nicotine dependence. The EOS group had more violent offenses and higher male/female ratio. Major depression and dysthymia disorder were equally distributed among the LOS and EOS group, but personality disorder (antisocial, narcissistic, borderline) was over-represented in the EOS (chi square, $p < 0.05$). Both the LOS and EOS groups showed time-dependent positive changes in CGI, HAM-D. GAF scores, as compared with baseline values (ANOVA, $p < 0.05$), but the magnitude of change was greater for the LOS. Abstinence rate of alcohol was 70% for the LOS and 40% for the EOS (chi-square, $p < 0.05$). Dropout rate was 23% for EOS and 13% for the LOS. Side effects were well tolerated: headache, restlessness, and appetite changes.

Conclusion: The results suggest that different modes of serotonin dysregulation in EOS and LOS dictate differential treatment responses to SSRI with respect to alcohol dependence and depression.

NR524 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Switching Patients with Schizophrenia from Injectables to Olanzapine

Alain Labelle, M.D., *Department of Psychiatry, IMHR ROH, 1145 Carling Avenue, Ottawa, ON K1Z 7K4, Canada*; Dominique Bourget, M.D., Luc J. Boulay, M.A., Jack Ellis, M.D., Pierre Tessier

Summary:

Objectives: Little is known about the feasibility of switching patients with schizophrenia from long-acting injectable antipsychotics to oral olanzapine. This study had two principle objectives: (1) to assess the feasibility of switching outpatients with schizophrenia from their long-acting injectable antipsychotic medication to olanzapine. (2) to assess the efficacy of olanzapine in improving psychopathology.

Method: This 14 week, open-label study included 25 stable outpatients (DSM-IV diagnosis of schizophrenia, schizophreniform, or schizoaffective disorder) who were receiving long-acting injectable antipsychotics. Following a screening visit, patients began treatment with olanzapine 10mg per day, which was initiated the day of their scheduled injection. Clinical assessments included the Clinical Global Impression of Improvement (CGI-I) and the Positive and Negative Symptom Rating Scale (PANSS). Adverse events were monitored and the Extrapyramidal Symptoms Rating Scale (ESRS) was also completed. Assessments were completed at weeks 0, 6, and 14.

Results: Results revealed that olanzapine significantly improved negative symptoms and reduced parkinsonism.

Conclusions: Switching patients from depot antipsychotics to olanzapine proved to be clinically beneficial as well as safe. As such, this study supports the switching of stable patients with residual psychotic symptoms and significant EPS from long-acting depot antipsychotics to olanzapine.

Funding: provided by the Zyprexa Research Fund, Eli Lilly Canada INC.

NR525 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Effects of Escitalopram on Anxiety Symptoms in Depression

R. Bruce Lydiard, M.D., *Department of Psychiatry, Medical University of South Carolina, 171 Ashley Avenue, #623, Charleston, SC 29425*

Summary:

Anxiety a common symptom in depressed patients, is associated with poor outcome and increased severity of the disorder. An optimal antidepressant drug should therefore also alleviate anxiety symptoms. Escitalopram is the active enantiomer of the selective serotonin reuptake inhibitor antidepressant citalopram. Both escitalopram and citalopram have been shown to improve depressive symptomatology. Recently, two randomized (one fixed and one flexible dose), double blind, eight-week, placebo-controlled, multicenter studies of escitalopram (10–20 mg/day) and citalopram (20–40 mg/day) were conducted in patients with major depressive disorder (DSM-IV). Both studies were of common design and had common patient entry criteria. Anxiety symptoms were measured by the Hamilton Depression Rating Scale (HAMD) anxiety subscale and the Hamilton Anxiety Scale (HAMA). The pooled data from these studies show that the effects of citalopram and escitalopram on HAMA and HAMD anxiety scores were statistically significant compared with placebo. The escitalopram 10 mg/day dose showed efficacy in improving anxiety symptoms in

the fixed-dose study. These data clearly demonstrate that escitalopram is efficacious in the treatment of anxiety symptoms in depression.

NR526 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Venlafaxine Extended Release Efficacy in SSRI Failure for Major Depression

Marc Cantillon, M.D., *Wyeth-Ayerst, 555 East Lancaster Avenue, St. Davids, PA 19087*; Michael E. Thase, M.D., Richard C. Shelton, M.D.

Summary:

Objective: Evaluate dosing efficacy of venlafaxine XR in depressed patients with failed SSRI treatment.

Methods: A total of 220 outpatients with lack of response or tolerance to SSRI within six months enrolled. Lack of SSRI response was defined as lack of improvement despite six weeks' adequate dosage. Lack of SSRI tolerance was defined as discontinuation due to intolerance to adequate dosage. Venlafaxine XR treatment was dichotomized into slow and fast dose-increase groups. The slow group increased from 75 to 150 mg/day by week 4, ≤375 mg/day by week 12. The fast group started at 150 mg/day and escalated to 300 mg/day by week 4, and 375 mg/day thereafter.

Results: The fast group showed significantly better response by week 6 on CGI-I (score of 1 or 2; $p < 0.001$) and HAM-D total ($p = 0.012$). Response was 27% for the slow group vs 42% for the fast group; 39% vs 51% at week 8; 48% vs 49% at week 12. No significant differences seen at week 12.

Conclusion: In depressed patients with SSRI failure, venlafaxine XR showed robust efficacy. Faster venlafaxine XR dosing increase resulted in quicker response. Broader mechanism of action of venlafaxine XR may represent higher standard of efficacy vs single-action agents such as SSRIs.

NR527 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Response to Treatment and Venlafaxine Extended Release Dose in Patients with GAD

Peter Shaw, *William Symons, 25 All Saints Avenue, Berks SL6 6EL, United Kingdom*; Alan Lenox-Smith, Alan Reynolds

Summary:

Objectives: Venlafaxine XR is effective in the treatment of generalized anxiety disorder (GAD). The current study was designed to assess the efficacy of venlafaxine XR in primary care patients with GAD without excluding comorbid moderate depression.

Methods: Patients enrolled in the study were >18 years who met DSM-IV criteria for GAD and have a HAM-A score ≥20. A MADRS score ≥23 excluded patients. Eligible patients were randomized to either venlafaxine XR 75 mg qd or placebo. After four weeks, the venlafaxine XR dose could be increased to 150 mg qd. The duration of treatment was 24 weeks.

Results: A total of 244 patients were enrolled. Overall, venlafaxine XR was superior to placebo on all major study endpoints (eg, HAM-A, $p = 0.05$). More patients receiving placebo had their dose increased during the study (80 vs 54, $p = 0.002$). Significant differences vs placebo were observed in those patients who had a dose increase for HAM-A ($p = 0.04$), HAD anxiety ($p = 0.012$), and depression ($p = 0.047$) subscales.

Conclusions: These results suggest that, in those patients where the investigator believed response was suboptimal, an increase in dose was an effective option.

NR528 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Citalopram in Adolescents with Mood and Anxiety Disorders: A Chart Review

Jeff Q. Bostic, M.D., *Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 725, Boston, MA 02114*; Jefferson B. Prince, M.D., Kenneth Brown, M.D., Suzanne Place, N.P.

Summary:

Despite a paucity of data, the selective serotonin reuptake inhibitors (SSRIs) have become a first-line pharmacotherapy for adolescent mood and anxiety disorders. This study assessed the effectiveness and tolerability of citalopram in adolescents with mood and anxiety disorders. Medical charts from 28 adolescents administered citalopram for mood and/or anxiety disorders at a community mental health center between 1998 and 1999 were retrospectively reviewed by an independent child psychiatrist. Adolescents began on 10 mg/day citalopram and titrated upward every two to four weeks as needed. The main outcome measures were the Clinical Global Impressions (CGI) Severity and Improvement scales for both depression and anxiety. Seventy-six percent of the adolescents with mood disorders demonstrated significant improvement on the CGI. Of the adolescents with anxiety, 82% had a significant clinical response. The average daily dose of citalopram was 30 mg/day and mild side effects of sedation, headache, and nausea were reported by 36% of patients. Eleven percent discontinued because of side effects, although none required medical intervention. This chart review suggests that citalopram may be effective and safe in the treatment of adolescent mood and anxiety disorders.

NR529 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Citalopram Compared with Paroxetine in Depressed Patients with Associated Anxiety

James W. Jefferson, M.D., *Department of Psychiatry, University of Wisconsin, 2711 Allen Boulevard, Middleton, WI 53562*; John Griest, M.D.

Summary:

Citalopram and paroxetine are selective serotonin reuptake inhibitor (SSRI) antidepressants that have been found to produce anxiolytic effects in clinical trials. This randomized, multicenter, double-blind, parallel-group, flexible-dose study compared the efficacy and safety of citalopram and paroxetine in patients with depression and anxiety. Male and female outpatients (N = 104) 18–65 years of age with DSM-IV major depression and mixed anxiety-depressive disorder (research criteria A,B,C, and D) were randomized to receive citalopram or paroxetine (20–40mg). The study consisted of a one-week, single-blind, placebo lead-in period, followed by double-blind treatment (24 weeks), a two-week, double-blind, down-titration period, and a two-week post-medication follow-up period (with the blind maintained). Both drugs produced clinically significant improvement of similar magnitude on measures of both depression and anxiety. Clinically significant body weight gain (≥7%) was more prevalent among paroxetine-treated patients (21.6%) than citalopram-treated patients (3.9%). During the post-medication follow-up period, the paroxetine group exhibited a trend toward more adverse events previously associated with an SSRI-discontinuation syndrome. These results indicate that citalopram and paroxetine are both effective in treating patients with mixed anxiety and depression. However, long-term treatment with paroxetine appears to be associated with clinically significant weight gain and a possibly greater risk of discontinuation effects.

NR530 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Psychotropic Treatment of the Mentally Retarded Who Are Mentally Ill

Nick C. Patel, Pharm.D., *Department of Pharmacology Practice, University of Texas, PHR 5.110, MC A1910, Austin, TX 78712*; M. Lynn Crismon, Pharm.D., A. John Rush, M.D., Allen J. Frances, M.D.

Summary:

Objective: To compare survey responses of clinicians in the public MHMR sector with experts completing The Expert Consensus Guideline Series (ECGS): Treatment of Behavioral and Psychiatric Problems in Mental Retardation.

Methods: The ECGS medication survey was sent to 85 psychiatrists providing care for the mentally retarded in the Texas public MHMR system. The two groups were compared on treatments of choice, first-line choices, and second-line choices. Results were evaluated by comparing 95% confidence intervals for clinician versus expert responses.

Results: 37 psychiatrists (43.5%) completed and returned the survey. Few differences between experts and clinicians were found regarding treatments for specific DSM-IV diagnoses. Both groups rated the following as treatments of choice: valproate for bipolar disorder, manic episode; newer atypical antipsychotics for schizophrenia; and SSRIs for obsessive-compulsive disorder and major depressive disorder. Clinicians rated venlafaxine (first-line) higher than experts (high second-line) for major depressive episodes. Clinicians rated venlafaxine and mirtazapine higher than experts as treatments for target symptoms of depression, self-injurious behavior, and aggression. Lithium augmentation of SSRIs for nonpsychotic depression was rated first-line by clinicians and second-line by experts.

Conclusions: Clinicians viewed treatment decisions similar to experts. Research needs to explore the extent to which physician prescribing is consistent with stated preferences. Funded in part by grants from Pfizer, Inc. and Texas Department of Mental Health & Mental Retardation.

NR531 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

A Placebo-Controlled, Double-Blind Study of Bupropion Sustained Release for Sexual Dysfunction

Charles DeBattista, M.D., *Psychiatry & Behavioral Sciences, Stanford University School of Medicine, 401 Quarry Road, #2137, Stanford, CA 94305-5723*; Hugh B. Solvason, M.D., Alan F. Schatzberg, M.D., Ellen Kendrick, B.A., Emily Loraas, B.A.

Summary:

Objective: Recent estimates on the rates of sexual side effects associated with SSRIs range from 30% to more than 70%. In this double-blind trial, the utility of improving SSRI-induced sexual side effects with a fixed daily dose of bupropion-SR was examined.

Method: Eligible patients were on a fixed, therapeutic dose of fluoxetine, paroxetine, citalopram (≥20 mg/day), or sertraline (50 mg) for at least 6 weeks and complained of SSRI-induced sexual side effects, such as lowered libido or delayed, diminished, or absent orgasm. Patients were randomly assigned to either placebo or 150 mg/day bupropion-SR added to their current SSRI for the 6-week trial. Assessments were performed at each visit (weeks 1, 2, 4, and 6) to monitor sexual functioning and depression symptoms.

Results: Forty-two patients were randomly assigned to treatment. Patients in the active treatment group (N = 21) noted a 21% improvement in sexual arousal, while there was no change in the placebo-treated patients (N = 21) ($p = 0.005$). Other measures of sexual dysfunction did not change significantly between groups. Mean baseline HDRS and BDI scores, which began low, remained low throughout the study.

Conclusions: Bupropion-SR as an antidote for SSRI-induced sexual dysfunction appears to result in significant improvement in sexual side effects attributed to SSRIs. The effects of bupropion may be more specific to arousal than to delayed orgasm.

NR532 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Modafinil as Adjunctive in Treatment of Fatigue and Hypersomnia in Major Depression

Charles DeBattista, M.D., *Psychiatry & Behavioral Sciences, Stanford University School of Medicine, 401 Quarry Road, # 2137, Stanford, CA 94305-5723*; Hugh B. Solvason, M.D., Ellen Kendrick, B.A., Alan F. Schatzberg, M.D.

Summary:

Objective: Modafinil is a stimulant recently approved by the FDA for idiopathic hypersomnia and narcolepsy. Stimulants have been used commonly as adjunctive agents in the treatment of depression. These stimulants target the fatigue and hypersomnia associated with major depression and standard antidepressant therapy. The purpose of this study was to investigate the utility of modafinil as an adjunctive treatment in depression.

Method: Patients who met DSM-IV criteria for major depression and who had an incomplete response to an adequate antidepressant trial were eligible for the study. Modafinil was added at a dose of 100–400 mg/day for 4 weeks to the patient's current antidepressant. At 2-week intervals, the patient's mood, fatigue, and cognitive symptoms were assessed.

Results: Fourteen patients entered the trial (thus far) with a mean baseline HDRS score of 23.6 and a mean Beck score of 24.2. Eleven of 14 patients completed the 4-week trial. Two discontinued because of side effects. At week 4, modest improvement was noted with mean HDRS and BDI scores of 18.2 and 18.6, respectively. Eight of the 11 patients who completed treatment reported improvement in fatigue and cognition.

Conclusions: Modafinil in doses of 100–400 mg/day appears to be a useful adjunctive agent in the treatment of major depression for targeting residual fatigue, hypersomnia, and cognition problems.

NR533 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Duloxetine: Clinical Evidence of Serotonergic and Noradrenergic Reuptake Blockade

Stephan Chalon, M.D., *Department of Clinical Pharmacology, Lilly Development Center, Rue Granbonpre, 11, Mont Saint Guibat 1348, Belgium*; Luc-Andre Granier, M.D., Francois Vandenhende, M.S., Marie Guillaume, M.D., Peter R. Bieck, M.D., Frank P. Bymaster, M.S., William Z. Potter, M.D.

Summary:

Duloxetine is an antidepressant with a mechanism of action involving inhibition of serotonin (5-HT) and norepinephrine (NE) reuptake. The capacity of duloxetine for these processes was tested in 12 healthy male subjects. Placebo (N = 12), desipramine (DMI) 50mg b.i.d. (N = 12), and two regimens of duloxetine: 80 mg/day and 60 mg b.i.d. (N = 6 each) were compared in a randomized, double-blind, three-way crossover study. Whole blood 5-HT, 48-hour urinary excretion of NE and its metabolites, and PD_{30} (iv pressor dose of tyramine increasing systolic blood pressure by 30 mm Hg) were measured at steady state (days 5–7). Both duloxetine regimens but not DMI affected 5-HT reuptake as evidenced by a whole blood 5-HT depletion. Both DMI and duloxetine induced a decrease in urinary excretion of NE metabolites. PD_{30} was significantly increased by DMI (+22.84 mg) but not by DU (<+2 mg). Biological assays support the conclusion that duloxetine

affects 5-HT and NE reuptake in vivo. Furthermore, our data suggest that the tyramine test may not be a sensitive tool for detecting NE reuptake after subchronic administration of a dual reuptake inhibitor. Published data supporting this hypothesis with another dual reuptake inhibitor (venlafaxine) will be discussed.

NR534 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Affinity of Duloxetine and Venlafaxine for 5HT and Norepinephrine Transporters

Frank P. Bymaster, M.S., *Department of Neuroscience, Lilly Research Labs, Lilly Corporate Center, Indianapolis, IN 46285*; Susan R. Hemrick-Leucke, M.S., Penny G. Threlkeld, M.S., Laura J. Ahmad, M.S., Janice L. Shaw, M.S., David L. Nelson, Ph.D., Robert K. McNamara, Ph.D.

Summary:

Objective: Inhibitors that block both norepinephrine (NE) and serotonin (5-HT) uptake may have greater efficacy in therapy of depression. In this study, we compared the blockade of monoamine transporters in vitro and in vivo by the dual uptake inhibitors duloxetine and venlafaxine.

Methods: The interaction of drugs with monoamine transporters was determined using in vitro uptake and transporter binding techniques and in vivo assessments of transporter blockade.

Results: Duloxetine blocked binding to the human NE and 5-HT transporters with K_1 values of 7.5 and 0.8 nM, respectively, and a ratio of 9. Venlafaxine blocked binding to the human NE and 5-HT transporters with K_1 values of 2480 and 82 nM, respectively, and a ratio of 30. Duloxetine more potently blocked ex vivo binding to 5-HT and NE transporters than venlafaxine. The depletion of 5-HT by the 5-HT transporter-specific neurotoxin p-chloramphetamine was blocked by duloxetine and venlafaxine with ED_{50} values of 2.3 and 5.9 mg/kg. The depletion of NE by the catecholamine transporter-specific neurotoxin 6-OHDA was blocked by duloxetine and venlafaxine with ED_{50} values of 12 and 94 mg/kg.

Conclusion: Duloxetine more potently blocks 5-HT and NE transporters in vitro and in vivo than venlafaxine and is a more balanced inhibitor of the two transporters.

NR535 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Efficacy and Safety of Duloxetine Treatment of Major Depression

Mark A. Demitrack, M.D., *Lilly Research Labs, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; David J. Goldstein, M.D., Craig Mallinckrodt, Ph.D., Yili Lu

Summary:

Duloxetine hydrochloride, a potent and balanced inhibitor of serotonin and norepinephrine reuptake, was evaluated for therapeutic efficacy and safety/tolerability in the treatment of major depression. In an 8-week, double-blind, placebo-controlled study, 173 patients (aged 18–65 years) were randomly allocated to placebo (N = 70), duloxetine (N = 70), or to fluoxetine 20 mg/day (N = 33), which served as a positive control group. Patients were required to have a $HAMD_{17}$ total score at baseline of ≥15 and a reduction of <30% in $HAMD_{17}$ total score during a placebo lead-in period. Patients were excluded if they had any current primary DSM-IV axis I diagnosis other than major depression or any anxiety disorder as a primary diagnosis within the past year, excluding specific phobias. Duloxetine was given in a forced titration regimen from 20 mg b.i.d. to a maintenance dose of 60 mg b.i.d. in weekly dose increments. Seventy-six percent of patients achieved the maximum allowable dose during the study. The primary efficacy measurement was $HAMD_{17}$ total score. Safety was evaluated on the basis of occurrence of treatment-emergent adverse events, discontinuation rates, vital signs, and laboratory analyses. A mixed-effects model, likelihood-based repeated measures analysis was used to assess mean changes in the $HAMD_{17}$ total score on an intent-to-treat basis. Duloxetine demonstrated statistically significant superiority to placebo and showed a favorable tolerability profile.

NR536 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Ropinirole for SSRI-Induced Sexual Dysfunction

John J. Worthington III, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114*; Naomi M. Simon, M.D., Nicole B. Korbly, B.A., Roy H. Perlis, M.D., Mark H. Pollack, M.D.

Summary:

Objective: SSRI-induced sexual dysfunction is a relatively common side effect of the SSRIs, occurring in approximately a third of treated patients, and is associated with significant distress and treatment noncompliance. Dopaminergic agents including methylphenidate, amantadine, and bupropion have been reported helpful for the treatment of SSRI-induced sexual dysfunction. Ropinirole is a dopamine agonist currently indicated for the adjunctive treatment of Parkinson's disease.

Methods: Outpatients treated in our clinical psychopharmacology unit for depressive or anxiety disorders are routinely assessed for SSRI-induced sexual dysfunction. Patients reporting sexual dysfunction on a stable dose of their SSRI were treated openly with ropinirole starting at 0.25 mg QHS and titrated up to 2 to 4 mg/day over four weeks as tolerated.

Results: Nine patients (two female, seven male), aged 42.8 ± 9.2 years were treated. Sexual dysfunction was monitored by each patient's psychiatrist with the MGH derivation of the Arizona Sexual Experience Scale (ASE) and the Clinical Global Impression of Improvement Scale (CGI-I). ASE scores assessed a minimum of four weeks after treatment with ropinirole at a mean dose of 1.8 ± 1.4 mg/day showed a 4-point improvement ($t = 2.45$, $df = 6$, $p < .05$).

Conclusion: These data suggest that the addition of ropinirole may represent a potentially useful adjunctive strategy for the treatment of SSRI-induced sexual dysfunction.

NR537 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Citalopram Treatment of Compulsive Shopping: An Open-Label Pilot Study

Lorrin M. Koran, M.D., *Department of Psychiatry, Stanford University, 401 Quarry Road, OCD Clinic #2363, Stanford, CA 94305-5721*; Kim D. Bullock, M.D., Heidi J. Hartston, Ph.D., Michael A. Elliott, M.A., Vincent J. D'Andrea, M.D.

Summary:

Open-label trials suggest that selective serotonin reuptake inhibitors (SSRIs) may be an effective treatment for compulsive shopping. To test the hypothesis that the SSRI citalopram is a safe, effective, and tolerable treatment for this disorder, a 12-week, open-label, flexible-dose trial was conducted in adult outpatients meeting diagnostic criteria. Citalopram treatment was started at 20 mg/day and titrated at two-week intervals to a maximum of 60 mg/day if significant response had not occurred. Twenty-one subjects (19 women and two men) were enrolled (mean age 44.9 years; mean age of onset 23.2 years). Citalopram produced marked improvements on the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) Shopping Version and the Clinical Global Impressions-Improvement (CGI-I) scale. Mean (±SD) Y-BOCS scores decreased from 22.0 (±7.2) at baseline to 6.33 (±9.35) at week 12. The week 12 mean (±SD) CGI-I score was 1.75 (±1.16); 80% of patients were classified as responders (CGI-I = 1 or 2).

Three patients discontinued the study because of side effects, two of whom were responders. Results suggest that citalopram may be an effective treatment for compulsive shopping.

NR538 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Safety Update on Lenticular Opacities: Benign Experience with Quetiapine

Alan M. Laties, M.D., *Scheie Eye Institute, Myrin Circle, 51 North 39th Street, Philadelphia, PA 19104*; Vikram Dev, M.D., Wayne Geller, M.D., Ihor W. Rak, M.D., Martin B. Brecher, M.D., Henry A. Nasrallah, M.D.

Summary:

The package insert for quetiapine in Canada and U.S. recommends periodic eye exams for cataract formation. All reports of lens opacities submitted to AstraZeneca between September 1997 (when quetiapine became available) and November 30, 2000, were examined. After the exposure of approximately 851,000 patients in the U.S., 45 cases of lens opacities were reported worldwide. Many of the patients reporting lens opacities had risk factors such as heavy smoking, hypertension, diabetes, and ocular trauma. An independent ophthalmologist's evaluation concluded that there appears to be no signal suggesting that lens opacities are related to quetiapine treatment. The possibility that the low number of lens opacities reported in patients taking quetiapine may be attributed to underreporting (as occurs with other prescription drugs), unknown duration of quetiapine use, or lack of eye exams should not diminish the value of these findings. Prospective studies comparing ocular status in patients receiving quetiapine versus other antipsychotics are needed to confirm these findings.

NR539 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Prevalence and Risks Associated with Antidepressant-Induced Mania

Joseph F. Goldberg, M.D., *Department of Psychiatry, Payne Whitney-NY Presbyterian Hospital, 525 East 68th Street, New York, NY 10021*; Aliza Rabin, B.A., Joyce E. Whiteside, B.A.

Summary:

The potential for antidepressants to induce manias in bipolar patients remains an area of tremendous controversy, although minimal data exist on either the scope or features of this phenomenon.

Lifetime medication histories were recorded for 48 DSM-IV bipolar outpatients from the Cornell Bipolar Disorders Research Clinic via direct interviews and record reviews. Frequencies, intensities, exposure durations and outcomes of antidepressant use were examined alongside illness characteristics of patients with or without histories of switches into mania/hypomania.

Results showed: (1) 33% of subjects had at least one lifetime antidepressant-induced mania; (2) switches typically arose a mean (SD) of 36.5 (34.1) days after antidepressant initiation; (3) switchers were more likely than non-switchers to have a history of substance abuse ($p < .001$) and to have had more antidepressant trials/years ill ($p < .05$); (4) 21% of SSRI exposures resulted in hypomania, as did 14% of bupropion trials, 6% of tricyclic trials, and 21% of novel antidepressant trials; (5) concomitant lithium or divalproex was not associated with a reduced risk for switching during antidepressant use; (6) mixed effect logistic regression models indicated a significant cumulative probability for switching with successive antidepressant trials.

Antidepressant-induced manias may arise in at least one-third of bipolar patients, with comparable frequency across antidepressant classes, and regardless of the presence of concomitant mood stabilizers. In most instances, switches were of mild severity and tended to resolve without hospitalization or marked functional impairment.

NR540 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Divalproex Sodium Treatment of Impulse Control Disorders

James A. Wilcox, D.O., *Department of Psychiatry, Texas Technical University, 4800 Alberta Avenue, El Paso, TX 79905-2709*

Summary:

In this study, 40 subjects with impulse control problems were treated with divalproex sodium and compared with 40 similar patients on other treatments, in a double-blind method. All subjects were adults. The subjects all suffered from impulse control disorders, with high Karolinska scores and DSM-IV diagnosis verified by objective criteria. Results were analyzed using student's t-test and multiple regression analysis. Scores were corrected using the Bonferoni procedure to minimize statistical artifacts. These results revealed remarkable improvement in impulsivity for individuals treated with divalproex ($t = 8.79$, $p < .001$). Use of divalproex was the only variable that changed the mean improvement of the Karolinska impulsivity scores in a positive way ($F = 9.48$, $p < .0001$). We conclude that divalproex sodium is a very effective treatment for the reduction of impulsive behavior and explosive behavior.

NR541 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Mirtazapine Onset of Action Compared with SSRIs: Response and Remission Rates

Albert J. Schutte, M.D., *International Marketing, NV Organon, Molenstraat 110, Oss 5342-CC, Netherlands*; Helga Van Oers, Ph.D.

Summary:

Objective: A pooled analysis was performed to compare the efficacy of mirtazapine with SSRIs.

Method: Data from four double-blind, controlled studies of mirtazapine vs. fluoxetine (two), paroxetine, or citalopram in depressed patients were pooled and reanalyzed. Data from the fluoxetine and the paroxetine studies (using HAMD-17) were combined (665 patients) and data from the fluoxetine with the citalopram study (using MADRS) (561 patients). Changes from baseline and responder rates (≥50% reduction in HAMD-17 or MADRS) were assessed, as well as the proportion of remitters (HAMD ≤7 or MADRS ≤12).

Results: Decrease from baseline was greater with mirtazapine, reaching significance on the HAMD-17 at weeks 1, 2, 4, 6, and endpoint and on the MADRS at weeks 1, 2, and 4. The proportion of responders as well as the proportion of remitters was higher on mirtazapine than SSRIs. The differences achieved significance for the responders at weeks 1, 2, 4, and 6 and for the remitters at weeks 2 and 4.

Conclusion: These results provide strong evidence that mirtazapine has a faster onset of antidepressant effect compared with the SSRIs.

NR542 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Mirtazapine Has Similar Short-Term and Long-Term Efficacy Compared with Venlafaxine

Albert J. Schutte, M.D., *International Marketing, NV Organon, Molenstraat 110, Oss 5342-CC, Netherlands*; Ilse Van Hensbeek, M.D., Helga Van Oers, Ph.D.

Summary:

Objective: To compare the onset of antidepressant activity and the efficacy and tolerability of two dual-acting antidepressants, mirtazapine and venlafaxine, in the long-term treatment of severely depressed patients with melancholia.

Method: This was a multicenter, randomized, double-blind, eight-week study with a 16-week extension phase. Patients with DSM-IV major depressive disorder with melancholic features and HAMD-17 ≥25 received mirtazapine (n = 78, 15–60 mg/day) or venlafaxine (n = 79, 75–375 mg/day) for eight weeks. Consenting patients responding to treatment continued on a double-blind basis (mirtazapine: n = 44, venlafaxine: n = 39). The primary efficacy variable was change from baseline on HAMD-17 and MADRS. Rates of responders (reduction ≥50%) and remitters (HAMD ≤7 or MADRS ≤12) were also analyzed.

Results: Both drugs reduced HAMD-17 scores to the same extent: the mean change from baseline was –7.1 for mirtazapine and –5.3 for venlafaxine at week 1. At weeks 1 and 2, the percentages of patients classified as HAMD-17 responders were 16.9 and 44.2 for mirtazapine and 6.7 and 30.7 for venlafaxine. The remission rates were 3.9%, 6.5% and 23.4% for mirtazapine and 1.3%, 5.3% and 16.0% for venlafaxine, at weeks 1, 2, and 4, respectively. MADRS scores showed similar results. Overall tolerability was good although more venlafaxine-treated patients discontinued for adverse events (p = 0.037) compared with mirtazapine; 15.2% vs. 5.1%, respectively. After 24 weeks, the decrease from baseline on HAMD-17 was similar for mirtazapine (21.3 ± 7.8) and venlafaxine (22.7 ± 5.0). The proportion of responders and remitters were also similar.

Conclusion: Onset of action of mirtazapine was at least as rapid as that of venlafaxine. Both dual-acting antidepressants, mirtazapine and venlafaxine, are effective and well-tolerated in long-term treatment.

NR543 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Open-Label Pilot Study of Topiramate in Adults with Prader-Willi Syndrome

Nathan A. Shapira, M.D., *Department of Psychiatry, University of Cincinnati, P O Box 100256, Gainesville, FL 32610*; Mary C. Lessig, B.S., Helen C. McCune, M.S., Wayne K. Goodman, M.D., Daniel J. Driscoll, Ph.D.

Summary:

Prader-Willi Syndrome (PWS) is a neurogenetic multisystem disorder characterized by infantile hypotonia, mental retardation, short stature, hypogonadism, obsessive-compulsive behaviors, self-injury, and hyperphagia with a high risk of obesity (1). Topiramate is a novel agent approved for the treatment of epilepsy and in controlled trials was associated with appetite suppression and weight loss (2). There are no reports of topiramate being utilized for PWS, but success has been noted in the treatment binge-eating disorder. This 8-week, open-label, flexible-dose (maximum 350 mg/day) study evaluated the efficacy and safety of topiramate in approximately 10 PWS adults. Weekly evaluations included scales for stereotypical behaviors and cognitive functioning as well as safety measures (e.g., blood pressure). Appetite was accessed by direct observation of the subject for 1 hour with free access to low-calorie food and a visual analogue scale before and after this hour. Four participants so far have completed the trial, all with weight loss (mean 1.81 lbs). Surprisingly, appetite tests showed a mean increase of 366.19 calories/hour. A salient finding was a dramatic reduction in self-injurious behavior (skin picking). Two participants exhibiting self-injurious behavior (SB) had marked improvements in the healing of their lesions and marked reductions in the time spent engaged in SIB.

NR544 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Melatonin Treatment for Tardive Dyskinesia: A Double-Blind, Placebo-Controlled, Cross-Over Study

Eyal Z. Shamir, M.D., *Day Care Department, Abarbanel Mental Health Center, 15 KKL Street, Bat-Yam 59100, Israel*; Foram Barak, M.D., Irena Shalman, M.D., Noshe Landon, Ph.D., Nava Zisapel, Ph.D., Avner Elizur, M.D., Ronit Weizman, M.D.

Summary:

Background: Antipsychotics remain the mainstay of drug intervention in the management of schizophrenia. However, long-term treatment with antipsychotics is associated with a variety of movement disorders, the most disabling of which is tardive dyskinesia (TD); which occurs in up to 50% of chronically hospitalized patients with schizophrenia. The pathophysiology of TD is still unclear. Both dopamine receptor supersensitivity and oxidative stress-induced neurotoxicity in the nigrostriatal system are apparently implicated (1). TD has no definite treatment, although atypical antipsychotics and the antioxidant vitamin E were reported to reduce TD symptomatology (2). The pineal hormone melatonin is a potent antioxidant and attenuates dopaminergic activity in the striatum and dopamine release from the hypothalamus. Thus, it may have a beneficial effect for both the treatment and prevention of TD.

Methods: We evaluated in a double-blind, placebo-controlled cross-over study, the efficacy of 10 mg/day melatonin for 6 weeks in 22 patients with schizophrenia suffering from TD.

Results: Mean±SD of decrease in Abnormal Involuntary Movement Scale (AIMS) score was 2.95 (SD = 2.14) for the melatonin group and 1.0 (SD = 1.34) for the placebo treatment group (p = 0.0001, MANOVA). A greater cumulative exposure to antipsychotics was associated with a better outcome. No adverse events or side effects were noted.

Conclusion: This is the first clinical evidence for efficacy of melatonin in the treatment of TD.

NR545 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Antidepressants Regulate the Expression of Brain-Derived Neurotrophic Factor (BDNF) and B Cell Lymphoma Protein-2 in Rat Brain

Haiyun Xu, Ph.D., *Department of Psychiatry, University of Saskatchewan, 103 University Drive, Saskatoon, SK S7N OW8, Canada*; Xin-Min Li, M.D.

Summary:

The efficacy of antidepressants has been attributed to their chronic effects. It was proposed that chronic antidepressants might exert neuroprotective effects on particular populations of brain neurons. To further test this hypothesis, we chose the neuroprotective proteins B cell lymphoma protein-2 (bcl-2) and brain-derived neurotrophic factor (BDNF) as target marks for their important role in the development and the survival of neurons. Adult male Sprague-Dawley rats were treated with the antidepressants amitriptyline (a classic tricyclic antidepressant) or venlafaxine (a new serotonergic/noradrenergic reuptake inhibitor) for 21 days, at the dose of 10 mg/kg in saline (vehicle). Immunohistochemistry experiments revealed that the immunoreactivity of both bcl-2 and BDNF in neurons of the prefrontal cortex, piriform cortex, and hippocampal formation of amitriptyline-treated rats was higher compared to control rats. Venlafaxine, however, increased the immunoreactivity of bcl-2 only at this dose. The results indicated the involvements of above neuroprotective proteins in the actions of the antidepressants amitriptyline and venlafaxine upon particular populations of brain neurons. (supported by CIHR, Canadian Psychiatric Research Foundation)

NR546 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Depakote Extended Release for Psychiatric Patients Experiencing Side Effects from Depakote

Lance P. Longo, M.D., *Department of Psychiatry, Sinai Samaritan, 1020 North 12th Street, 4th Floor OHC, Milwaukee, WI 53233*

Summary:

Divalpioex ER is a newly formulated hyrophilic polymer matrix controlled-release formulation that produces lower peak-trough blood level fluctuation than divalproex delayed-release tablets, and in clinical trials it appears to have a favorable side effect profile. Although it is FDA approved for migraine headache prophylaxis it has not yet been studied in psychiatric populations. Based on initial anecdotal clinical experience, we hypothesized that divalproex ER would be effective and well tolerated, perhaps conferring the additional benefit of enhanced compliance as a result of once-daily dosing requirements.

Ten patients with bipolar I or bipolar II disorder (some with other axis I or axis II comorbidity) who exhibited side effects that limited their compliance or tolerability to divalproex were switched to the new once-daily ER formulation at an equivalent bioavailable dose. Patients were evaluated over 12 weeks to monitor clinical status (CGI-clinical global impressions, and GAF-global assessment of functioning) and a 7-point Likert side effect rating scale. Laboratory assessment included serial divalproex blood levels, liver function tests, and complete blood counts.

Our results substantiated that divalproex ER was effective (nine of 10 patients showed equal or mildly improved clinical status), well tolerated (five of 10 had reductions in side effects), and led to enhanced medication compliance in certain individuals. We hope that these pilot findings stimulate interest in more rigorous controlled clinical trials of divalproex ER in psychiatric patients.

NR547 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Divalproex Sodium Treatment of Alcohol Withdrawal

Lance P. Longo, M.D., *Department of Psychiatry, Sinai Samaritan, 1020 North 12th Street, 4th Floor OHC, Milwaukee, WI 53233*; Todd Campbell, Ph.D., Sandy Hubatch, R.N.

Summary:

Preliminary studies and anecdotal observations suggest that the anticonvulsant divalproex sodium may be a safe and efficacious alternative to benzodiazepines for acute alcohol withdrawal and may offer additional promise as a relapse prevention agent by tempering protracted withdrawal symptoms. Although the efficacy of benzodiazepines is supported by extensive literature, their use in outpatient settings is limited by abuse potential, psychomotor side effects, and pharmacologic synergism with alcohol—thus making physicians wary of medical/legal liability risks and prohibiting more extensive outpatient management of this condition.

We conducted an open pilot study comparing divalproex to standard benzodiazepines (chlordiazepoxide, lorazepam) in a sample of alcoholics (N = 16) admitted for detoxification. Subjects were randomly assigned to one of three groups: 1) standard benzodiazepine detoxification 2) divalproex (loading dose) 5-day detoxification, or 3) divalproex detoxification plus 6-week maintenance. Subjects were administered a battery of screening and assessment instruments and were entered into the study if their CIWA-Ar scores were ≥8 and <20 (indicating moderate alcohol withdrawal).

Divalproex treatment was well tolerated at loading doses of 20 mg/kg and led to rapid symptom resolution (reduction in CIWA scores) comparable to benzodiazepines at 12- and 24-hour intervals. No divalproex-treated subjects suffered adverse events or required benzodiazepines, and at 6-week follow up all divalproex-treated patients had lower liver transaminase levels than at baseline (presumably because they were drinking less). At 6-week follow-up a greater percentage of patients in the divalproex maintenance group were completely abstinent than either detoxification-only group, and none relapsed to heavy or daily drinking. Our pilot study suggests that divalproex may be a safe and efficacious alternative to benzodiazepines in selected patient populations.

NR548 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Compliance, Type of Medication, and Quality of Life

Letitia T. Postrado, Ph.D., *Department of Psychiatry, University of Maryland, 685 West Baltimore, MSTF Building, Room 300, Baltimore, MD 21201*

Summary:

Objective: This study aims to examine the association of medication compliance with quality of life (QOL) in schizophrenic patients receiving atypical antipsychotic medications and compare the results on a sample of patients who were taking conventional antipsychotics.

Methods: The Schizophrenia PORT Project Team surveyed a stratified random sample of 719 persons with schizophrenia in two states. Of this total, 165 were taking atypical antipsychotics, and 444 were taking conventional medications. The survey used the Lehman Quality of Life Instrument to measure patients' subjective quality of life. A 4-point scale was used to determine degree of medical compliance.

Findings: Compliance with medications was significantly associated with greater overall life satisfaction ($p < 0.05$), higher satisfaction with family ($p < 0.01$), daily activities ($p < 0.01$) and health ($p < 0.05$) among persons who were receiving atypical antipsychotic medications. Further, compliance and greater satisfaction with social relations were related at a nearly significant level ($p = 0.065$). In contrast, compliance with medications was not correlated with any domain of subjective quality of life among patients who were taking conventional medications.

Conclusion: Association between medication compliance and subjective quality of life was affected by type of antipsychotic medication (atypical versus conventional) among patients with schizophrenia.

NR549 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Olanzapine-Fluoxetine Combination for Difficult-to-Treat Depression

Douglas J. Williamson, M.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Scott W. Andersen, M.S., Luann E. Van Campen, Ph.D., Todd M. Sanger, Ph.D., Sofia Paul, Ph.D., Sara A. Corya, M.D., Gary D. Tollefson, M.D.

Summary:

Background: Up to 30% of patients with major depression are resistant to conventional antidepressant treatment (1), and response rates are lower when psychotic symptoms are present. Subsequent therapy may include combinations of antidepressants or various augmentation strategies. (2) Efficacy of an olanzapine-fluoxetine combination (OFC) was investigated in difficult-to-treat forms of depressions: treatment-resistant depression (TRD) and depression with psychotic features (DPF).

Methods: Both studies employed an 8-week, double-blind design. In study 1, subjects with non-bipolar TRD without psychotic features (N = 28) were randomly assigned to OFC or olanzapine or fluoxetine monotherapy. In study 2, subjects with DPF (N = 124) were randomly assigned to OFC, olanzapine monotherapy, or placebo.

Results: For TRD, OFC had significantly greater improvement from MADRS baseline than either monotherapy. For DPF, OFC

had significantly greater improvement on HAMD-24 total score than placebo and significantly greater improvement on HAMD-24 responder analysis than olanzapine or placebo. In both studies, OFC had a comparable safety response to olanzapine and showed no significant increases in extrapyramidal symptoms.

Conclusion: OFC showed significant improvement over olanzapine or fluoxetine monotherapy and placebo in patients with difficult-to-treat forms of depression.

NR550 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Efficacy of Tomoxetine Versus Placebo in School-Age Children with ADHD Who Failed Psychostimulant Treatment

John H. Heiligenstein, M.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; David W. Dunn, M.D., Joan Busner, Ph.D., Mark Stein, Ph.D., Christopher J. McDougle, M.D.

Summary:

Objective: To compare the efficacy of tomoxetine, a novel, non-stimulant, selective noradrenergic enhancer, was compared with placebo in school-age children who meet DSM-IV criteria for ADHD and have failed treatment with psychostimulants.

Methods: Two identical multicenter (17 sites total) double-blind, placebo-controlled studies were conducted in the United States. Patients were required to meet diagnostic and severity of illness criteria for ADHD following structured and semi-structured interviews. Patients were stratified based on prior history of treatment with psychostimulants. Patients with a prior history of treatment with psychostimulants were randomized to nine weeks of treatment with tomoxetine or placebo. The primary analysis was an intent-to-treat comparison of tomoxetine vs. placebo.

Results: In the two studies combined, efficacy data were available for 119 patients who had previously been treated with any psychostimulant. Of these, 33 (28%) had failed treatment with psychostimulants, by parent report. Tomoxetine (n = 14) was found to be superior to placebo (n = 19) in reducing ADHD symptoms (p = .027).

Conclusion: Tomoxetine is effective in treating school-age children who have had an inadequate response to treatment with psychostimulants.

NR551 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Efficacy of Tomoxetine Versus Placebo in School-Age Children with ADHD: Inattentive Subtype

John H. Heiligenstein, M.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Karen D. Wagner, M.D., Charles D. Casat, M.D., Joan Busner, Ph.D., Jeffrey H. Newcorn, M.D., Keith E. Saylor, Ph.D., Nora Galil, M.D.

Summary:

Objective: To compare the efficacy of tomoxetine, a non-stimulant, selective noradrenergic enhancer, with placebo in school-age children meeting DSM-IV criteria for ADHD, inattentive subtype.

Methods: Two identical multicenter (17 sites total) double-blind, placebo-controlled clinical trials were conducted in the United States. Patients were required to meet diagnostic and severity of illness criteria for any ADHD subtype using structured and semi-structured interviews. Patients were stratified based on prior history of treatment with any psychostimulant then randomized to nine weeks of treatment. The analysis consisted of an intent-to-treat comparison of tomoxetine vs. placebo in school-age children who met DSM-IV criteria for the inattentive subtype of ADHD.

Results: For the two studies combined, 48 primarily inattentive children were randomized to tomoxetine (n = 24) and placebo (n = 24). Tomoxetine was found to be superior to placebo (p = .003) on the primary efficacy outcome instrument and on additional measures of efficacy.

Conclusion: The data provide convincing evidence of the efficacy of tomoxetine for the treatment of the inattentive subtype of ADHD in school-age children.

Research funded by Eli Lilly and Company, Indianapolis, Indiana 46285.

NR552 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Efficacy of Tomoxetine Versus Placebo in School-Age Girls with ADHD

John H. Heiligenstein, M.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Joseph Biederman, M.D., Christopher J. Kratochvil, M.D., Nora Galil, M.D., Scott A. West, M.D., Graham J. Emslie, M.D.

Summary:

Objective: To compare the safety and efficacy of tomoxetine, a nonstimulant, selective noradrenergic enhancer, with placebo in school-age girls with ADHD.

Methods: Two identical multicenter (17 sites total) double-blind, placebo-controlled, clinical trials were conducted in the US. Patients were required to meet diagnostic and severity of illness criteria for DSM-IV ADHD using structured and semi-structured interviews. Patients were stratatifed based on prior history of treatment with any psychostimulant, then randomized to nine weeks of treatment with tomoxetine, methylphenidate (included as a positive control), or placebo in the stimulant naïve stratum or to nine weeks of treatment with tomoxetine or placebo in the stimulant prior-exposure stratum. Methylphenidate was included to validate the study design. A subset analysis (ITT) of the total sample of randomized patients was conducted to determine the efficacy of tomoxetine vs. placebo in girls.

Results: Efficacy data were available for 51 girls (tomoxetine, n = 30), (placebo, n = 21). Tomoxetine was found to be superior to placebo (p = 0.002). Statiscally significant efficacy was seen one week following randomization and remained so for the remainder of the study.

Conclusion: Data from these trials provide convincing evidence of the efficacy of tomoxetine in school-age girls with ADHD. Treatment with tomoxetine was well tolerated.

Research funded by Eli Lilly and Company.

NR553 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Olanzapine Treatment for PTSD: The Continuation Phase

Frederick Petty, M.D., *Department of Psychiatry, University of Texas at Southwestern, 4500 South Lancaster Road, Suite 116A, Dallas, TX 75216*; Virginia Gajewski, R.N., Patricia Borman, Jason Worchel, M.D., Alina Suris, Ph.D., Andra Teten, B.A.

Summary:

The antipsychotic olanzapine, showed efficacy in treating the aviodant, intrusive, and hyperarousal symptoms of PTSD in our core eight-week study (Petty et al). Based on these promising results a multi-site, open label, six-month maintenance study of olanzapine in veterans with severe, chronic, combat-induced PTSD was conducted.

Patients received an extended treatment of olanzapine (5–20 mg per day) for six months following their completion of the eight-week study. The primary outcome measures administered monthly were the Clinician Administered PTSD Scale (CAPS), and the Clinical Global Impressions (CGI) Improvement Scale. Secondary outcome measures included the Hamilton Rating Scales for Depression and for Anxiety (HRSD, HRSA), and the

Brief Psychiatric Rating Scale (BPRS). A structured social functioning interview (SAS) and Quality of Life questionnaire (QOL-BV) were completed at months 3 and 6.

Results demonstrated no significant change in any of the outcome measures from the final week (week 8) of the core study to the end (month 6) of the follow-up study.

This presentation is designed for clinicians and researchers dealing with the treatment and study of PTSD.

Eli Lilly Corporation provided partial funding for this project.

NR554 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Escitalopram: Potent and Rapid in Chronic Mild Stress Model of Depression

Mariusz Papp, Ph.D., *Institute of Pharmacology, Polish Academy of Science, 12 Smetna Street, Krakow 31-343, Poland*; Connie Sanchez, D.Sc.

Summary:

Objective: The selective serotonin reuptake inhibitor citalopram is the racemic of an S-(+)-enantiomer, escitalopram, and an R-(–)-enantiomer, R-citalopram. Escitalopram mediates citalopram's 5-HT reuptake inhibitory potency, illustrated by the in vitro IC50 values in rat brain synaptosomes: 2.1 and 275nM for escitalopram and R-citalopram, respectively.

Method: The present investigation studied escitalopram in the chronic mild stress (CMS) model of depression in rats. The CMS model consists of sequential exposure to a variety of mild stressors for a prolonged period. This results in behavioral hedonic deficits, measured as decreased consumption of a 1% sucrose solution.

Results: Escitalopram (5 and 10mg/kg, s.c. per day) reversed the CMS-induced decrease in sucrose intake, to a similar extent as tricyclic antidepressants. However, escitalopram had a substantially faster onset of action. The first significant effects on the CMS-induced deficit in sucrose consumption were seen within the first week of treatment with escitalopram. Tricyclic antidepressants typically require three to four weeks before the first significant increases of sucrose intakes can be observed.

Conclusions: These results suggest that escitalopram has antidepressant potential. Moreover, the onset of antidepressant action seen with escitalopram in the CMS model of depression is more rapid than that seen with tricyclic antidepressants.

NR555 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Antipsychotic Medication and Insulin Resistance

Tony A. Cohn, M.D., *Centre for Addiction and Mental Health, 1001 Queen Street, West, Toronto, ON M6J 1H4, Canada*; Gary J. Remington, M.D., Lawrence Leiter, M.D., Homa Kameh, M.S.C.

Summary:

Objective: This report represents an interim analysis of data on 50 consecutive patients from an ongoing study addressing the issue of weight gain and related side effects of antipsychotic medication treatment.

Method: Patients were on a single antipsychotic medication for at least three months. Those on concomitant lithium or tricyclic anti-depressants were excluded. For the purpose of this analysis patients were divided into the following three medication groups: clozapine (10), olanzapine (11), and other (29). Homa's index, a measure of insulin resistance was calculated using fasting glucose and insulin data. Groups were compared for Homa's index, fasting insulin, fasting triglyceride, body mass index (BMI), waist circumference, and blood pressure.

Results: The clozapine and olanzapine groups were similar on all the above variables. These two groups were combined and compared with patients on other antipsychotics. BMI was similar but significant differences were found in insulin resistance, fasting insulin levels, and triglycerides. Waist circumference and blood pressure followed the same trend.

Conclusion: These preliminary results suggest that antipsychotic treatment with both clozapine and olanzapine is associated with insulin resistance compared with other antipsychotics. This association is independent of BMI and may predispose these patients to the development of diabetes and coronary heart disease.

NR556 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Concurrent Validity and Sensitivity to Change of the Schedule for the Assessment of Drug-Induced Movement Disorders (SADIMoD)

Anton J.M. Loonen, M.D., *Delta Psychiatric Hospital, PO Box 800, Poortugaal, NL 317 ODZ, Netherlands*; Lowijs N.M. Perquin, M.D., Dianne A. Van Hemert, M.S.C., Jessica Wesselius, M.D., Pieter Kempe, M.S.C., Cees H. Doorschot, M.D.

Summary:

Objective: Measurement of the characteristics and suitability of the newly developed instrument: Schedule for the Assessment of Drug-Induced Movement Disorders (SADIMoD).

Method: Using the results of an open trial of the acute effects of sertindole in acutely admitted psychotic patients [20 males/10 females; 36.9 ± 11.0 years old], the concurrent validity with the Barnes Akathisia Scale (BAS), Abnormal Involuntary Movement Scale (AIMS), Fahn-Marsden Dystonia Movement Scale (FMDMS), Webster's Parkinson Disease Rating Scale (WPDRS), Positive and Negative Syndrome Scale (PANSS), and Montgomery-Nsberg Depression Rating Scale (MADRS) was assessed. Moreover, it was examined whether the SADIMoD is more sensitive to change.

Results: At entry, one-third of the patients suffered from ataxia of at least mild severity. The highest Spearman correlation coefficients (.88 – .96; highly significant $p < .01$) were found for ratings on the SADIMoD subscales and their corresponding scales. Apart from the existence of relationship between PANSS motor retardation and mannerism with respectively SADIMoD Parkinsonism and Dystonia subscale scorings, no evidence exists for a relationship between mental symptoms and motor signs. Comparing the change of the scores after the initiation of treatment, the SADIMoD showed a similar or larger (vs. BAS, WPDRS) sensitivity than the comparators.

NR557 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Escitalopram Mediates Citalopram's Inhibition of Dorsal Raphe Nucleus (DRN) 5HT Neural Activity

Peter B. Bergqvist, Ph.D., *Clinic OPS, AstraZeneca R & D, Lund S-22187, Sweden*; Lise T. Brennum, Ph.D., Connie Sanchez, D.Sc.

Summary:

Objective: Citalopram is a racemic mixture of the S-(+)-enantiomer, escitalopram, and the R-(–)-enantiomer, R-citalopram. In vitro pharmacological studies suggest that escitalopram, which is in late Phase III development, is a selective inhibitor of serotonin (5-HT) that is approximately twice as potent as citalopram. For example, in rat brain synaptosomes, escitalopram and citalopram show IC_{50} values of 2.1 and 3.9nM, respectively. Based on potentiation of 1-5-HTP-induced behaviors in rats, escitalopram is a potent 5-HT reuptake inhibitor, whereas R-citalopram is inactive in this model. Moreover, escitalopram, but not R- citalopram, is active in animal models predicting antidepressant activity, such as Porsolt's forced swim test. The present study assessed the effects

acute intravenous administration of citalopram and its enantiomers on neuronal activity of 5-HT cells in the rat dorsal raphe nucleus (DRN).

Method: The study employed extracellular single unit recording.

Results: SSRIs inhibit serotonergic neuron firing by activating autoreceptors on the DRN cell body. Escitalopram and citalopram, but not R-citalopram, dose-dependently reduced the firing activity of 5-HT cells in the DRN. In this model, escitalopram was approximately twice as potent as citalopram (ED_{50} 0.18 and 0.35 mol/kg, respectively).

Conclusions: These results support the hypothesis that escitalopram mediates citalopram's pharmacological activity.

NR558 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Is Amisulpride Effective for Schizophrenia? A Systematic Review

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Summary:

Objectives: Amisulpride is one of the novel atypical neuroleptics used for treating schizophrenia. As well as its reputed tendency to cause fewer movement disorders, it is claimed that it may improve particularly negative symptoms. A systematic review and metanalysis was undertaken aiming to evaluate the clinical and adverse effects of amisulpride for those with schizophrenia in comparison with placebo and typical and atypical neuroleptics.

Methods: Searches of relevant randomized controlled trials (RCTs) in electronic databases (Biological Abstracts, Cochrane Library, EMBASE, MEDLINE, PsycLIT) were supplemented by reference searching and contacting authors. Data were analyzed on an intention-to-treat basis. Relative risk (RR), weighted mean difference (WMD) and 95% confidence intervals (CI) were calculated for dichotomous outcomes.

Results: Review included data from 15 RCTs. Nine studies comparing with typical neuroleptics, suggest that amisulpride, especially at high doses, seemed to be better on global improvement (Fixed RR 0.71 95%CI 0.56–0.88), mental state (WMD −3.51 95%CI −6.25 to −0.78), and treatment of negative symptoms (WMD −2.51 95%CI −4.34 to −0.66). The use of amisulpride was less prone to need an antiparkinsonian medication (RR 0.63 95%CI 0.51–0.77) and may be more acceptable (RR 0.77 95%CI 0.66–0.90) than conventional drugs. A single trial compared with another atypical, risperidone, and no differences were recorded on efficacy or acceptability.

Conclusions: Amisulpride is an effective antipsychotic, with a favorable side-effect profile and better action on negative symptoms, when compared with typical antipsychotics.

NR559 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Escitalopram: Potent Anxiolytic Effects in Rodent Models of Anxiety

Connie Sanchez, D.Sc., *Department of Neuropharmacology, H Lundbeck A/S, Ottiliavej 9, Copenhagen-Valby Dk-2500, Denmark*

Summary:

Objective: Selective serotonin (5-HT) reuptake inhibitors, such as citalopram, show beneficial effects in anxiety disorders (e.g. panic and generalized anxiety) and are approved for these disorders in many countries. The S-(+)-enantiomer escitalopram mediates citalopram's 5-HT reuptake inhibitory potency, exemplified by the in vivo ED_{50} values for potentiation of 1-5-HTP-induced head twitches in rats: 2.5 and >97 mol/kg, respectively. This study assessed escitalopram's anxiolytic potential in two models of anxiety.

Method: The two models of anxiety included: two-compartment black and white box models in mice and rats; and the footshock-induced ultrasonic vocalisation (USV) model in adult rats. The black and white box protocol models aspects of generalised anxiety. USV reflects aspects of panic anxiety.

Results: In the rat, escitalopram showed a significant anxiolytic-like profile in the two-compartment black and white box model over a broad dose range (0.0003–0.3 mol/kg). Similarly, escitalopram produced a significant anxiolytic-like effect in the mouse black and white box model. Escitalopram abolished USV (ED_{50} = 1.6 mol/kg). R-citalopram was inactive or showed only weak activity in these models.

Conclusions: Escitalopram produces potent anxiolytic-like effects in animal models of generalised anxiety and panic anxiety. Moreover, escitalopram accounts for citalopram's anxiolytic activity.

NR560 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Quetiapine Reduces the Gene Expression of P75NTR and Promotes Cell Survival

Ou Bai, Ph.D., *Department of Psychiatry, University of Saskatchewan, 103 University Drive, Saskatoon, SK S7N 0W8, Canada*; Hong Qing, Ph.D., Xin-Min Li, M.D.

Summary:

Although the atypical antipsychotic agent quetiapine is widely used to ameliorate symptoms of schizophrenia, the exact mechanisms underlying its therapeutic efficacy remains unknown. Recent studies indicate that apoptosis may be involved in the pathophysiology of schizophrenia. The p75NTR (p75 neurotrophin receptor) can mediate the apoptosis of neurons when expressed in the absence of Trk receptors. In a recent study, we investigated the effects of quetiapine on p75NTR and cell survival. PC12 cells were treated with differing concentrations of quetiapine. The changes in p75NTR mRNA were determined by northern blot analyses. MTT assays were used to assess cell survival after NGF and serum withdrawal. These results demonstrate that (1) quetiapine downregulates the expression of p75NTR mRNA in dose and time-depended patterns, and (2) quetiapine protects differentiated PC12 cells from apoptosis. The effects of quetiapine on gene expression of p75NTR and cell survival indicate that the mechanisms of quetiapuine may potentially be involved in neuroprotection.

NR561 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

A Prospective Treatment Study of Inteferon-Induced Depression in Hepatitis C

Peter Hauser, M.D., *Department of Psychiatry, Portland VAMC, P O Box 1034, B3MHDC, Portland, OR 97207*; Harvinder Aurora, M.D., Jaswinder S. Khosla, M.D., Mangla S. Gulati, M.D., Mitchel A. Kling, M.D., Susan Reed, N.P.

Summary:

Although symptoms of depression are among the most common side effects of alpha interferon (IFN-α) therapy, there have been no systematic neuropsychiatric studies prior to and following implementation of IFN-α therapy in patients with hepatitis C and the incidence of IFN-α-induced major depressive episodes (MDD) remains unknown. Furthermore, there have been no prospective studies that have assessed the efficacy of antidepressants in IFN-α-induced MDD. The purpose of this study is to determine the frequency of MDD in patients treated with IFN-α and, in those patients who develop MDD secondary to IFN-α therapy, to medicate them with the antidepressant citalopram. After signing in-

formed consent to participate in our study, patients with hepatitis C were administered a structured psychiatric interview (SCID) and depression symptom rating scale (Beck depression inventory or BDI) prior to starting IFN-α. Fifty patients without evidence of a current psychiatric disorder and with BDI scores less than 10 were enrolled. Patients were followed weekly using the BDI once IFN-α was begun. If patients BDIs were 18 or greater, they were reevaluated and patients who met criteria for MDD were treated with citalopram. Of the 38 patients who have been on at least two months of interferon therapy, 12 (32%) met criteria for MDD. Eighty-three percent (10/12) of patients with MDD responded to citalopram (BDI less than 10) within the dosage range of 20 to 60 mg. Only one patient was required to discontinue IFN-α therapy. The results of our prospective study suggest that MDD is a common side effect of IFN-α therapy in nonpsychiatrically ill patients with hepatitis C. However, the vast majority of these patients with IFN-α-induced MDD respond to citalopram treatment, thus allowing them to complete a full course of IFN-α therapy.

NR562 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Risperidone Treatment for Combat-Related PTSD

George Bartzokis, M.D., *Department of Psychiatry, UAMS, 4301 West Markham Street, Slot 554, Little Rock, AR 72205*; Thomas W. Freeman, M.D., Vince Roca, Ph.D.

Summary:

Reported here are the initial results from a double-blind, placebo-controlled, parallel-group, single-site trial to evaluate the efficacy and safety of risperidone, a novel antipsychotic, in veteran patients with chronic combat-related posttraumatic stress disorder (PTSD) who were referred to a residential PTSD treatment program. A baseline evaluation and titration of the medication was accomplished while the subjects participated in the month-long residential program. Upon discharge, subjects received an additional three months of outpatient treatment with placebo or 3 mg/day of risperidone. A total of 73 subjects were enrolled and 70 were randomized. The data from the 48 subjects who completed the entire four-month study were analyzed (22 were on risperidone and 26 on placebo). Risperidone was well tolerated: only four subjects discontinued the study due to complaints of side effects (two on risperidone and two on placebo). The principal dependent measures were the total score on the Clinician-Administered PTSD Scale (CAPS), and its three subscores (B; re-experiencing, c; Avoidance, d; Arousal scores). Secondary measures were anxiety (HAM-A), and depression (HAM-D). Data were analyzed using analysis of covariance, with baseline scores as the covariate and medication condition as the independent variable.

There were significant medication differences on the CAPS total ($F = 5.89$, $p = .019$) and CAPS-D subscale ($F = 9.01$, $p = .004$). Medication effects on the CAPS-B ($F = 3.83$, $p = .06$) and CAPS-C ($F = 1.0$, $p = .32$) subscales were not statistically significant (all $df = 1, 45$). Outcome mean scores were lower (i.e., better) on all CAPS measures in the treated group. Medication did not significantly affect depression (HAM-D, $F = 2.25$, $df = 1, 37$, $p = .14$). However, there was a highly significant medication effect on anxiety (HAM-A, $F = 10.03$, $df = 1, 37$, $p = .003$).

NR563 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Frequency of Neurological Side Effects with Atypical Antipsychotics and Haloperidol: Results from the EIRE Study

Paz Gonzalez, M.D., *Department of Psychiatry, University of Oviedo, Julian Claveria 6, #3, Oviedo 33006, Spain*; Julio B. Bobes, Ph.D., Margarida Garcia, Psy.D., Javier Rejas, M.D., Fernando Rico-Villademoros, M.D., Alberto Porras-Chavarino, Ph.D., Gonzalo Hernandez, M.D.

Summary:

Objective: The aim of this study was to assess the frequency and management of neurological side effects with risperidone, olanzapine, quetiapine, and haloperidol.

Methods: A cross-sectional, multicenter study was carried out by 61 spanish psychiatrists (The EIRE Collaborative Group). Outpatients meeting DSM-IV criteria for schizophrenia and taking a single antipychotic for at least four-weeks were consecutively entered into the study. Evaluations comprised demographic and clinical characteristics, CGI-severity scale, and a modified-UKU that included an ad-hoc question to evaluate side-effects management.

Results: A total of 636 evaluable patients (out of 669 recruited) were assessed. The average doses were those seen commonly in the clinical setting: 5.3 mg/d (RIS), 13.5 mg/d (OLAN), 360.5 mg/d (QUE) and 10.6 mg/d (HAL). The frequency of neurological side effects is shown in the table below. Concomitant use of antiparkinsonian drugs was significantly greater with haloperidol (55.7%) and risperidone (24.8%) as compared with olanzapine (8.3%) and quetiapine (7.0%). The most frequent action taken to manage this side effect was the use of antidote followed by dose-reduction.

	HAL(n=131) %	OLAN(n=228) %	QUE(n=43) %	RIS(n=234) %
Akathisia	36.8	11.4[a,b]	2.6[a,b]	19.7[a]
Dystonia	12.3	5.3[a]	2.6	4.1[a]
Rigidity	34.4	9.7[a,b]	7.9[a]	18.0[a]
Hypokinesia/akinesia	47.2	26.0[a,b]	25.0[a]	35.0[a]
Hyperkinesia	8.3	1.9[a]	7.9	3.2[a]
Tremor	48.4	14.2[a,b]	15.8[a]	25.3[a]

[a] χ^2 :$p<0.05$ vs haloperidol; [b] χ^2 :$p<0.05$ vs risperidone.

Conclusion: Neurological side effects are highly frequent with haloperidol and to a much lesser extent with risperidone. These effects required an action in a substantial number of subjects.

This study was nonducted on behalf of the EIRE Collaborative Group

NR564 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Frequency of Obesity in a Spanish Schizophrenic Patient Under Antipsychotics: Results from the EIRE Study

Margarida Garcia, Psy.D., *Biometrica, Aristides Maillol 15, Barcelona 08028, Spain*; Julio B. Bobes, Ph.D., Javier Rejas, M.D., Fernando Rico-Villademoros, M.D., Alberto Porras-Chavarino, Ph.D., Gonzalo Hernandez, M.D.

Summary:

Objective: The aim of this study was to assess the frequency of obesity in a Spanish schizophrenic population treated with atypical antipsychotics and haloperidol.

Methods: A retrospective, cross-sectional, multicenter study was carried out by 61 Spanish psychiatrists (The EIRE Collaborative Group) in 636 evaluable, consecutive, outpatients meeting DSM-IV criteria for schizophrenia and treated with risperidone (RIS, n = 234), olanzapine (OLAN, n = 228), quetiapine (QUE, n = 43), and haloperidol (HAL, n = 131) for at least four weeks. Demographic and clinical characteristics were collected.

Results: The average doses of antipsychotics were: 5.3 mg/d (RIS), 13.5 mg/d (OLAN), 360.5 mg/d (QUE) and 10.6 mg/d (HAL). Out of 636 patients, 96 (15.2%) were obese, with no gender differences; 15% for males and 15.4% for females, but remarkably higher than the prevalence for corresponding normative Spanish population: 7.8%, 7.3%, and 8.4%, respectively. The table below shows the percentage of obesity according to type of therapy at baseline and at present:

	HAL(n=131)[a]		OLAN(n=228)[a]		QUE(n=43)[b]		RIS(n=234)[a]	
Weight Category by BMI	Baseline	Actual	Baseline	Actual	Baseline	Actual	Baseline	Actual
Normal weight (<25)	42,7%	35,7%	52,9%	37,4%	54,8%	52,4%	53,5%	41,6%
Overweight (≥25 & <30)	46,8%	46,5%	39,5%	46,3%	31.0%	33,3%	37,4%	45,5%
Obese (≥30)	10,5%	17,8%	7,6%	16,3%	14,3%	14.3%	9,1%	12,8%

[a] McNemar :p<0.000; [b] :p= not significant

Conclusion: Obesity was highly frequent within Spanish Schizophrenic under antipsychotic therapy, without differences according to gender. Obesity frequency was no different according to type of therapy, but all of them except quetiapine showed a significant weight gain although duration of treatment was much shorter.

This study was conducted on behalf of the EIRE Collaborative Group.

NR565 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Pramipexole in Treatment-Resistant Depression: A 16-Week Naturalistic Study

Lorenzo Lattanzi, M.D., *Department of Psychiatry, University of Pisa, Via Roma 56, Pisa I-56100, Italy*; Paolo Cassano, M.D., Liliana Dell'osso, M.D., Stefano Pini, M.D., Alfredo Gemignani, M.D., Annalisa Bassi, M.D., Giovanni B. Cassano, M.D.

Summary:

Objective: The aim of this study was to assess the tolerability and antidepressant efficacy of adjunctive pramipexole, a D_2-D_3 dopamine agonist, in patients with drug-resistant depression.

Methods: Inpatients with major depressive episode [MDE] (DSM-IV) and absolute drug resistance were recruited. Pramipexole was added to antidepressant treatment, at increasing doses from 0.375 to 1.0 mg/day. MADRS and CGI scales were administered at baseline, week 2,4,8,12,16. Two independent response criteria were adopted: a >50% reduction of MADRS total score and a score of 1 or 2 on CGI-I at endpoint. Side effects were assessed by DOTES.

Results: A total of 29 patients (17 bipolar) were included (21 women; mean age 52.9 years). Current MDE was lasting from 21.7 months. Mean dose of pramipexole was 0.95 ± 0.35mg/day. Mean follow-up was 12.5 ± 5.1 weeks. Mean scores on MADRS decreased from 34.5 ± 7.3 at baseline to 4.6 ± 11.5 at endpoint ($p < 0.001$) and CGI-S decresed from 4.6 ± 0.8 at baseline to 2.8 ± 1.3 at endpoint ($p < 0.001$). At endpoint, 65.5% (19/29) of patients were responders on MADRS and 75.9% on CGI-I. Five out of the 29 patients, discontinued pramipexole for adverse events.

Conclusions: These preliminary data suggest that pramipexole adjunction to antidepressant treatment may be effective and well tolerated in patients with resistant depression.

Practitioners involved with treatment of resistant depression.

NR566 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Effects of ECT on Behavior of Psychiatric Inpatients with Different Diagnoses

Mustafa K. Saadani, M.D., *Department of Psychiatry, King Khalid N.G. Hospital, P O Box 9515, Jeddah 21423, Saudi Arabia*; Ahmed Saad, M.D., Mona Mansour, M.D., Abdelnaser Omar, M.D.

Summary:

Background: Electroconvulsive therapy (ECT) is an effective agent in improvement of psychotic symptoms.

Method: The behavior of 244 patients with different psychotic diagnoses (per ICD-10 criteria) before and after ECT was assessed with the Behavioural Observation Schedule (BOS).

Results: Improvement in behavior after ECT was significant for all diagnoses: recurrent depression ($z = 5.71$), schizophrenia ($z = 8.51$), mania ($z = 5.68$), bipolar affective disorder ($z = 3.30$), single depressive episode ($z = 2.80$), schizoaffective disorder ($z = 4.11$), delusional disorder ($z = 2.67$), and puerperal psychosis ($z = 2.02$). There was no significant relationship between the improvement of behavior after ECT and different demographic variables.

Conclusions: ECT has a significant improving effect on psychotic behavior regardless of patient diagnosis. Moreover, the clinical improvement in behavior after ECT does not change in relation to different demographic variables.

NR567 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Peak Heart Rate During ECT Seizures: Reflections on Clinical Efficacy

Conrad M. Swartz, M.D., *Department of Psychiatry, Southern IL University, P O Box 19642, Springfield, IL 62794-9642*

Summary:

Objective: A goal for monitoring ECT seizure is stimulus dose regulation, analogous to drug dose regulation by blood drug concentration. Useful blood drug concentrations must reflect both efficacy and drug dose. Analogous ECT monitoring should reflect both efficacy and electrical dose. A previous study found that peak HR increases with electrical dose.

Method: For 24 drug-free acute ECT patients, the relationship between length of ECT course and average peak HR relative to individual maximum peak HR was examined. Left frontal to right temporal stimulus electrodes were used.

Results: Fewer ECT sessions were needed by patients who maintained peak HRs closer to their maximum ($r = 0.74$; two-tailed $t = 5.20$, $p = 0.00003$). The minimum course length of six ECT sessions was received by 14 patients; their peak HRs averaged 6.5 (SD = 3.5) bpm below maximum. For the 10 patients who received more ECT sessions, peak HR averaged 18.1 (SD = 10.3) bpm below maximum. This 178% difference was highly significant (one-tailed $t = 3.94$, $df = 22$, $p = 0.00035$). Minimum course patients showed lower post-ECT severity (1.3, SD = 0.6) than other patients (1.8, SD = 0.8; one-tailed $t = 1.42$, $df = 22$, $p = 0.08$), on a 1 to 5 masked global rating.

Conclusions: Peak HR should be clinically useful in stimulus dose regulation. The large effect size suggests that the site of ECT therapeutic effect is near the medullary cardioacceleratory area.

NR568 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Repetitive Transcranial Magnetic Stimulation as Primary Monotherapy in Major Depression

Rainer Rupprecht, M.D., *Department of Psychiatry, University of Munich, Nussbaumstrasse 7, Munich 80336, Germany*; Peter Zwanzger, M.D., Cornelius Schuele, M.D., Thomas C. Baghai, M.D., Patrick Mikhaiel, M.D., Robin Ella, M.D., Frank Padberg, M.D.

Summary:

Objective: In the majority of prior rTMS studies in major depression, rTMS was either used as add-on treatment or applied in pharmacotherapy-refractory patients. Moreover, the relationship

between the individual responses to rTMS and other non-pharmacological antidepressant interventions has not been characterized. In the present study, we therefore investigated the therapeutic efficacy of rTMS monotherapy as primary treatment and to what extent sleep deprivation (SD) may predict the clinical response to rTMS.

Method: Thirty-one patients suffering from a major depressive episode were treated for 10 days using left prefrontal 10-Hz rTMS at 100% motor threshold intensity. All patients were free of psychotropic medication for at least 1 week prior to and during rTMS.

Results: After rTMS patients showed an overall significant clinical improvement (30% reduction in Hamilton Rating Scale for Depression [HRSD] score). 42% of patients responded to rTMS with at least a 50% reduction of HRSD scores. In responders, the response remained stable during consecutive antidepressant pharmacotherapy. No positive association between the individual responses to rTMS and SD was observed.

Conclusion: rTMS monotherapy exhibits clinically significant antidepressant effects that warrant further investigation. SD, however, does not appear to be a useful predictor for the outcome of rTMS treatment.

NR569 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Use of Divalproex Sodium Extended-Release Tablets in Bipolar Affective Disorder

John F. Delaney, M.D., *Department of Psychiatry, West Pennsylvania Hospital, 4815 Liberty Avenue, Suite 123, Pittsburgh, PA 15224*; Rose Hammond, D.P.H.

Summary:

Objective: To evaluate the extended release form of divalproex sodium in bipolar affective disorder.

Method: Ten patients with the diagnosis of bipolar affective disorder who had been stabilized by the use of divalproex sodium in the past were chosen to determine if the extended release form of the drug would provide adequate blood levels with once-a-day dosing. These patients ranged from 18 to 55 years of age and had the diagnosis made at least three years prior to the start of the study. All patients were stabilized on divalproex sodium of at least 1000mg in divided doses. The study was designed so that patients would have a baseline valproic acid level and then be switched to the extended release form of divalproex sodium. After two weeks a clinical interview was conducted and another blood level was drawn. Symptoms of mood instability including hypomania and depression were evaluated. After one month patients were again seen for a brief clinical visit and blood levels were drawn again.

Results: All patients in this study showed no real difference in terms of their symptoms. All patients had a slight decrease in valproic acid levels with the extended release product but only one had to have an adjustment by increasing the dose.

Conclusion: The use of the extended release form of divalproex sodium has demonstrated good clinical efficacy and represents a significant improvement over multiple daily doses.

NR570 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Cingulate Activity as a Possible Predictor of Repetitive Transcranial Magnetic Stimulation Treatment Outcome

Peter Eichhammer, M.D., *Department of Psychiatry, University of Regensburg, Universitaetsstrasse 84, Regensburg 93053, Germany*; Alexander Kharraz, M.D., Rainer Wiegand, M.D., Goran Hajak, M.D.

Summary:

Objective: Prefrontal cortex and paralimbic activity appear to be involved in the action of repetitive transcranial magnetic stimulation (rTMS) as an antidepressant (Teneback et al., 1999). The present study was designed to investigate the role of cingulate activity as a predictor of rTMS treatment outcome.

Methods: 15 patients with a DSM-IV diagnosis of a pharmacologic treatment sensitive major depression were scanned by ECD (99m Tc)-BICISATE (NeuroliteR)-SPECT immediately before and then 3 days after 2 weeks of daily rTMS treatment. All patients enrolled had a fixed antidepressive medication during the treatment period. HAMD and MADRS ratings were obtained at baseline and at end of the study.

Results: TMS antidepressant responders showed a significantly lower cingulate activity at baseline then nonresponders ($p = 0.018$). Moreover, all depressive patients with psychotic features were nonresponders to TMS.

Conclusions: In line with Teneback et al., TMS seems to act preferentially on paralimbic regions. Activity in the cingulate appears to differ between treatment responders and nonresponders to TMS and additionally between depressive patients with and without psychotic features.

NR571 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Association Between Anxiety and Remission from Depression After Acute ECT

Karen A. Snyder, B.S., *Department of Psychiatry, Mayo Foundation, 200 First Street, SW, Rochester, MN 55905*; Martina Mueller, M.S., A. John Rush, M.D., Max Fink, M.D., Teresa A. Rummans, M.D., Rebecca S. Knapp, M.D., Melanie Biggs, Ph.D., Charles H. Kellner, M.D., Mustafa Hussain, M.D., Georgios Petrides, M.D., Keith Rasmussen, M.D., Glenn E. Smith, Ph.D., M. Kevin O'Connor, M.D.

Summary:

Introduction: This study examines the impact of anxiety on the outcome of acute. ECT for major depression.

Method: In the ongoing NIMH-funded, multicenter, randomized trial evaluating continuation ECT versus pharmacotherapy, 253 patients received an index course of bilateral ECT. Patients who remitted and remained remitted for 1 week (interim week) were randomly assigned to the continuation phase. Anxiety was determined using baseline HRSD items #10 (psychic anxiety) and #11 (somatic anxiety).

Results: On item 10, 57% (12/21) of the minimal anxiety group (subscore 0–1) sustained remission through the interim week compared to 47% of the severe anxiety group (subscore 3–4) (chi-square, $p = 0.46$). On item 11, 54% (25/46) with minimal anxiety sustained remission compared to 41% (50/123) with severe anxiety ($p = 0.16$). Among less depressed (HRSD ≤ 32 minus items 10–11), low scores for somatic anxiety were significantly associated with sustained remission ($p = 0.02$). This association did not hold for those having depression scores >32 ($p = 0.37$).

Conclusion: Rates of sustained remission were higher among those with lower baseline anxiety. The relationship between somatic anxiety and sustained remission, while not significant, is suggestive of a trend. This relationship is stronger and statistically significant among patients with less severe depression at baseline compared to patients with more severe depression.

NR572 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

EEG Correlates of Dissociative States: Concurrent Mind and Brain States

Christa Kruger, M.D., *Department of Psychiatry, University of Pretoria, P O Box 667, Pretoria 0001, South Africa* C. Werdie Van Staden, M.D.

Summary:

Objective: Concurrent EEG correlates of experimentally induced dissociative states were studied following suggestions of a relationship between dissociation and EEG background activity. Previous studies, however, could only infer a nontemporal association between a dissociative tendency and neurophysiological parameters, since a measure of dissociative states at the time they present had not yet been developed.

Method: Induced dissociative states were examined for canonical correlations with changing background EEG activity among 11 outpatients with complex partial epilepsy. Dissociative states were induced by hyperventilation, photic stimulation, and staring into a mirror. Dissociative states were measured by the State Scale of Dissociation (SSD) during each of these experimental conditions. Concurrent EEG background activity was examined by spectral analysis.

Results: Canonical analyses yielded the following significant correlations between dissociative states and concurrent EEG activity: amnesia with widespread theta activity; identity alteration with frontal delta activity; identity confusion with widespread fast wave activity; hypermnesia with right mid-temporal activity in all four wavebands; and depersonalization with frontal delta as well as with widespread theta and fast wave activity.

Conclusion: Examining concurrent neurophysiological parameters of dissociative states is an advance on previous studies, which were restricted to examining an association between a dissociative tendency and neurophysiological features.

NR573 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Textual Associations and the Assessment of Semantic Networks in Schizophrenia

Avi Peled, M.D., *Department of Rehabilitation, Sha'ar Menashe Mental Health Center, Mobile Post Hefer, Hadera 38814, Israel;* Itamar Netzer, M.D., Rena Kurs, B.A., Ilan I. Modai, M.D.

Summary:

Background and Objectives: Collins and Quillian (1970) proposed that semantic representations in the human brain could have a "network-like" theoretical construct. Thought disorders in schizophrenia have been described as disturbances in spread of activation (Manschreck et al. 1988) within semantic networks. Semantic networks are typically evaluated indirectly via reaction times of priming tasks. Since medications could affect the reaction time of patients, we sought to investigate semantic networks directly (independent of time) by having patients (and control subjects) rate textual associations in sentences with various degrees of organization.

Methods: Twenty-eight schizophrenia patients and 27 normal control subjects were asked to rate associative relationships between concepts in sentences on a scale from 1 (i.e., total dissociation) to 10 (complete association). The task contained three sets of sentences: organized meaningful sentences, intermediately organized sentences, and completely disorganized sentences (i.e., incomprehensible). To avoid order effects sentences were randomly mixed at presentation.

Results: Compared to control subjects, schizophrenia patients demonstrated increased standard deviations in rating associative values between concepts in the sentences, moreso in disorganized sentences. Inadequate ability to identify and rate associations in disorganized sentences is discussed in the context of disordered semantic networks of schizophrenia patients.

NR574 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Therapeutic Interactive Voice Response for Chronic Pain Relapse Prevention

Magdalena R. Naylor, M.D., *Department of Psychiatry, University of Vermont, 54 West Twin Oaks Terrace, #14, South Burlington, VT 05403*; John E. Helzer, M.D.

Summary:

Objective: To test whether interactive voice response (IVR) can be used to improve adherence to pain coping skills learned in cognitive behavioral therapy (CBT) and prevent the relapses frequently described in the literature.

Method: Ten subjects with chronic pain participated in ten weeks of group CBT followed by four months of Therapeutic Interactive Voice Response (TIVR). Our specially designed TIVR is based on a computerized telephone system in which callers are asked questions and respond using the telephone keypad. It was created to reinforce pain coping skills and provide messages for relaxation, sleep induction, and emotional support that can be accessed by patients on demand.

Results: Within-subjects analysis showed that maximum positive change for nearly all outcome measures occurred at the post TIVR point. For some measures, improvement was significant post TIVR despite the fact they had not been significant after CBT. Statistically significant measures included SF-36 Mental Health Composite Score ($p < .0004$) MPQ pain ($p < .01$), CSQ Catastrophizing ($p < .0006$), TOPS Total Pain Experience ($p < .03$), and Perceived Family/Social Disability ($p < .02$).

Conclusions: Our preliminary results suggest that TIVR can be used to improve coping skills adherence and prevent relapse in chronic pain. We predict TIVR could also reduce health care utilization.

NR575 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Prolonged Time Lapse in Repeated Rubber Hand Illusion in Schizophrenia

Shmuel Hirschmann, M.D., *Open Ward B, Shaar Menashe Mental Health Center, Mobile Post Hefer, Hadera, IL 38814, Israel*; Claudia Lamstein, M.D., Ilan I. Modai, M.D., Michael Ritsner, M.D., Avi Peled, M.D.

Summary:

Background: The rubber hand illusion (RHI) is a tactile sensation referred to an alien limb. RHI has been explained by a spurious reconciliation of visual and tactile inputs reflecting functional connectivity in the brain and was used to explore alterations of functional connectivity in patients with schizophrenia.

Method: 28 schizophrenia patients and 19 healthy volunteers participated in the study. RHI was achieved with two paintbrushes simultaneously stroking the hand of the subject, hidden from view by a screen, as well as an artificial hand placed within view. After positive report of the illusion, participants were exposed to one of two texts, a neutral nonsense paragraph or a text that negated creation of an illusion. The RHI was repeated and the lapses of time to creation of the illusion as well as its quality were compared to the initial RHI.

Results: Negative context did not influence the creation of illusion. A significant shortening of RHI time was reported in healthy volunteers but not in schizophrenia patients (healthy control subjects: time 1 = 121.8 sec [SD = 80.0], time 2 = 52.3 sec [SD = 62.3]; $t = 3.1$, $p = 0.006$; schizophrenia patients: time 1 = 75.5 sec [SD = 66.4], time 2 = 86.2 [SD = 90.0]; $t = -0.66$, $p = 0.052$).

Conclusions: The disorder in the learning processes related to illusion in schizophrenia patients may indicate disturbances in functional brain connectivity, bypassing motor dysfunction.

NR576 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Effects of Psychotherapy for Personality Disorders

Ludwig Teusch, M.D., *Department of Psychiatry, EV University, Grutholzallee 21, Castrop-Rauxel, D 44577, Germany*; Hildegard Boehme, Jobst Finke, M.D., Markus T. Gastpar

Summary:

Background: There is increasing interest in data about the efficacy of psychotherapeutic strategies alone or when combined with medication in the treatment of patients with personality disorders.

Methods: The efficacy of an inpatient client-centered treatment program (CCT) was studied prospectively in 142 patients with personality disorders and additional depressive, anxiety, or eating disorders (ICD-10).

Results: Significant changes (e.g., in mood, self-esteem, and social adjustment) were achieved up to discharge and remained stable at 1-year follow-up. The efficacy with regard to individual variables or the total result could not be enhanced by a combination with psychopharmacological treatment (CCT+MED; N = 46), mainly antidepressants. Within the subgroups of patients with socially deviant (F60.0–2), emotionally unstable/borderline (F60.3) and histrionic/narcissistic personality disorders (F60.4, F60.8), CCT was significantly superior in the reduction of depression (BRMES-ratings), whereas the response was enhanced by medication in the subgroup of patients with socially dependent "cluster C"-personality disorders (F60.5–7).

Conclusions: The results are discussed with regard to client-centered therapeutic concepts and the further development of differential combination strategies.

NR577 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Switching to Olanzapine Treatment in Naturalistic Community Care

Douglas Noordsy, M.D., *Department of Psychiatry, Dartmouth College, 1555 Elm Street, Manchester, NH 03101*; Christopher O'Keefe, M.A., Thomas Liss, B.S.

Summary:

Objective: To evaluate outcomes of the decision to switch to olanzapine treatment in a CMHC setting.

Methods: This report presents 12-month outcomes of 105 patients switched to olanzapine and 49 patients remaining on conventional antipsychotics.

Results: The olanzapine group demonstrated significant improvement at 12 months compared with baseline across multiple measures of symptoms, side effects, and psychosocial function. The olanzapine group was more symptomatic and functionally impaired at baseline and demonstrated significantly greater improvement in symptoms and side effects burden at 12 months. Psychosocial outcomes for the olanzapine group were significantly improved compared with baseline. The olanzapine group had significantly lower rates of sheltered employment and higher rates of competitive employment post-baseline relative to their previous three-year trend. There was a trend toward the olanzapine group demonstrating a greater rate of improvement in medication follow-through than the reference group. The olanzapine group also demonstrated significantly greater reductions in partial hospital and hospital services.

Conclusions: Olanzapine is effective in managing markedly to severely ill patients with psychotic disorders in a CMHC setting. The rate of improvement in psychosocial outcomes for the olanzapine group was equal or superior to the reference group despite being comprised of more severely ill patients.

This project was funded by a grant from Lilly Research Laboratories.

NR578 Wednesday, May 9, 12:00 p.m.-02:00 p.m.

Symptom-Specific Group Therapy for Medicated Inpatients with Schizophrenia

Anne-Marie Shelley, Ph.D., *Bronx Psychiatric Center, 1500 Waters Place, Ward 18, Bronx, NY 10461*; Joseph Battaglia, M.D., Jeffrey Lucey, M.D., Albert Ellis, Ph.D., Lewis A. Opler, M.D.

Summary:

Objectives: To examine whether medicated chronic schizophrenic inpatients show improvements when a cognitive-behavioral symptom-specific group therapy (SSGT) program is added to standard pharmacotherapy and routine clinical care.

Methods: 25 patients were assessed on the Positive and Negative Syndrome Scale (PANSS). Problem symptoms were matched to appropriate treatment groups including positive symptoms, negative symptoms, attention, and affect regulation. Patients received three to five sessions of group per week (total of 50–100 sessions), re-assessed on the PANSS, and compared with a control group of 23 inpatients, receiving pharmacotherapy and routine clinical care only.

Results: Patients receiving SSGT showed a 22% decrease in total symptom severity on the PANSS. The improvement occurred on the positive, negative, and general symptom scales, and on four of the five PANSS factors: negative symptoms, dysphoric mood, activation, and autistic preoccupation. Controls did not show a change from baseline.

Conclusions: Both the study and control groups were receiving medication plus routine care, and had symptoms in the mild to moderate range. The results suggest that improvement in symptoms with pharmacotherapy plateaus. The addition of symptom-specific groups using cognitive-behavioral and psychoeducational methods leads to further significant improvements. The treatment groups of our program have been manualized, and we are planning a double-blind, random allocation study.

NR579 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Paroxetine Versus Multimodal Behavior Therapy in the Treatment of Trichotillomania: A Pilot Study

Annett Neudecker, *Department of Psychiatry, University of Hamburg Hospital, Martinistrasse 52, Hamburg 20246, Germany*; Michael Rufer, M.D., Iver E. Hand, M.D., Rocco M. Zaninelli, M.D.

Summary:

Objective: To compare the SSRI paroxetine and multimodal behavior therapy as treatments for trichotillomania.

Method: Patients with trichotillomania as defined by DSM-IV criteria were recruited into this pilot study, and chose either multimodal behavior therapy (MBT) or treatment with the SSRI paroxetine. MBT patients had 45 weekly individual outpatient sessions, paroxetine patients were treated with 20 to 60 mg daily for 12 weeks and received bi-weekly supportive contacts. At the baseline and endpoint assessments, severity of hairpulling was determined with the Psychiatric Institute Trichotillomania Scale (PITS). Comorbid psychiatric symptomatology was measured using the Beck Depression Inventory (BDI), Yale-Brown Obsessive Compulsive Scale (Y-BOCS), and the German-language Social Insecurity Scale (SIS).

Results: Of the 40 patients enrolled (39 female, 1 male), 20 patients entered each treatment group. Four patients in the MBT group and two patients in the paroxetine group discontinued treatment prematurely. The mean PITS score at baseline was 20 (SD = 4); 60% of the patients had a BDI score >11, and 63% demonstrated high social insecurity on the SIS. At the posttreatment assessment the PITS score was reduced by 45% in both groups. There was also a significant decrease in the mean BDI score for

both treatments (MBT: –46%, $t = 3.7$, $p < 0.01$; paroxetine: –20%, $t = 2.5$, $p < 0.05$) The mean Y-BOCS score was 3.2 at baseline and 2.6 at study end. MBT patients showed a greater improvement in the social skills component of the SIS. The mean paroxetine dose after 12 weeks was 38 mg.

Conclusions: Both MBT and paroxetine treatment led to a significant reduction in the symptoms of trichotillomania. Interestingly, the patients in this study did not manifest severe OCD symptoms.

NR580 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

DSM-IV: Self-Evaluation by Psychiatrists

Rael D. Strous, M.D., *Department of Psychiatry, Beer Yaakov Mental Health Center, P O Box 1, Beer Yaakov 70350, Israel*; Rafael Stryjer, M.D., Yehuda Baruch, M.D., Dana Ofir, M.D., Raya Lapidus, M.D., Faina Bar, M.D., Mordechai Weiss

Summary:

Conjecture suggesting a high incidence of mental illness among psychiatrists is based on hearsay with limited substantiating evidence. However, studies investigating mental illness in psychiatrists have struggled to address the presence of DSM-IV syndromal illness. Psychiatrists attending an educational symposium were instructed to complete anonymously a self-evaluation questionnaire in which they were asked to self-diagnose and indicate the presence of DSM-IV illness according to axis I syndromes and axis II traits. 110 responses were received (response rate: 52.1%). Overall, 90% of respondents indicated the presence of at least one syndrome or trait according to a 5-point Likert scale of severity. The most common disorders on axis 1 and axis 2 were "mood disorder" and "narcissistic traits," respectively, with the least common being "psychotic disorder" and "schizotypal traits." Female psychiatrists reported more impairment, particularly among axis I disorders. The number of axis I and axis II disorders reported decreased with subjects' age. Psychiatric disorders as self-diagnosed according to DSM-IV criteria may manifest with a high prevalence in psychiatrists. Our findings suggest the need for a greater sensitivity to the mental health of psychiatrists and may be of importance in encouraging the implementation of special programs in training and ongoing occupational support.

NR581 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Long-Term Donepezil in Affective Illness

Frederick M. Jacobsen, M.D., *Department of Psychiatry, George Washington University, 1301 20th Street, NW, Suite 711, Washington, DC 20036-6023*; Lillian Comas-Diaz, Ph.D.

Summary:

Objectives: Determine in a naturalistic follow-up study the long-term utility, tolerability, and safety of the acetylcholinesterase inhibitor donepezil for treatment of memory loss, dry mouth, and constipation in affectively ill patients as well as donepezil's effects on the course of affective illness.

Methods: Non-demented bipolar/unipolar outpatients took donepezil 2.5–10 mg/day for >6 months. A retrospective chart review with ratings for memory dysfunction, sleep, mood stability, and CGI scale was conducted for patients who had undergone monthly clinical monitoring. Contributory factors to cognitive dysfunction, affective stability, and drug interactions were assessed.

Results: Preliminary findings for 32 patients (21 women, 11 men; mean age = 47.8 ± 9.4 years) taking donepezil (6.3 ± 3.0 mg) for 17.8 ± 10.7 months indicated that most continued to benefit from treatment. Major side effects were diarrhea and insomnia. Insomnia and hypomania were lessened by morning administration and dose reduction. Most patients who reported diminishing memory effects over time had first-degree relatives with Alzheimer's disease. Longitudinal data on memory dysfunction and mood will be presented.

Conclusions: In affectively ill patients complaining of psychotropic-associated memory loss, long-term treatment with donepezil appears beneficial and well tolerated. Diminishing memory benefits may signal a heritable progressive decline in cholinergic function.

NR582 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

The Geography of Psychiatric Education in the U.S.

William R. Yates, M.D., *Department of Psychiatry, University of Oklahoma at Tulsa, 4502 East 41st Street, Tulsa, OK 74135*; Ted R. Yates

Summary:

Objectives: The equal distribution of psychiatrists in the U.S. contributes to mental health access problems. The objective of this study is to examine the correlation between the geographic distribution of first-year psychiatry residency positions and the geographic distribution of psychiatrists in the U.S.

Method: Variables for this study were abstracted from multiple public information resources including the 2000 U.S. Census, state health profiles from the Health Services Resource Administration (DHHS), and the AMA Graduate Medical Directory. Statistical analysis included non-parametric rank order comparisons using Statview software. Geographic analysis included use of ArcView and ArcInfo software.

Results: The distribution of psychiatrists in the U.S. varied from a low of 4.7 per 100,000 population (Idaho) to a high of 43.5 psychiatrists per 100,000 population (District of Columbia). First-year psychiatry residency training positions also varied widely from 0 per 1,000,000 population (multiple states) to 35.0 per 1,000,000 population (District of Columbia). Psychiatrist distribution correlated highly with first-year positions (Spearman rank order correlation Rho = .50, $p < .0001$).

Conclusions: This study finds a significant correlation between the geography of first-year psychiatry residency positions and practicing psychiatrists. Future public policy decisions about the psychiatric physician workforce and number of psychiatric residency positions should consider these geographic factors.

NR583 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Reboxetine Treatment of Depressed Patients with HIV Infection

Adriana Schoffel, M.D., *Department of Psychiatry, UFRGS, Padre Chagas 147/905, Porto Alegre, RS 905-70080, Brazil*; Paulo Abreu, Ph.D., Alessandra Spode, Joel Correa

Summary:

Objective: We examined the efficacy of reboxetine in an open 12-week trial of HIV-seropositive outpatients with major depressive disorder.

Method: Thirteen HIV-seropositive patients with DSM-IV major depressive disorder were treated with 8 mg/day of reboxetine for 12 weeks. The depression symptoms were assessed with the Montgomery-Asberg Depression Rating Scale (MADRS) at weeks 2, 4, 6, 8, 10 and 12.

Results: Of 13 patients receiving reboxetine, three discontinued treatment (one for developing bipolar disorder). Of the 10 patients who completed the trial, nine (90%) were classified as full responders with more than a 70% reduction in MADRS score, and one (10) was classified as a nonrespondent. The symptoms reduced 50% by the fourth week. The most common adverse effects were insomnia and sweating.

Conclusions: Depressed HIV-seropositive outpatients respond to reboxetine comparably to other outpatient populations. This

suggests that reboxetine may have a role in the treatment of depression in HIV-seropositive patients and appears to be well-tolerated. Symptoms will reduced by 50% after 4 weeks.

NR584 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Assessment of the Impact of Lipodystrophy Syndrome on the Quality of Life in HIV-1 Infected Patients

Araceli Rousaud, *ICPP, Hospital Clinic, Villarroel 170, Barcelona 08036, Spain*; Jordi Blanch, M.D., Josep M. Gatell, Ph.D., Esteban Martinez, Ph.D., Josep M. Peri

Summary:

Introduction: Present antiretroviral therapy has given longer survival for HIV-infected patients; but it has also brought new important problems such as the lipodystrophy syndrome (LDS). The objective of our study was to assess the impact of LDS on quality of life.

Methods: Cross-sectional, nonrandomized, open-label, observational study was performed assessing characteristics, data about HIV-1 infection, and treatment adherence of consecutive outpatients who were clinically stable and were taking HAART for more than one year. Patients with LDS completed the Dermatology Life Quality Index (DLQI) for measuring impact of body image changes in quality of life.

Results: Of 150 interviewed patients, 79 (51 men and 28 women) fulfilled criteria for LDS. Only self-reported physical status was significantly ($p = 0.009$) better in patients without LDS. Patients with LD were taking HAART for more time ($p = 0.009$). Dimensions of quality of life belonging to perceptions, daily activities, and treatment were the most influenced by body changes. Impact on DLQI was higher in women than men in dimensions belonging to perceptions ($p = 0.004$), daily activities ($p = 0.009$), and interpersonal relationship, specifically sexuality ($p = 0.033$). Intravenous drug users presented a greater impairment than non-IVDU in dimensions related to perceptions (0.009), free-time activities ($p = 0.010$), and total score (0.011).

Conclusions: Women and IVDU suffered a greater impact in their DLQI due to LDS than men and non-IVDU, respectively.

NR585 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Axis I and II Psychiatric Disorders Among Patients at a Sexually Transmitted Disease Clinic

Heidi E. Hutton, Ph.D., *Department of Psychiatry, Johns Hopkins School of Med, 600 North Wolfe Street, Meyer 4-119, Baltimore, MD 21287-7413*; Constanine G. Lyketsos, M.D., Jonathan Zenilman, M.D., Emily J. Erbelding, M.D.

Summary:

Background: Sexually transmitted disease (STD) clinic patients are at high risk for HIV infection and are a major focus of HIV prevention. Because untreated psychiatric disorders, including substance abuse, may significantly compromise the success of HIV risk-reduction interventions, we estimated the prevalence of these disorders in STD clinic patients. In such HIV at-risk populations, little data exist on psychiatric disorders and STDs.

Methods: A systematic sample of patients presenting to a publicly-funded STD clinic were recruited for participation in a study on mood disorders and STD risk behaviors. Seventy-two patients consented to the Structured Clinical Interview for DSM-IV.

Results: Thirty-nine percent (28/72) suffered from current Axis I psychiatric disorders. Of these, seven (25%) met criteria for mood disorder; 13 (18.1%) met criteria for substance dependence. Twenty-nine percent (21/72) presented with a personality disorder. Antisocial personality disorder was found to be highly prevalent among males (9/34; 25%). Ten percent of the total sample had severe symptoms to warrant urgent referral for psychiatric evaluation.

Conclusion: Psychiatric and other substance use disorders are common among patients in a STD clinic, and may significantly limit the success of standard HIV risk reduction. STD clinics may serve as important sites for psychiatric case identification.

Source of Funding: NIH Award 1 RO1MH6066-01A1; PI: Emily Erbelding, MD

NR586 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Bupropion Sustained Release Treatment of Depression in HIV-Positive and AIDS Patients

M. Beatriz Currier, M.D., *Department of Psychiatry, University of Miami, PO Box 016960, Miami, FL 33101*; German Molina, M.D., Thomas Robertson, Psy.D., Sergio M. Arcey, M.D., Mercy Matos, M.D.

Summary:

Objectives: To date, there have been no prospective studies of bupropion SR among depressed HIV/AIDS patients. The purpose of this study was to 1) evaluate the efficacy and safety of bupropion SR in the treatment of depression among 20 HIV seropositive adult outpatients and 2) determine if clinical variables such as HIV disease staging, chronicity of HIV illness, and chronicity of depression were significantly associated with depression treatment response.

Methods: Outpatients with HIV spectrum illness, ages 18–75 years, with baseline Beck Depression Inventory (BDI) scores > 15, baseline Mini Mental State Exam (MMSE) scores >20, and a SCID-confirmed DSM-IV diagnosis, 7 major depressive disorder with no other axis I active diagnosis were recruited into a 6-week, open-label study of bupropion SR (flexible dose 100–300 mg/day as tolerated). Responders were defined by a Clinical Global Improvement (CGI) score of "much improved" or "very much improved" and a 50% reduction in baseline BDI scores and Hamilton Depression Rating Scale (HDRS-17) scores.

Results: Twenty patients (six women, 14 men, mean age-40.2 years) were treated with bupropion SR 100–300 mg/day. The HIV-sample included asymptomatic, symptomatic, and AIDS patients. Twelve of the patients (60%) responded to bupropion SR at a mean dose of 264 mg/day. Treatment responders had significantly lower CD4 cell counts than the nonresponders; however, other clinical variables such as HIV disease staging, viral load, and chronicity of depression were not significantly associated with depression treatment response. Five patients (25%) discontinued the study secondary to adverse events. Completers reported mild and transient adverse events including headaches, insomnia, and anxiety symptoms.

Conclusions: Preliminary findings suggest bupropion SR is effective for the treatment of depression in HIV/AIDS patients regardless of HIV disease staging. Furthermore, it appears to be well tolerated among patients with AIDS-related medical conditions. Double-blind, placebo-controlled trials are needed to confirm these findings.

NR587 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Impact of a Smoke-Free Policy on Medication Use in a Psychiatric Facility

Norma C. Josef, M.D., *Walter Reuther Hospital, 30901 Palmer Road, Westland, MI 48186-9529*; Venkataramana S. Lingam, M.D., S. Ramalingam, M.D., Cynthia Quince, Pharm.D., Patricia Camazzola, Pharm.D.

Summary:

Cigarette smoking remains the most preventable contributor to health problems, disability, and health expenditures in the United

States. The prevalence of cigarette smoking in the U.S. in 1994 was 25.5% in the normal population and as high as 50% in the psychiatric groups. According to the Centers for Disease Control and Prevention, the approximately four million smoking-related deaths may decrease with the implementation of nonsmoking policies in public facilities. In March 1999, a nonsmoking campus policy was implemented in a midwest state adult psychiatric inpatient facility. Concurrent chart review of 80 identified smoking patients at baseline and 3 and 6 months after policy implementation, collected data on diagnosis, smoker status, cardiovascular and psychotropic medication use, and seclusion/restraints utilization. The results showed that the use of anxiolytic, antidepressant, antipsychotic, cardiac, and bronchodilator medications decreased during the 6 months after policy implementation based on the facility's pharmacy expenditures by as much as 25%. Seclusion/restraints measures remained constant. Based on the limitations of the study, it is difficult to determine if the nonsmoking policy independently caused the results, but it suggests a correlation that merits further exploration.

NR588 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Longitudinal Development of Panic and Other Anxiety Disorders in Patients with Dizziness

Jeffrey P. Staab, M.D., *Department of Psychiatry, University of Pennsylvania, 3400 Spruce Street, 11 Founders Building, Philadelphia, PA 19104*; Michael J. Ruckenstein, M.D.

Summary:

Objective: An association between dizziness and anxiety disorders has been described, but the course of illness is unclear. This study examined predisposing factors and medical-psychiatric etiologies of dizziness and anxiety to improve diagnostic clarity and treatment.

Methods: Records of 81 consecutive patients diagnosed with an anxiety disorder by the psychiatrist in a multi-specialty neurotology center were reviewed. The onset of dizziness relative to anxiety, predisposing factors for anxiety (e.g., childhood anxiety), and neurotologic diagnoses were determined.

Results: Thirty-four patients had panic disorder and/or agoraphobia, and three had subthreshold panic as their sole diagnosis. Four patients developed a neurotologic condition after the onset of panic. Twelve patients developed panic and 16 more a specific phobia as a complication of their neurotologic illness. Eight patients had generalized anxiety disorder, but six manifested their illness only after the onset of a neurotologic condition. Three patients developed PTSD and otologic trauma from head injuries. Thus, 41 patients had full or subthreshold panic as the primary etiology of their dizziness. Twenty-nine developed panic or phobic behaviors as a complication of a neurotologic condition, and six others had low-grade GAD exacerbated by dizziness. Predisposing factors did not distinguish patients with a primary anxiety disorder from those with neurotologic comorbidity.

Conclusions: Panic disorder is a common cause of dizziness, but neurotologic illnesses have a propensity to induce anxiety disorders. The role of predisposing factors remains unclear.

NR589 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Psychiatric Consultation to Primary Care Physicians by Phone and E-Mail

Donald M. Hilty, M.D., *Department of Psychiatry, University of California at Davis, 2230 Stockton Boulevard, Sacramento, CA 95817*; Rick Ingraham, M.D., Samuel Yang, M.D., Thomas F. Anders, M.D.

Summary:

Telemedicine technology (videoconferencing, phone, electronic mail, and web site) is one strategy to improve the accessibility and quality of mental health care, particularly for rural areas. The University of California, Davis Health System developed a Physician Assistance, Consultation and Training Network (PACT Net) in an attempt to enhance the care of persons with developmental disabilities in rural California, with grant support from the California Department of Developmental Services. PACT Net is a warm line with 24-hour turnaround, and it employs a multispecialty panel (psychiatry, developmental pediatrics, medical genetics, neurology, pharmacology, pharmacy, physical medicine, and rehabilitation, etc.) to provide free, practical, phone, or e-mail physician-to-physician consultation. A pilot study was conducted to test the hypothesis that primary care physician satisfaction with ability to provide care would be enhanced for those who received physician consultation via phone or e-mail means compared to usual care (no consultation). Data were collected on 30 consultations: 25 by phone and five by e-mail; 24 occurred within 24 hours; average duration of the consultation was 38 minutes. The primary reasons for psychiatric consultation were for management of agitation/behavioral disturbance and mood disorders. Satisfaction was prospectively measured using a scale from 1 (very low) to 7 (very high). Primary care physician respondents rated their baseline satisfaction with: 1) pre-existing local services at 3.37; 2) the timeliness of the PACT Net consultation at 5.45; 3) the quality of the communication at 6.3; and 4) the overall quality and utility of the consultation at 6.2. Specialists rated their satisfaction with quality of the communication at 6.45 and the ease of the service at 6.46. The findings of this study and other studies using telemedicine will be discussed.

NR590 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Life Events, Irritability, and Myocardial Infarction

Renerio Fraguas, Jr., M.D., *Department of Psychiatry, University of Sao Paulo, Rua Drovidio Pires Campos S/N, Sao Paulo, SP 05015-021, Brazil*; Ana N.E. Pereira, M.D., David A. Wilson, M.D., Bernardino Tranchesi Jr., M.D.

Summary:

Background: Psychological factors have been associated with increased risk for myocardial infarction (MI). Life events (LE) are external and verifiable and their impact may differ among patients. This study investigated the association between self-perceived patterns of reaction to LE and MI.

Design: In this institution-based, case-control study, 45 infarcted patients were compared with 30 uninfarcted patients who had coronary disease.

Methods: LE were investigated over the 12 months preceding MI. The Social Readjustment Rating Scale was used as a checklist. Patients qualified their reactions according to eight patterns: interruption of activities, necessity to reorganize life activities, depression, anxiety, irritability, helplessness, and feelings of defeat and disturbance.

Results: Three significant LE in the last 12 months occurred in 23% of younger infarcted patients, 9% of middle-aged infarcted patients, and in none of the uninfarcted patients. Middle-aged infarcted patients reported significantly more frequent irritability associated with life events (57%) than the younger infarcted group (35%) and uninfarcted (32%) ($p = 0.002$).

Conclusions: The higher frequency of irritability as a pattern of reaction to life events in the middle-aged infarcted group is clinically important. Together with hostility and anger, irritability may be part of an emotional spectrum of reactions associated with increased risk for MI.

NR591 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Reproductive Psychiatry Patient Characteristics: Consultation Versus Outpatients

Terri L. Kipnis, M.S.C., *Department of Psychiatry, BC Women's, H214-4500 Oak Street, Vancouver, BC V6H 3N1, Canada*; Annie J. Kuan, B.A., Diana Carter, M.B., Fred Ott, O.T.

Summary:

Objective: To compare how standard clinical data differ between reproductive psychiatry patients in a consultation-liaison (C-L) service versus an outpatient program at a women's maternity hospital.

Method: Information collected consecutively from 30 outpatient initial assessments and 30 antepartum/postpartum inpatient consultations were retrospectively compared. The outcome measures included demographic data, Global Assessment of Functioning (GAF) scale score, DSM-IV axis I diagnoses, past psychiatric history, reasons for referral, and treatment recommendations.

Results: Pilot analyses revealed that the C-L inpatients did not differ from the outpatients in age, GAF, or antepartum/postpartum status. However, the two groups did differ in reasons for referral, psychiatric diagnoses and past history, socioeconomic status, and treatment interventions/recommendations. The C-L inpatients were more likely to be diagnosed with substance use disorders and adjustment disorders that were not identified in the primary reason for referral. Outpatients were most often diagnosed with mood disorders that were identified upon referral.

Conclusions: The results lead us to conclude that more education is needed for referring hospital staff, thus allowing for more accurate identification of all psychiatric conditions, including the dually diagnosed.

NR592 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Change in Depression Status in Patients with Acute Coronary Syndrome (ACS)

Claus H. Sorensen, M.D., *Research Unit, Ringkjobing AMT, Amtsradhuset Torvet 7, Ringkobing DK-6950, Denmark*; Erik Friis-Hasche, M.D., Per Bech, M.D.

Summary:

Objective: To examine the prevalence and assess the point of onset in the pathogenesis of depression in recently discharged ACS patients in relation to cardiovascular and prognostic factors.

Method: The Major Depression Inventory was completed by 800 Danish patients at discharge after ACS and at six weeks, six months, and 12 months after discharge. Relevant information was obtained from the hospital notes.

Results: Sixteen percent [C.I. 15.9–16.1%] had a depression at discharge. Depressed and nondepressed patients had the same age, 59 years s.d 9.5. There were no differences in major cardiovascular risk/prognostic factors between depressed and nondepressed patients.

At the six weeks contact 16.6% [C.I. 16.5–16.7%] had a depression. Only 47% of depressed at discharge were still depressed six weeks later. Patients remaining depressed were more frequently women OR 3.2 [C.I. 1.7–5.5], single OR 3.8 [C.I. 1.2–9.1], and previously depressed OR 9.8 [C.I. 5.6–21.4] compared with nondepressed. They were also more frequently diabetic, had larger infarcts, lower ejection fraction and workload, and were less frequently prescribed beta blockers but more frequently ACE inhibitors and diuretics compared with nondepressed.

Conclusion: This is the first study to asses and re-examine ACS-patients for depression with a diagnostic tool. There is a large turnover of patients with depression. Interventions should be aimed at those at risk for continuous depression; women, singles and previously depressed.

NR593 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Nicotine Withdrawal as a Risk Factor for Delirium

Jaime Santander, M.D., *Department of Psychiatry, Catholic University, Apo Quindo 3990, OF. 502, Santiago, Chile*; Sergio Ruiz

Summary:

Background: There is strong evidence about cholinergic mechanisms in the etiology of delirium, but the nicotinic system has not received attention. There is no information about the effect of nicotine withdrawal in patients with nicotine dependence and its relation with delirium.

Objective: To asses the association between delirium and nicotine withdrawal in medical inpatients of a general hospital.

Method: We assessed inpatients of the service of medicine of two general hospitals. Two groups were established, patients with nicotine dependence (DSM-IV criteria) and nonsmokers. We assessed the patients daily for delirium using DSM-IV criteria, Delirium Rating Scale and Mini-Mental Scale Exam.

Results: The sample was comprised of 85 medically ill nonsmokers in the control group and 44 medically ill and nicotine-dependent patients. The age was the main risk factor of delirium ($p = 0.0048$). In patients older than 60 years, we found delirium in 28 % of the control group and 63.6% of the nicotine-dependent group. In these older nicotine-dependent patients, the nicotine withdrawal was an independent risk factor of delirium ($p = 0.036$)

Conclusion: The nicotine withdrawal seems to be an independent risk factor of delirium in medical patients older than 60 years.

NR594 Wednesday, May 9, 12:00 p.m.-2:00 p.m.

Family and Social Factors Associated with Well-Being in Adolescents with Diabetes

Consuelo De Dios, M.D., *Department of Psychiatry, Hospital La Paz, Paseo Castellana 261, Madrid 28046, Spain*; Jose L. Agud, M.D., Arancha Ortiz, M.D., Angela Palao, Caridad Avedillo, Isabel Gonzalez, M.D.

Summary:

Introduction: Psychosocial well-being is an important treatment outcome criterion in type 1 diabetes mellitus.

Objective: To evaluate family and social factors that influence well-being in diabetic adolescents.

Method: Self-reports were obtained from 55 adolescents and their families using the following scales: Moos Family Environment Scale, Well-being, Diabetic Care Family Support, Diabetic Care Health Professional Support, and Diabetic Care Friends' Support Questionnaires. Metabolic control was measured by HbA_{1c}.

Results: Adolescents' total general well-being correlates with family cohesion ($r = 0.48$), organization ($r = 0,30$), and conflict ($r = 0,50$). Adolescents' depression rate increases with family conflict ($r = 0,36$), autonomy ($r = 0,40$) and with less cohesion ($r = 0,42$). Positive well-being is greater in adolescents perceiving their families as offering greater specific diabetic support ($r = 0,54$); they also have greater general well-being ($r = 0,36$) and are less depressed ($r = 0,31$). Gender, cohesion, and family history accounted for 43% of the depression variance as measured in the well-being scale (adjusted $R^2 = 0,43$). Male adolescents' positive well-being increases with more cohesive families, more specific family support, less control, and more specific friends' support (adjusted $R^2 = 0,75$). Family cohesion increases adolescents' energy ($R^2 = 0,52$) and total general well-being ($R^2 = 0,64$).

Conclusion: Diabetic treatment teams need to pay attention to general family factors as well as to specific diabetic family support to diabetic adolescents, in order to improve adolescent's well-being.

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NR595 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Community Prevalence of Nausea: Psychological, Social, and Somatic Factors

Tone T. Haug, M.D., *Department of Psychiatry, University of Bergen, Haukeland University Hospital, Bergen 5022, Norway*; Arnstein Mykletun, Ph.D.

Summary:

Background: Nausea is a commonly reported symptom with a point prevalence of about 12% in the community. Nausea is a prominent symptom in functional gastrointestinal disorders and these conditions are strongly related to anxiety and depression.

Aims: This study examines the relationship between anxiety disorders, depressions, and nausea in a large community sample.

Methods: A questionnaire that asked about physical and mental health and demographic and life-style factors was sent to all adults 20 years and above, a total of 97,197 persons. 62,651 persons returned the questionnaire. Presence of nausea, heartburn, diarrhea, and constipation during the last year was recorded. Anxiety disorders and depressions were based on self-rating of the Hospital Anxiety and Depression Scale (HADS).

Results: Forty-eight percent reported one or several gastrointestinal complaints during the last year. 15.3% had an anxiety disorder and 10.4% a depression. Presence of anxiety disorders carried the highest risk for nausea (OR 3.42). Presence of depression also increased the risk, but less than anxiety (OR 1.47). Demographic factors, life-style factors, and extragastrointestinal conditions did not reduce the OR of anxiety disorders and depressions to any significant extent.

NR596 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Panic Attacks, Chest Pain, and Ischemia in Post-Menopausal Women: An Epidemiologic Perspective

Jordan W. Smoller, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114*; Mark H. Pollack, M.D., Sylvia Wassertheil-Smoller, Ph.D., Beth Bartholomew, M.D., Bruce Barton, Ph.D., David Scheffield, Ph.D., Judith Hsia, M.D.

Summary:

Objective: Examine the association between panic attacks, chest pain, and ischemia in postmenopausal women.

Methods: A total of 3,128 women ages 50–79 enrolled in a 10-center ancillary study of the Women's Health Initiative (WHI) underwent 24-hour ambulatory electrocardiogram monitoring (AECG) and were asked about the presence of panic attacks (feeling suddenly frightened or anxious, accompanied by ≥4 symptoms on the panic symptom checklist) in the past six months.

Results: A total of 342 women (10.9%) reported full panic attacks in the past six months. Episodes of chest pain during AECG were reported by 334 women (11.0%). Chest pain was more common among women who reported panic attacks (23.4%) compared with those who did not (10.5%) (OR = 2.61, 95% CI:1.92–3.53). Of the 12 women who had ST depression during an episode of chest pain, five (41.7%) had reported panic attacks in the past six months. Those with panic were more likely (OR = 3.23, 95% CI:1.05–9.99) to have episodes of chest pain accompanied by ST depression than were those without panic. Chest pain without ST depression was also reported more frequently by women with panic attacks (21.6%) than women without (10.4%) ($p < .0001$).

Conclusion: A recent history of panic attacks may be associated with an increased risk of both ischemic and non-ischemic chest pain among postmenopausal women.

Sponsor: Glaxo-Wellcome

NR597 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Panic in Women Across the Life Cycle: Clinical Presentation and Response to Sertraline

Anita L.H. Clayton, M.D., *Department of Psychiatry, University of Virginia, 2955 Ivy Road, Northridge #210, Charlottesville, VA 22908*; Rege S. Stewart, M.D., Cathryn M. Clary, M.D.

Summary:

Objective: The objective of the study was to examine the differential clinical presentations and response to sertraline treatment in women across the adult life cycle.

Methods: Pooled data were analyzed from four double-blind, placebo-controlled sertraline treatment studies of patients who met DSM-III-R criteria for panic disorder.

Results: Data were available on a sample of 338 women (mean age = 40 years, SD = 11) analyzed by age and compared to 335 men (mean age = 36 years, SD = 10). Clinical presentation of panic disorder in the total sample of women differed from men in terms of later age of onset and significantly lower history of alcohol and/or substance abuse. Post-menopausal women reported significantly lower ($p < 0.05$) anticipatory anxiety, panic attack frequency, and panic severity than younger women and nonsignificantly lower avoidance and anxiety sensitivity. No effect on treatment response was found for younger women based on oral contraceptive (OC) status or for post-menopausal women based on hormone replacement therapy (HRT) status. Sertraline was well tolerated, with women reporting a higher incidence of diarrhea than men.

Conclusion: In this treatment sample, the clinical presentation of panic was less severe in post-menopausal women compared to women of reproductive age. Response to sertraline was unaffected by reproductive status or concomitant use of either OCs or HRT.

NR598 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Efficacy and Safety as One Combined Outcome in Clinical Trials

Jacobo E. Mintzer, M.D., *Department of Psychiatry, Medical University of South Carolina, 5900 Core Road, Suite 203, North Charleston, SC 29406*; Dennis Sweitzer, Ph.D., Jamie Mullen, Ph.D.

Summary:

Using data from a 4-month, multicenter, open-label trial of quetiapine (N = 553) and risperidone (N = 175) in adult outpatients with psychotic disorders, we present simple endpoints that incorporate efficacy and tolerability. Assessments included the CGI, PANSS, and an EPS checklist. Quetiapine and risperidone groups both showed improvements on all efficacy measures. Proportion of patients rated as "much" or "very much" improved according on the CGI was higher in the quetiapine group throughout the trial but was significantly so ($p < 0.05$) at only one timepoint. EPS in both groups declined during the treatment period. Risperidone patients were more likely than were quetiapine patients to have an EPS event and more likely ($p < 0.001$) to have EPS requiring adjustment of study medication or adjunctive medication. More patients taking quetiapine were rated as "much" or "very much" improved (according to the CGI) with no worsening of any EPS and were significantly so at all assessments between 2 weeks and 3 months ($p < 0.05$). Similarly, significantly ($p < 0.02$) more patients in the quetiapine group showed >30% improvement in PANSS total score with no worsening of any EPS symptoms at all assessments. These results illustrate that significant differences in clinical benefit may be overlooked by separate analyses of efficacy and safety.

NR599 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

The Treatment of OCD: A Missed Chance

Damiaan Denys, M.D., *Department of Psychiatry, UMC, Heidelberglaan 100 PO85500, Utrecht 3508 GA, Netherlands*; M. Van Tatenhove, M.D., Harold Van Megen, M.D., H. G. M. Westenberg, Ph.D.

Summary:

Background: On average, before they receive a correct diagnosis, patients with obsessive-compulsive disorder (OCD) see three to four doctors and spend over 9 years seeking treatment. Moreover, it takes an average of 17 years from the onset of OCD for patients to obtain appropriate treatment.

Objectives: The current study was conducted to catch insight into the management strategies of OCD.

Method: 200 outpatients with OCD, admitted at the University Medical Center in Utrecht. the Netherlands were evaluated for severity as measured with the Y-BOCS and previous treatments.

Results: The average number of previous treatments was 3.42. Mean Y-BOCS score at entry was 25.77. Mean disease duration was 15.7 years. 28% of the sample received a combination of drugs and behavioral therapy at any time, 21% received behavioral therapy only, and 35% received medication only. Of those who received appropriate medication, only 10% got an adequate dose according to the expert consensus guidelines.

Conclusions: These results show that OCD still tends to be undertreated for a number of reasons.

NR600 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Quetiapine Addiction for Treatment-Refractory OCD

Damiaan Denys, M.D., *Department of Psychiatry, UMC, Heidelberglaan 100 PO85500, Utrecht 3508 GA, Netherlands*; Harold Van Megen, M.D., H. G. M. Westenberg, Ph.D.

Summary:

Background: The addition of atypical antipsychotic agents to serotonin reuptake inhibitors (SRIs) has benefited patients with treatment-refractory obsessive-compulsive disorder (OCD). Since quetiapine has similar serotonergic and dopaminergic receptor binding profiles, we tested the hypothesis that quetiapine addition would be beneficial in patients with treatment-refractory OCD.

Method: We recruited 12 patients with primary OCD (per DSM-IV criteria) and no other axis I disorder. All subjects had OCD for at least 10 years, a mean Y-BOCS score of 31.1/40, and were unresponsive to at least two different, 8-week SRI trials at maximum dose. An SRI was continued throughout the trial and 100 mg/day of quetiapine was added. In the absence of response (Y-BOCS score >25%) and if there were no limiting side effects we increased the dose of quetiapine to 150 mg/day, and after 2 more weeks to 200 mg/day.

Results: For study completers (10 patients), Y-BOCS scores decreased 33% on average.

Conclusion: These results suggest that treatment-refractory OCD patients without comorbidity may respond to the addition of quetiapine to ongoing SRI therapy. To date, this is the first study that found the addition of quetiapine to be efficacious in treatment-refractory OCD.

NR601 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

A Flexible-Dose Study of Paroxetine Treatment of PTSD

Lee D. Ruggiero, B.S.C., *SmithKline and Beecham, 1250 South Collegeville Road, Collegeville, PA 19425*; Cornelius D. Pitts, R.P.H., Kerry Dillingham, M.S.C.

Summary:

The efficacy and safety of paroxetine versus placebo were assessed in a double-blind, placebo-controlled, multicenter study conducted in North America. Three hundred and seven patients (151 paroxetine, 156 placebo) diagnosed with PTSD per DSM-IV criteria comprised the intention-to-treat population. Following a 1 week placebo run-in period, patients who scored ≥50 on the Clinician Administered PTSD Scale (CAPS-2) at baseline and who satisfied all other inclusion/exclusion criteria were randomly assigned to receive either paroxetine or placebo for a 12-week treatment period. All patients assigned to active treatment initiated therapy at 20 mg daily and were permitted dosage elevations in 2-week intervals to a maximum daily dosage of 50 mg daily. The primary efficacy parameters were the change from baseline to study endpoint in the CAPS-2 total score and the proportion of responders based on the Global Improvement item of the Clinical Global Impression (CGI-I).

Results: Statistically significant differences were demonstrated in favor of paroxetine in the CAPS-2 change from baseline (adjusted mean difference = −10.6, 95% CI = −16.2 to −5.0; $p < 0.001$). Similarly, in the CGI responder analysis, 58.8% of paroxetine patients were classed as responders compared to 38.0% of placebo patients. The odds of being a responder to paroxetine compared to placebo at week 12 was 2.6, indicating a statistically significant benefit of paroxetine over placebo (95% CI = 1.6 to 4.3; $p < 0.001$). Statistically significant differences favoring paroxetine over placebo were also demonstrated in the re-experiencing; avoidance/numbing, and hyperarousal symptom clusters of the CAPS-2. In psychosocial functioning as measured by the Sheehan Disability Scale, statistically significant differences in favor of paroxetine over placebo were observed in the total score as well as the work, social life, and family life items. Ten (6.4%) placebo-treated and 18 (11.9%) paroxetine-treated patients withdrew from the study due to adverse experiences. No remarkable changes in vital signs or laboratory parameters were observed in either treatment group. The most common adverse experiences were nausea, somnolence, dry mouth, asthenia, and abnormal ejaculation. This study shows that paroxetine is safe and effective in a daily dosage range of 20–50 mg for the treatment of PTSD.

NR602 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Defense Mechanisms in Anxiety Disorders

Enrique Chavez-Leon, M.D., *Universidad Anahuac, Av Lomas Anahuac s/n Lomas Anahuac, Huixquilucan 52760, Mexico*; Martha P. Ontiveros-Uribe, M.D., Carmen Lara-Munoz, Ph.D.

Summary:

Objective: Few studies of anxiety disorders have been conducted in Mexico, and there has been little published evidence about the importance of the defense mechanisms that are present in these disorders. In this study we identified the differential use of defense mechanisms in normal control and in patients with anxiety disorders alone or complicated with mood disorders.

Method: The study sample comprised 48 consecutive outpatients with anxiety disorders from the National Institute of Psychiatry (Mexico) who agreed to participate and complete a demographic questionnaire and the Defense Style Questionnaire (DSQ) during their first visit. The validity and reliability (Cronbach's alpha = 0.897) of the DSQ was established in a sample of 261 psychiatric patients and controls before its application. Axis P disorders were ascertained reliably with face-to-face semistructured interview (SCID I). This group had 32 patients with pure anxiety disorders and 16 patients with anxiety disorders associated with mood disorders. 32 subjects were included in the control group.

Results: A comparison of patients with anxiety disorders, patients with anxiety disorders associated with mood disorders, and

controls showed that both patient groups used more projection, regression, inhibition, acting out, fantasy, splitting, help rejecting, undoing, and reactive formation than the controls. The patients with anxiety disorders used more somatization and denial than both the controls and the group of patients with anxiety and mood disorders.

Conclusions: There is a clear difference in the defense mechanisms used by the illness groups and the normal subjects, but only subtle differences between the illness groups.

NR603 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Genetic Polymorphism of Catechol-O-Methyltransferase (COMT) in Panic Disorder

Yong-Lee Jang, M.D., *Department of Psychiatry, Samsung Medical, 50 Ilwon-dong Kangnam-gu, Seoul 135-710, Korea*; Bum-Hee Yu, M.D., Kyoung-Sik Yun, M.D., Jong-Min Woo, M.D., Young-Sik Lee, M.D., Chul Na, M.D.

Summary:

Background: Catecholámine metabolism is known to be associated with the pathophysiology of anxiety disorders, including panic disorder. Two alleles of the human catechol-*O*-methyltransferase (COMT) gene correspond to high (H) and low (L) activities of the enzyme, respectively. We examined the genetic effects of COMT on panic disorder and the relationships between the genetic polymorphism and some physiological and psychological parameters in panic patients.

Method: We recruited 51 patients who met the DSM-IV criteria for panic disorder and 45 control subjects who had no medical or psychiatric illnesses. We measured physical parameters (skin temperature, electromyography, electrodermal response) using a biofeedback system (J&J 1-410 model) and assessed psychological parameters (anxiety and depression levels) with Spielberger State-Trait Anxiety Inventory (STAI) and Beck Depression Inventory (BDI). Genetic polymorphism was identified using PCR-based restriction fragment length polymorphism analysis (RFLP).

Result: We found that panic disorder was significantly associated with the L allele ($\chi^2 = 8.662$, $p = 0.003$) and genotype ($\chi^2 = 8.453$, $p = 0.015$) of the COMT gene. In addition, the homozygous LL genotype showed lower skin temperature change during a stressful task than other genotypes ($F(2, 10) = 4.807$, $p = 0.034$). Treatment was less effective in panic patients with the LL genotype than patients with other genotypes ($F(2, 48) = 4.983$, $p = 0.011$). There was no significant association between the COMT genetic polymorphism and psychological parameters.

Conclusion: The result of this study suggests the COMT genetic polymorphism plays an important role in panic disorder. The LL genotype might be related to the pathophysiology and treatment response of panic disorder.

NR604 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Factor Analysis of Symptoms in OCD

Dennis L. Murphy, M.D., LCS, *NIMH-NIH, NIH Clinical Center, 10/3D41, Bethesda, MD 20892-1264*; Lauren W. Cochran, Mark J. Smith, M.D., Benjamin D. Greenberg, M.D., Yung-Mei Leong, M.A., B. Lucy Justement, R.N.

Summary:

Despite progress in our ability to successfully treat obsessive-compulsive disorder (OCD) with behavior therapy and medication, the identification of homogeneous subgroups of patients with OCD has remained elusive. Once identified, such subgroups may be of value in future genetic, neurobiological, and treatment response studies. The purpose of this study was to evaluate the relationships between OCD symptom categories using factor analysis and, by comparing our results with previous findings, to determine whether or not these factors are consistent across patient populations.

In this study, 156 OCD patients completed the Thoughts and Behaviors Inventory (TBI) and their symptom subcategory scores were calculated using the 13 symptom subcategories derived from the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) Symptom Checklist. A principal-components factor analysis revealed a four-factor solution accounting for more than 60% of the variance in the data set, namely: 1) aggressive/sexual/religious obsessions and checking, 2) symmetry and ordering, 3) hoarding, and 4) contamination and cleaning. Because these factors correspond exactly with the symptom clusters previously described by another group, these findings help to validate the existence of specific symptom subtypes, which may be useful in delineating meaningful homogeneous subgroups of OCD patients.

NR605 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Paroxetine and the Rate of Remission in the Treatment of GAD

Kevin M. Bellew, B.S., *Department of Neuroscience, GlaxoSmithKline, 1250 South Collegeville Road, Collegeville, PA 1426-0989*; James P. McCafferty, B.S., Rocco M. Zaninelli, M.D., Malini Iyengar, Ph.D., Daniel B. Burnham, Ph.D.

Summary:

Objective: To determine the rate of remission among patients with generalized anxiety disorder (GAD) treated with paroxetine.

Method: Data from two randomized, double-blind, placebo-controlled studies of paroxetine were reviewed to determine rates of remission among GAD patients. In both studies, patients were treated for eight weeks. One study evaluated two fixed doses of paroxetine (20 mg and 40 mg), while a second evaluated a range of paroxetine doses (20–50 mg). Remission was defined as a Hamilton Rating Scale for Anxiety (HAM-A) total score of seven or less.

Results: In the fixed-dose study, 30% of patients in the 20 mg group and 36% of patients in the 40 mg group achieved remission (LOCF). These rates were significantly larger than the 20% rate of remission achieved by the placebo group ($p < 0.027$ for both doses compared with placebo). Among patients completing the study (OC), 36% of patients in the 20 mg group and 42% of those in the 40 mg group achieved remission compared with 24% in the placebo group ($p < 0.027$ for 40 mg vs placebo). In the flexible-dose study (LOCF), 36% of paroxetine patients (mean dose ± SD = 26.8 mg ± 7.5) achieved remission compared with 23% of those treated with placebo (p vs placebo = 0.009). Completers achieved a remission rate of 43% in the paroxetine group and 26% in the placebo group (p vs placebo = 0.006).

Conclusion: Paroxetine at doses of 20–50 mg is an effective treatment for patients with GAD with up to 43% of patients achieving full remission, a clinical scenario in which the patient is indistinguishable from healthy counterparts.

NR606 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Posttraumatic Stress and Depressive Reactions Among Adolesents in Nicaragua After Hurricane Mitch

Armen K. Goenjian, M.D., *Department of Psychiatry, UCLA NPI, 501 Via La Selva, Redondo Beach, CA 90277*; Luis Molina, M.D., Alan Steinberg, Ph.D., Robert S. Pynoos, M.D.

Summary:

Objective: To determine the severity of PTSD and depressive reactions among adolescents in Nicaragua after Hurricane Mitch, and the relation of these reactions to variables including DSM IV

objective and subjective features of hurricane exposure, death of family members, and thoughts of revenge.

Method: Six months after the hurricane, 158 adolescents from three differentially exposed cities were evaluated using a hurricane exposure questionnaire, the CPTSD-RI and DSRS.

Results: Severe levels of posttraumatic stress and depressive reactions were found among the most exposed group (Posoltega). PTSD, depression, and objective hurricane-related exposure scores followed a "dose of exposure" pattern, congruent with rates of death and destruction across the cities. Hurricane impact, objective and subjective hurricane-related experiences, and having thoughts of revenge after the hurricane accounted for 68% of the variance in PTSD severity. Severity of PTSD, death of a family member, and sex accounted for 59% of the variance in severity of depression. There was a high correlation between CPTSD-RI and DSRS scores, and B category and DSRS scores.

Conclusion: Adolescents in Nicaragua who have had severe exposure to Hurricane Mitch have developed severe and chronic PTSD and comorbid depression. Their recovery is vital to the social and economic recovery of a country already ravaged by years of political violence and poverty. Trauma/grief-focused intervention is urgently needed for these adolescents.

NR607 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Paroxetine Improves Quality of Life and Functional Disability in Patients with GAD

Janet M. Flisak, R.N., *Department of Neuroscience, GlaxoSmithKline, 1250 South Collegeville Road, Collegeville, PA 19246-0989*; Kelly Grotzinger, Ph.D.

Summary:

Objective: The anxiolytic effect of paroxetine in the treatment of generalized anxiety disorder (GAD) has been demonstrated in a placebo-controlled trial. The study included measures of functionality as well-as scales to assess patient's perception of health-related quality of life. We report here the analysis of these outcome measures.

Methods: Patients were randomized to receive either paroxetine or placebo in an eight-week, double-blind study. ANOVA methods were used to assess changes in the Sheehan Disability Scale(SDS) and EuroQol(EQ-5D). The SDS measures functional impairment across three subscales: work, social life/leisure activities, family life/home responsibilities. The EQ-5D measures quality of life and covers the domains of mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. EQ 5D responses were converted into health-state utilities using standardized tariffs.

Results: After eight weeks of treatment, mean decreases from baseline in SDS total scores were approximately two-fold greater in paroxetine-treated patients (20mg, $p = 0.005$; 40mg, $p = <0.001$) than placebo controls. EQ-5D utility scores improved for both 20mg and 40mg paroxetine regimens with statistical significance achieved in the 40mg group ($p < .001$). Patients who took paroxetine 40mg had twice the increase in utility scores as patients on placebo. Paroxetine treatment was also associated with a significantly greater improvement in global health ($p < 0.001$).

Conclusion: In addition to paroxetine relieving the core anxiety symptoms of GAD, the data support improvement in patients' social and physical functioning and health-related quality of life.

NR608 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Paroxetine: Effective Treatment for GAD Regardless of Patient Gender, Race, or GAD Severity?

Daniel B. Burnham, Ph.D., *Department of Neuroscience, GlaxoSmithKline, 1250 South Collegeville Road, Collegeville, PA 19426-0989*; Malini Iyengar, Ph.D., Kevin M. Bellew, B.S., James P. McCafferty, B.S., Rocco M. Zaninelli, M.D.

Summary:

Objective: The selective serotonin reuptake inhibitor (SSRI) paroxetine at 20 and 40 mg/day is superior to placebo in treating GAD outpatients over eight weeks (Bellew et al.). A covariate analysis was done on this sample. The lifetime prevalence of generalized anxiety disorder (GAD) among women (6.6%) is almost twice that of men (3.6%) (Kessler et al).

Method: Analysis of covariance models with effects of treatment, site, covariate, and treatment by covariate interaction were studied. At study endpoint, p-values were calculated for each effect. A 10% level of significance was used for tests of interaction; other effects were tested at a 5% level.

Results: Change from baseline in Hamilton Anxiety (HAM-A) total score:

Subgroup	Placebo Mean (SD)	n	20 mg Mean (SD)	n	40 mg Mean (SD)	n
Male	–9.6 (0.9)	79	–12.0 (0.9)	86	–12.6 (0.9)	86
Female	–9.7 (0.8)	101	–13.0 (0.8)	102	–12.0 (0.8)	111
White	–9.7 (0.7)	147	–12.4 (0.7)	154	–12.0 (0.7)	175
Non-White	–9.7 (1.4)	33	–13.3 (1.4)	34	–13.7 (1.7)	22

No covariate effects and treatment-by-covariate interactions were seen for the above subgroups or for duration of GAD expressed as a continuous covariate ($p \geq 0.34$). Although patients with higher baseline HAM-A total scores showed more improvement than patients with lower scores regardless of treatment ($p < 0.001$), the superiority of paroxetine over placebo was not affected by this covariate. Overall, the treatment effect remained significantly in favor of paroxetine ($p < 0.05$) after adjusting for either of these 4 covariates.

Conclusion: Paroxetine is effective in treating GAD regardless of patient gender, race, or disease covariates.

NR609 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Paroxetine Treatment of GAD: An Analysis of Response by Dose

James P. McCafferty, B.S., *Department of Neuroscience, GlaxoSmithKline, 1250 South Collegeville Road, Collegeville, PA 19426-0989*; Kevin M. Bellew, B.S., Rocco M. Zaninelli, M.D.

Summary:

Background: Two placebo-controlled clinical trials demonstrated the efficacy of paroxetine in the treatment of generalized anxiety disorder (GAD). The findings from a fixed-dose study clearly established that 20 mg/day of paroxetine is an effective regimen as evidenced by a response rate of 68%. We analyzed the results from a 331 patient, eight-week, flexible dose trial (20–50 mg/day) to assess whether patients who did not respond to 20 mg of paroxetine would benefit from higher doses.

Methodology: The data set analyzed was derived from 87 paroxetine patients who were titrated to doses greater than 20 mg/day. Point estimates of response and 95% confidence limits were tabulated using conventional methodology. Response to treatment was defined as a clinical global impression (CGI) improvement rating of moderate or marked improvement.

Results: 69.0% (CI = 59.3%, 78.9%) of patients who had an insufficient benefit while receiving 20 mg regimen of paroxetine responded when titrated to a higher dose. The point estimates and 95% CI of response rates for the various doses used in the titration scheme are as follows:

Paroxetine Dosage	No. of Patients Receiving Dose	Point Estimate of Response (95% CI)
30 mg	87	0.34 (0.24, 0.45)
40 mg	47	0.49 (0.34, 0.64)
50 mg	21	0.33 (0.12, 0.55)

The higher doses of paroxetine were well tolerated; termination of treatment because of an adverse event was reported for only four patients (sexual dysfunction two nausea one asthenia.

Conclusion: The evidence from the fixed-dose study shows that most GAD patients will respond to a 20 mg/day regimen of paroxetine. These analyses derived from the flexible-dose study support that GAD patients who do not respond to a dose of 20 mg may respond to higher doses, up to 50 mg/day.

NR610 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Quetiapine Effectiveness in Reducing Anxiety: Clinical Evidence

Andrew J. Cutler, M.D., *Department of Psychiatry, Coordinated Research of Florida, 807 West Morse Boulevard, Suite 101, Winter Park, FL 32789*

Summary:

Objective: Quetiapine has proven short-term and long-term efficacy in the treatment of acute and chronic stable schizophrenia. Its favorable tolerability profile includes no greater incidence of EPS than placebo across the entire dose range, no sustained elevation of plasma prolactin, and minimal weight gain. In addition to the high 5-HT_2:D_{2A} receptor binding ratio, quetiapine has affinity for 5-HT_{1A}, 5-HT_6, and H_1 receptors.

Methods: A meta-analysis was performed on data from three placebo-controlled (n = 42) and four haloperidol-controlled (n = 723) six-week trials in patients with schizophrenia. Mean changes from baseline in BPRS individual item of anxiety and BPRS Factor I (a combined measure of somatic concern, anxiety, guilt feeling, and depressive mood) were analyzed using an ANOVA on the pooled database.

Results: Quetiapine, 100 to 750 mg/d, produced significantly greater reductions in anxiety item scores compared with placebo (–0.70 vs –0.16, $P < 0.0001$) or haloperidol (–56 vs –0.39, $P = 0.017$). Quetiapine also produced significantly greater reductions in BPRS Factor I scores compared with placebo (0.59 vs –0.29, $P = 0.0002$) and haloperidol (–0.48 vs –0.34, $P = 0.0035$).

Conclusions: The results suggest quetiapine is effective in reducing anxiety in patients with psychotic symptoms.

NR611 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Sertraline Treatment of Panic Disorder: A Naturalistic Study

Jeronimo Saiz-Ruiz, M.D., *Department of Psychiatry, Hospital Ramon Y Cajal, Ctra. Colmenar Viejo KM 9, 100, Madrid 28034, Spain*; Manuel Gomez-Beneyto, M.D., Jose R. Gutierrez-Casares, M.D., Joan Massanaronquillo, M.D., Angela Ibanez-Cuadrado, M.D., Inmaculada Exposito, Ph.D., Alberto Porras-Chavarino, Ph.D.

Summary:

Objectives: To assess the tolerability and effectiveness of sertraline in a large number of patients with panic disorder in daily clinical practice.

Methods: In this open-label, non-comparative study, 886 outpatients with panic disorder were treated with sertraline (25–200 mg/day) for six months. Patients were assessed after one, two, four, and six months with the Hamilton Anxiety Rating Scale (HAM-A), item 7 of the Clinical Anxiety Scale (CAS), the Clinical Global Impression of Severity (CGI-S) and Improvement (CGH), and two visuo-analogic self-evaluation scales (VAS) for fear and avoidance.

Results: A total of 858 patients completed the study. The mean final daily dose was 89.1 mg. The mean HAM-A score decreased from 28.6 at baseline to 7.8 after six months of treatment. At final visit, 88.7% of patients were free of panic attacks; 47.7% did not experience fear and 40.9% did not have avoidance; 70.8% were not ill and 68.6% showed a market improvement.

A total of 196 patients (22.1%) reported at least one adverse event with nausea (6.5%) being the most frequent adverse event. Only 3.6% of patients discontinued due to adverse events.

Conclusions: Sertraline is an effective and relatively well tolerated treatment for panic disorder in daily clinical practice.

This study was supported by a research grant from Pfizer Spain.

NR612 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Comorbidity and Severity of Pathological Gambling

Jeronimo Saiz-Ruiz, M.D., *Department of Psychiatry, Hospital Ramon Y Cajal, Ctra. Colmenar Viejo KM 9, 100, Madrid 28034, Spain*; Angela Ibanez-Cuadrado, M.D., Ignacio Perez de Castro, Ph.D., Jose Fernandez-Piquer, Ph.D.

Summary:

Objective: To determine the frequency of psychiatric comorbidity among treatment-seeking pathological gamblers, compare the clinical and psychosocial severity of the comorbid and non-comorbid groups, and investigate differences in D2 dopamine receptor gene (DRD2).

Method: Sixty-nine consecutive pathological gamblers applying to a specialized outpatient treatment program were evaluated with structured interviews, self-report questionnaires, and psychological scales and were genotyped for a DRD2 polymorphism.

Results: A comorbid psychiatric disorder was present in 63% of the sample. The most frequent diagnoses were personality disorders (43%), alcohol abuse/dependence (34%), and adjustment disorders (17%). Subjects with associated comorbidity showed higher severity in gambling scores and psychological scales. Significant differences in DRD2 allele distribution were found.

Conclusions: Psychiatric comorbidity is common among pathological gamblers and associated with increased clinical severity. DRD2 gene could be a liability genetic factor for psychiatric comorbidity in pathological gambling.

NR613 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Panic Disorder and OCD in a Hyperventilation Challenge Test

Fabiana L. Lopes, M.D., *Institute of Psychiatry, University FED Rio Jan, Min Octavio Kelly 467, AP1204-B, Niteroi, RJ 24220-300, Brazil*; Antonio E. Nardi, M.D., Alexandre M. Valenca, M.D., Isabella Nascimento, M.D., Marco A. Mezzasalma, M.D., Walter A. Zim, M.D.

Summary:

Background: Stress-induced hyperventilation produces symptoms that people are prone to misinterpret as life-threatening if they are unaware of the consequences of overbreathing. Our aim was to observe the induction of panic attacks by a hyperventilation challenge test in a series of panic disorder and obsessive-compulsive disorder (OCD) patients (DSM-IV).

Method: We randomly selected 28 panic disorder patients, 21 OCD patients, and 28 normal volunteers. All patients were drug free for a week. They were induced to hyperventilata (30 breaths/min) for four minutes. Anxiety scales were applied before and after the test.

Results: A total of 64.3% (n = 18) panic disorder patients, 9.5% (n = 2) OCD patients and 3.6% (n = 1) of control subjects had a panic attack after hyperventilating ($X^2 = 3.99$, d.f. = 2, p = 0.026).

Limitations: The hyperventilation challenge test has a low sensitivity for panic disorder.

Conclusion: In this challenge test the panic disorder patients were more sensitive to hyperventilation than OCD patients and

normal volunteers. The induction of panic attacks by voluntary hyperventilation may be an easy test for validating the diagnosis in some specific panic disorder patients.

NR614 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Predictors of Sertraline Response in Generalized Social Phobia

Michael A. Van Ameringen, M.D., *Department of Psychiatry, McMaster Medical Center, 1200 Main Street, West, Hamilton, ON L8N 3Z5, Canada*; Catherine L. Mancini, M.D., Jonathan Oakman, Ph.D., Peter Farvolden, Ph.D., John R. Walker, Ph.D., Roger Lane, M.R.C.

Summary:

Objective: The purpose of this study was to examine the predictors of response to sertraline treatment of generalized social phobia (GSP).

Method: Predictors of response to treatment were examined in a large placebo-controlled, multisite study of sertraline in GSP (N = 204).

Results: Following 20 weeks of treatment, the response rate for sertraline and placebo were 53% and 29%, respectively. Demographic variables did not predict across several different measures of response to treatment. Baseline symptom severity was strongly related to outcome in the placebo-treated group (e.g. on the SP-MFQ, r = .63, p < .01), and weakly related to outcome in the sertraline-treated group (r = .20, p < .05, t-test of slope difference = 3.10, p < .01). For patients in the sertraline group who were minimally, much, or very much improved (CGI) at week 2 of treatment, 82% finished much improved or very much improved, while for those unchanged at week 2 of treatment, only 42% finished the trial much or very much improved.

Conclusion: Demographic variables did not predict response to treatment. Severity of symptoms at baseline predicts response to placebo treatment but not response to sertraline treatment. An early response bodes well; however, a lack of early response is nonpredictive of subsequent improvement.

NR615 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Topiramate for Weight Control in SSRI-Treated Anxiety Disorder Patients

Michael A. Van Ameringen, M.D., *Department of Psychiatry, McMaster Medical Center, 1200 Main Street, West, Hamilton, ON L8N 3Z5, Canada*; Catherine L. Mancini, M.D., Beth Pipe, B.S.C., Peter Farvolden, Ph.D.

Summary:

Objective: Selective serotonin reuptake inhibitors (SSRIs) have become the first-line pharmacological treatment for anxiety disorders. Although effective, the use of SSRI medications can be associated with significant adverse events, including weight gain. Based on the successful use of anticonvulsants in the treatment of mood and anxiety disorders and the fact that topiramate has been found to be associated with weight loss in affective disorders, topiramate was added to the treatment of patients with a primary DSM-IV anxiety disorder who experienced a significant weight gain with SSRI treatment, in an attempt to induce weight loss.

Method: Topiramate was added to the SSRI in ten anxiety disorder patients, starting at a dose of 25mg/day and titrated up to a maximum daily dose of 200 mg/day. Subjects' weight was monitored across subsequent monthly clinic visits.

Results: SSRI-treated subjects in this sample gained an average 9.53 (*SD* = 3.28) kg.. Following the addition of a mean dose of 150.00 (*SD* = 44.72) mg/day of topiramate for 6.66 (*SD* = 2.87) weeks, subjects, on average, lost 4.60 (SD = 2.66) kg..

Conclusions: While the efficacy of topiramate in the treatment of anxiety disorders remains to be established in placebo-controlled trials, topiramate may have a role in managing weight gain in SSRI-treated patients.

NR616 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Appearance of Panic Disorder in Terms of Comorbid Anxiety Disorders

Milan Latas, M.D., *Institute of Psychiatry KCS, Pasterova 2, Belgrade 11000, Yugoslavia*; Vladan Starcevic, M.D., Goran Trajkovic, Goran Bogojevic, M.D.

Summary:

Objective: To compare ages of onset of panic disorder in patients with panic disorder and agoraphobia (PDA) with and without comorbid anxiety disorders (CAD): specific phobia, generalized anxiety disorder, and social phobia.

Method: 124 consecutive outpatients with principal diagnosis of PDA participated the study. Diagnoses of PDA and CADs were made on the basis of SCID-I for DSM-IV. Ages of onset of PDA and CADs were defined as ages when patients meet DSM IV criteria for the disorders. Ages of onset of panic disorder of patients with and without CAD were compared by 2-tailed t-test.

Results: Patients with only one CAD were older at the age of onset of panic disorder than patients without CAD (specific phobia: 31.0 vs. 30.1; generalized anxiety disorder: 31.3 vs. 29.8; social phobia: 31.2 vs. 30.5) but differences were not statistically significant. Patients with jointly CADs were older than patients without CADs (31.4 vs. 28.0) and difference was statistically significant (t = –2.6; p = 0.021).

Conclusion: Patients with PDA with CAD were older at the age of onset of panic disorder than patients with PDA without CAD. This could be due to adaptation on symptoms of anxiety in patients with previous CAD and consequently later noticing of symptoms of PDA.

NR617 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Social Anxiety Disorder in Primary Care

Raz Gross, M.D., *Department of Epidmiology, Columbia University, 600 West 168th St. PH-18 R 303, New York, NY 10032*; Mark Olfson, M.D., Marc Gameroff, M.A., Adriana Feder, M.D., Myrna M. Weissman, Ph.D.

Summary:

Background: Despite evidence for extensive disability and comorbidity associated with social anxiety disorder (SAD), information on its prevalence and presentation in urban primary care settings is limited. Moreover, fear and avoidance of situations that involve possible scrutiny by others may prevent SAD patients from seeking help from their primary care providers.

Method: Data were taken from a survey conducted on a systematic sample (N = 209) of patients from a primary care practice to examine the prevalence, clinical features, psychiatric comorbidity, impairment, mental health treatment, and primary care visits of patients with SAD.

Results: Lifetime and current prevalence of SAD were 5.7% and 3.8%, respectively. Substance use disorders were far more common among patients with SAD compared to patients with other psychiatric disorders (40.0% vs. 3.3%, p = 0.01). Prevalence of major depression was high in both groups (20.0% and 26.6%). SAD patients were functionally impaired, made fewer primary care visits compared to all other patients, and only 41.7% reported receiving mental health treatment in the past year.

Conclusion: Prevalence of SAD was less than one-half that found in most community surveys, and mean number of primary care visits of patients with SAD was significantly lower. These

results, and the finding that fewer than one-half of patients with SAD received past year mental health treatment suggest substantial unmet need for care, especially in view of available effective treatments for SAD.

NR618 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Depression, Anxiety, and Glycemic Control in Diabetes

Raz Gross, M.D., *Department of Epidmiology, Columbia University, 600 West 168th St. PH-18 R 303, New York, NY 10032*; Mark Olfson, M.D., Marc Gameroff, M.A., Adriana Feder, M.D., Myrna M. Weissman, Ph.D.

Summary:

Background: Diabetes mellitus (DM) and its complications constitute a major health problem in modern societies. Maintaining optimal glycemic control (GC) is a primary goal in DM. Studies suggest that depression is highly prevalent among adults with DM but are less consistent with regard to the association between depression and poor glycemic control. Such an association would suggest that treatment of depression might have favorable effects on outcomes in diabetes.

Method: We linked data on psychiatric disorders, collected in a survey of systematic sample of urban, low-income, mostly Hispanic primary care patients (N = 1005), to medical records and laboratory databases. Patients with DM were identified (N = 321) and compared to non-diabetics. Correlation between depression, anxiety, and Hemoglobin Alc (HbAlc), the gold standard measure of recent glycemic control, were studied cross-sectionally and longitudinally.

Results: Prevalence of current depression, anxiety, and substance use were high in both diabetic and non-diabetic patients. Among diabetics, glycemia was not well controlled in both depressed and non-depressed groups. Results on the relationship between anxiety and glycemic control will be presented.

Conclusion: These findings raise the possibility that in the presence of other fundamental risk factors, e.g., low socioeconomic status, the effect of depression on glycemic control may be overridden. A comprehensive psychosocial intervention should direct resources to improved access to care, patient education, and social welfare.

NR619 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Does Pre-Existing Anxiety Disorder Predict Response to Paroxetine in Irritable Bowel Syndrome

Sanjay Gupta, M.D., *Department of Psychiatry, Olean General Hospital-Psychiatric Net, 2221 West State Street, Olean, NY 14760*; Prakash S. Masand, M.D., Thomas L. Schwartz, M.D., David E. Kaplan, M.D., Subhdeep Virk, M.D., Kari Lockwood, R.N., Michael Wade

Summary:

Background: IBS is the most common disorder seen by gastroenterologists. There is bidirectional comorbidity of IBS and psychiatric illness. Various antidepressants, particularly TCAs, have been used to treat IBS. An unanswered question remains: does the presence of a pre-existing psychiatric disorder predict response to an antidepressant in IBS? Ours is the first study to address this question.

Method: Twenty subjects diagnosed with IBS (Rome criteria) treated for 12 weeks with 20 to 40 mg of paroxetine. At baseline a structured clinical interview for DSM-IV was administered to diagnose co-existing psychiatric illness utilizing interactive voice response system to measure symptom improvement. For dichotomous variables, improvement was defined as not having symptoms for four or more days during the last study week. For continuous variables, improvement was defined as having at least 50% reduction from first week to last week of study.

Results: Ten patients had anxiety disorder and IBS while 10 patients had only IBS. Both subgroups had similar improvement in abdominal pain ($p = 0.650$), constipation ($p = 1.00$), and diarrhea ($p = 0.143$). Patients with anxiety had a similar change in the number of bowel movements compared with patients without anxiety ($p = 0.91$, Wilcoxon Rank Sum Test). No difference was found in the two subgroups on the measures of incomplete emptying ($p = 0.559$), bloating, or abdominal distension ($p = 0.622$). Both groups had similar improvement in PGI scores.

Conclusions: The presence of a pre-existing psychiatric disorder is not necessary to predict a response to paroxetine in patients with irritable bowel syndrome.

NR620 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Functional Impairment Associated with GAD

Mark Olfson, M.D., *Department of Psychiatry, Columbia University, 1051 Riverside Drive, Box 24, New York, NY 10032*; Carlos Blanco-Jerez, M.D., Jeanine Christiana, B.A., Mary T. Guardino, B.A.

Summary:

Background: Generalized anxiety disorder (GAD) commonly occurs in combination with other psychiatric disorders. This poster examines whether comorbid GAD contributes to disability associated with major depressive disorder (MDD), panic disorder (PD), postraumatic stress disorder (PTSD), social anxiety disorder (SAD), and obsessive compulsive disorder (OCD).

Method: Data were analyzed from a random national sample of participants in the 2000 National Anxiety Disorders Screening Day (n = 4,145) who completed a questionnaire with six disorders from the Mini Neuropsychiatric Inventory (MINI) and the Sheehan Disability Scale (SDS). Difference of means tests were performed comparing participants with (1) no disorder, GAD alone, and GAD and other disorders; and, (2) each disorder alone and each disorder with GAD, but not other disorders.

Results: GAD was strongly associated with functional impairment. Mean SDS ratings of GAD alone (N = 426, 9.7 (SD = 6.4)) were intermediate between no disorder (N = 1,254; 4.6 (5.2)) and GAD and other mental disorders (N = 1,934; 16.4 (7.8), $F = 1646.7$, $df = 3,185$, $p < .001$). In four of five disorders, comorbid GAD significantly increased SDS scores. As compared with MDD alone, MDD comorbid with GAD was associated with a 27% increase in SDS scores.

Conclusions: GAD is associated with substantial functional impairment. When GAD occurs in combination with common psychiatric disorders, it compounds disability. Psychiatrists should remain alert to the possibility that GAD is complicating the clinical course of their patients with common anxiety and mood mental disorders.

NR621 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Pentagastrin-Induced Sleep Panic Attacks

Marilla Geraci, M.S.N., *CCNURS Department, NIMH/NIH, 10 Center Drive, MS C1368, Bethesda, MD 20892-1368*; Todd Anderson, M.A., Shiyoko Slate-Cothren, M.H.A., Una D. McCann, M.D., Robert M. Post, M.D.

Summary:

Pharmacological challenges with pentagastrin have been shown to produce panic attacks in approximately half of patients with social phobia and panic disorder. However, the pharmacological specificity of this phenomenon has been criticized because patients with anxiety disorders can develop panic under situations of high environmental stress. The present studies were conducted

in an effort to eliminate the potential confound of nonspecific environmental stress in the induction of pentagastrin-induced panic, by performing challenges during sleep. Studies were conducted in seven subjects (four with panic disorder and three with social phobia) who had previously developed pentagastrin-induced panic while awake. Subjects were equipped with standard sleep montages prior to sleep, and intravenous catheters permitting remote venous access were placed. During the transition from stage 2 to stage 3 sleep, subjects received infusions of normal saline and pentagastrin (0.6ug/kg over one minute) in fixed order, separated by 10 minutes. Pentagastrin, but not saline, caused subjects to awaken within 30 seconds after drug infusion. Two of four panic disorder and two of three social phobia subjects reported experiencing panic attacks, as measured by a panic attack inventory. Pentagastrin infusion was associated with increases in ACTH and cortisol, regardless of whether subjects reported panic or not. These results indicate that patients with anxiety disorders can experience pentagastrin-induced panic in the absence of high environmental arousal, and suggest that pentagastrin-related increases in cortisol and ACTH can occur without panic attacks.

NR622 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Fluoxetine Treatment for OCD in Children and Adolescents: A Placebo-Controlled Clinical Trial

Daniel A. Geller, M.D., *Department of Pediatrics (OCD), McLean Hospital, 115 Mill Street, Belmont, MA 02478*; Sharon L. Hoog, M.D., John H. Heiligenstein, M.D., Randall K. Ricardi, D.O., Roy Tamura, Ph.D., Stacy Kluszynski, M.S., Jennie G. Jacobson, Ph.D.

Summary:

Objective: This double-blind, placebo-controlled study assesses efficacy and safety of fluoxetine treatment for children and adolescents with OCD.

Methods: Patients (N = 103) ages 7 to 17 had primary psychiatric diagnoses of OCD (DSM-IV) with symptoms of at least moderate severity (CGI-Severity ≥ 4 and Children's Yale-Brown Obsessive Compulsive Scale (CY-BOCS)>=16, one or more symptoms present for >=6 months). After a one-week screening phase, patients entered a 13-week, double-blind, acute treatment phase, receiving fluoxetine 20–60mg or placebo. Change from baseline to endpoint in CY-BOCS total score was the primary efficacy measure. Additionally, fluoxetine's effects on secondary anxiety and depression and safety were analyzed.

Results: Fluoxetine was associated with statistically significantly greater reductions in CY-BOCS total score than placebo (p = 0.026). Fluoxetine-treated patients demonstrated significantly higher rates of response (defined as >=40% reduction in CY-BOCS total score) compared with placebo-treated patients (p = 0.030). Fluoxetine-treated patients experienced numerically, but not significantly, greater reductions in CY-BOCS obsessions subtotal than did placebo-treated patients (p = 0.102). For CY-BOCS compulsions subtotal, the difference between treatment groups was statistically significant in favor of fluoxetine (p = 0.015). Percentages of both serious adverse events were similar in fluoxetine- and placebo-treated groups.

Conclusion: Fluoxetine 20–60mg daily is effective and safe for treatment of OCD in children and adolescents.

NR623 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Paroxetine Treatment of Chronic PTSD With and Without Psychiatric Comorbidity

Katherine L. Beebe, Ph.D., *Department of Neurosciences, GlaxoSmithKline, 1250 South Collegeville Road, Collegeville, PA 19426-0989*; Mary Oldham, Ph.D., Kerry Dillingham, M.S.C., Cornelius D. Pitts, R.P.H., Rocco M. Zaninelli, M.D.

Summary:

Objective: To evaluate the effects of paroxetine on specific symptom severity in PTSD patients with and without comorbid mood and anxiety disorders.

Method: Data were pooled from the intent-to-treat populations of three 12-week, placebo-controlled, multinational studies conducted to evaluate the efficacy and tolerability of paroxetine 20mg–50mg daily. These were adult outpatients with chronic PTSD. Comorbidity was assessed with the Mini International Neuropsychiatric Inventory (MINI). Outcome measures were the change from baseline to study endpoint in the Clinician Administered PTSD Scale (CAPS-2) total score and the Sheehan Disability Scale (SDS) Work, Social Life, and Family Life scores.

Results: There were 416 patients with PTSD alone (PTSD-a) and 310 patients with PTSD plus a comorbid mood or anxiety disorder (PTSD-c). Reduction of the CAPS-2 total score was significantly greater for paroxetine than for placebo in both diagnostic groups (PTSD-a: −11.23, 95% CI [−15.99, −6.47], p < 0.001); (PTSD-c: −13.70, 95% CI [−19.99, −7.41], p < 0.001). Improvement in family and social life as assessed with the SDS, was also statistically greater for paroxetine-treated patients among both diagnostic groups. However, only for the PTSD-a group, was paroxetine statistically superior to placebo in improving work adjustment. Paroxetine was well tolerated by both groups, with no substantial difference in the incidence of adverse events.

Conclusion: Paroxetine is effective and well tolerated in the treatment of adult men and women with PTSD both with and without comorbid mood and anxiety disorders.

NR624 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Paroxetine Efficacy in Male and Female Patients with PTSD

Cornelius D. Pitts, R.P.H., *Department of Neurosciences, GlaxoSmithKline, 1250 South Collegeville Road, Collegeville, PA 19426-0989*; Katherine L. Beebe, Ph.D., Lee D. Ruggiero, B.S.C., Mary Oldham, Ph.D., Kerry Dillingham, M.S.C., Rocco M. Zaninelli, M.D.

Summary:

Objective: To evaluate the efficacy and safety of paroxetine in both male and female patients with posttraumatic stress disorder (PTSD) treated with paroxetine.

Method: Data were pooled from three randomized, double-blind, placebo-controlled trials (n = 1,180) investigating the efficacy and safety of paroxetine in the management of PTSD. These trials were of 12 weeks duration and evaluated paroxetine in dosages ranging from 20–50 mg daily. Primary efficacy measures were the Clinician Administered PTSD scale (CAPS-2), and the Clinical Global Impressions, global improvement item (CGI-I). Secondary measures included CAPS-2 symptom clusters, Davidson Trauma Scale (DTS), and the Sheehan Disability Scale (SDS). All patients were required to have a baseline CAPS-2 score of at least 50. The baseline scores for these efficacy parameters were similar for both genders.

Results: For male patients (n = 428), the mean difference between active and placebo treatments for the CAPS-2 total score (LOCF) was −8.93 (95% C.I.: [−14.10, −3.75]). For female patients (n = .752) the mean difference between treatments was −11.48 (95% C.I.: [−15.39, −7.57]). Both comparisons were statistically significant (p < 0.001) in favor of paroxetine. A responder analysis employing the CGI-I also showed statistical significance of paroxetine over placebo for both male and female patients (males: Odds/Ratio = 2.36 (95% C.I.: [1.57, 3.57]; females: Odds/Ratio = 2.20 (95% C.I.: [1.62, 2.99]; p < 0.001 for both genders). Both genders also demonstrated statistical significance for paroxetine over placebo in the CAPS-2 clusters, DTS, and SDS analyses. Paroxetine was well tolerated in both genders.

Conclusion: Paroxetine is an effective and well-tolerated treatment of PTSD in both male and female patients.

NR625 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Quality-of-Life Assessments in PTSD Treated with Paroxetine

Rocco M. Zaninelli, M.D., *Department of Neurosciences, GlaxoSmithKline, 1250 South Collegeville Road, Collegeville, PA 19426-0989, Germany*; Katherine L. Beebe, Ph.D., Lee D. Ruggiero, B.S.C., Mary Oldham, Ph.D., Kerry Dillingham, M.S.C., Cornelius D. Pitts, R.P.H.

Summary:

Objective: To evaluate improvements in quality of life (QOL) and psychosocial functioning in patients with posttraumatic stress disorder (PTSD) treated with paroxetine.

Method: Data were reviewed from two randomized, double-blind, placebo-controlled, 12-week studies to assess improvements in quality of life during the treatment of PTSD. One study employed a flexible dosage range of paroxetine (20–50mg), while the other used a fixed-dose strategy (20 mg and 40 mg). QOL and overall PTSD efficacy were interrogated as follows:

- Sheehan Disability Scale (SDS) total score and SDS individual item scores assessing work life, social life, and family life.
- Specific items of the CAPS-2 assessing subjective distress, social and occupational functioning.
- Clinician Administered PTSD Scale (CAPS-2) total score.

Results: In the flexible dose study (n = 307), the improvement in the paroxetine SDS total score was significantly larger compared with placebo (difference = –2.6 [95% C.I. = –4.4, –0.7] p = 0.007). Also, the SDS items assessing work, social and family life significantly favored paroxetine. The CAPS-2 items assessing subjective distress, social and occupational functioning also demonstrated statistical advantage for paroxetine over placebo. In the fixed-dose study (n = 551), improvement in the SDS total score for paroxetine was significant relative to placebo for both the 20mg and 40mg treatments (difference = –2.44 [95% CI = –4.12, –0.76] p = 0.005; difference = 1.98 [95% CI = 3.70, –0.26] p = 0.024 respectively). The SDS social and family life and CAPS-2 quality-of-life items were all significant in favor of paroxetine compared with placebo for both doses. In both studies, these QOL data parallel the overall efficacy demonstrated by statistically significant superiority achieved for paroxetine in the CAPS-2 total score analyses.

Conclusion: Successful treatment of PTSD with paroxetine is associated with improvement in QOL domains as well as pharmacologic efficacy.

NR626 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Insight as a Predictor of Outcome in Behavioral Group Therapy for OCD

Joseph A. Himle, Ph.D., *Department of Psychiatry, University of Michigan, 1500 East Medical Center Drive, Ann Arbor, MI 48109-0840*; Amy S. Janeck, Ph.D., Daniel Fischer, M.S.W., Michelle L. Van Etten, Ph.D.

Summary:

Poor insight into the senselessness of symptoms of obsessive-compulsive disorder (OCD) has been theoretically linked to poor treatment response, yet few studies have examined this directly. Sixty-four OCD patients who completed 7 weeks of cognitive behavioral group therapy participated in this study. Patients completed the Yale-Brown Obsessive Compulsive Scale (Y-BOCS) and other measures of psychopathology. Insight was measured using question #11 on the Y-BOCS scale ("Do you think your concerns are reasonable?"). After controlling for pretreatment levels of symptom severity, depression, age, and gender, patients with "excellent to good insight" (N = 47) experienced better post-treatment outcomes (mean = 13.4) than those with "fair to poor insight" (N = 17; mean = 21.2; p = 0.02). The group with less insight reported a "moderate" level of symptoms, whereas the group with better insight reported a "mild" level of symptoms posttreatment. The data suggest that patients with poorer insight can still benefit from treatment but may experience a less favorable outcome. This indicates a need to assess insight and apply interventions accordingly. This presentation is intended for clinicians and clinical researchers interested in treatment for obsessive-compulsive disorder.

NR627 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Sertraline in PTSD: Temporal Pattern of Response

Cathryn M. Clary, M.D., *CNS Medical, Pfizer, Incorporated, 235 East 42nd Street, 235/10/20, New York, NY 10017-5755*; Jonathan R.T. Davidson, M.D., Lawrence R. Landerman, Ph.D., Gail Farfel, M.D.

Summary:

Objective: The objective of the study was to analyze the temporal pattern of response among core PTSD symptom clusters.

Methods: Pooled data were analyzed from two double-blind, placebo-controlled sertraline treatment studies of patients meeting DSM-III-R criteria for posttraumatic stress disorder (PTSD).

Results: 191 patients were treated with sertraline (80% female; mean age = 39 years), and 194 patients were treated with placebo (72% female; mean age = 38). F-values for the treatment group by time interaction for the four core PTSD symptom clusters found the strongest effect for numbing (F = 24.0), followed by hyperarousal (F = 15.4) and avoidance (F = 10.4), with a weak but still significant sertraline versus placebo effect for intrusion (F = 7.0). Results found improvement in PTSD symptomatology due to sertraline occurred in a distinct, temporal progression, with initial damping of hyperarousal followed, successively, by improvement in symptoms of numbing, intrusions, and avoidance. Much of the early benefit of sertraline in treating the hyperarousal cluster derived from improvement in symptoms of anger and hostility.

Conclusion: Sertraline was found to have a differential treatment effect on the core PTSD symptom clusters, both in terms of effect size and the time sequence of improvement.

NR628 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Sertraline Versus Imipramine Treatment of Comorbid Panic Disorder and Major Depression

Mihaly Arato, M.D., *Department of Psychiatry, University of Calgary, 1403 29th Street, NW, Calgary, AB T2N 2T9, Canada*; Ulla M. Lepola, M.D., Carol Austin, M.D.

Summary:

Objective: The objective of the study was to evaluate the efficacy and tolerability of sertraline and imipramine in patients with panic and depression comorbidity.

Methods: Patients meeting a DSM-IV diagnosis of panic disorder and concurrent major depression were randomly assigned in a 2:1 ratio to 26-weeks of double-blind treatment with either sertraline or imipramine. Primary outcome measures were panic attack frequency and the Montgomery-Åsberg Depression Rating Scale (MADRS) score.

Results: 138 patients were treated with sertraline (76% female; age in years: 40.3, SD = 10.4; mean weekly frequency of full panic attacks: 7.2, SD = 8.9; mean MADRS score: 28.5, SD = 5.4), and 69 patients were treated with imipramine (70% female; age in years: 40.3, SD = 9.8; mean weekly frequency of full panic attacks: 7.2, SD = 9.9; mean MADRS score: 28.7, SD = 5.4). Both the

symptoms of panic disorder and of major depression responded significantly and equivalently to both sertraline and imipramine. Among study completers, CGI-I responder rates were 87% with sertraline and 91% with imipramine. Overall, sertraline was better tolerated with fewer discontinuations due to adverse events (12% versus 23%, $p < 0.05$).

Conclusion: Both sertraline and imipramine were found to be highly effective treatments for both panic disorder and major depression.

NR629 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Effectiveness of Sertraline in the Long-Term Treatment of Panic Disorder: Treatment Response, Sexual Functioning, and Weight Gain

Robert B. Pohl, M.D., *Department of Psychiatry, Wayne State University, 2751 East Jefferson, Suite 200, Detroit, MI 48207*; Peter J. Holland, M.D., Henry Chung, M.D., Cathryn M. Clary, M.D.

Summary:

Objective: The objective of the current analysis was to examine clinical response and tolerability in panic disorder patients receiving sertraline for up to 90 weeks.

Methods: Data were drawn from a multicenter relapse prevention trial that had followed three acute (10-week) double-blind, placebo-controlled studies of sertraline for the treatment of panic disorder. The acute trials were followed by an additional 52 weeks of open-label sertraline treatment, then responders (CGI-I of 1 or 2) were reassigned randoms to drug or placebo. Tolerability, including weight change (utilizing body mass index—BMI) and sexual dysfunction (including patient-rated satisfaction) were examined in patients receiving sertraline for ≥62 weeks.

Results: 189 sertraline patients completed 10 weeks of treatment; 76% were classified as CGI responders. At week 62, 97.5% of completers maintained their response; of the nonresponders, 57% (N = 44) became responders by week 26. 41 patients received sertraline for 62–90 weeks, of these, 36.5% reported a sexual adverse event; by the last visit, all but one patient had complete resolution of the sexual side effect, and 80% maintained/improved their sexual satisfaction compared to baseline. 76% maintained or improved their BMI toward the ideal range. No patients of normal weight at baseline became obese over the long term.

Conclusion: Long-term sertraline treatment for panic disorder was effective and generally well-tolerated; sexual side effects resolved over time, and severe weight change leading to BMI obesity was minimal.

This work was supported by Pfizer, Inc.

NR630 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Does Treatment with SSRIs Block the Behavioral and Physiological Effects of Pentagastrin?

Christina M. Morgan, M.A., *Department of Psychiatry, UF de Sao Paulo, R Botucatu 740, Sao Paulo, SP 04023-900, Brazil*; Marilla Geraci, M.S.N., Josette Desfayes, M.S.N., Robert M. Post, M.D., Una D. McCann, M.D.

Summary:

Introduction: Pentagastrin, a cholecystokinin agonist, produces anxiety and panic in patients with panic disorder and social phobia. Previous studies have suggested that pentagastrin-induced anxiogenesis may be mediated via the 5HT system. This study sought to determine the effects of treatment with selective serotonin reuptake inhibitors (SSRIs) on the response to pentagastrin in patients with anxiety disorders.

Methods: 18 subjects with panic disorder (N = 9) or social phobia (N = 9) underwent placebo and pentagastrin challenges in random order before and after at least 8 weeks of open treatment with a stable dose of fluoxetine or sertraline. Behavioral, cardiovascular, and neuroendocrine responses were obtained.

Results: Comparisons of pre- and posttreatment ratings show significant clinical improvement with SSRI treatment. As expected, pentagastrin infusion led to increases in anxiety, physical symptoms of panic attacks, pulse rate, cortisol, and ACTH. Pentagastrin's behavioral and cardiovascular effects were not attenuated by treatment with SSRIs. Treatment with SSRIs did not alter the pentagastrin-induced cortisol increase but significantly delayed the pentagastrin-induced ACTH increase ($p = 0.046$).

Discussion: Treatment with SSRIs does not block pentagastrin-induced anxiety in subjects with panic disorder and social phobia but may alter patterns of pentagastrin-induced hormonal response. These findings suggest that pentagastrin's behavioral effects are not mediated via the 5HT system.

NR631 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

PTSD and MDD: The Role of Overlapping Symptoms in Diagnostic Comorbidity

C. Laurel Franklin, M.S., *Department of Psychiatry, Rhode Island Hospital, 235 Plain Street, Suite 501, Providence, RI 02905*; Mark Zimmerman, M.D.

Summary:

Objective: Studies of PTSD have found high levels of comorbid major depression (MDD). One reason suggested for the high comorbidity is the symptom overlap between PTSD and MDD. The present study, from the Rhode Island Hospital MIDAS project, investigated the contribution of the three PTSD-MDD overlapping symptoms (anhedonia, concentration problems, and sleep problems) to the diagnosis of PTSD.

Method: A sample of 393 psychiatric outpatients who reported experiencing a traumatic event on the Structure[4] Clinical Interview for DSM-IV (SCID) were used in these analyses. Sensitivity and specificity of the PTSD criteria were calculated. In a separate analysis, the frequency of the PTSD symptoms was compared in patients with and without MDD. This analysis was done for all patients reporting a trauma and for only those patients diagnosed with PTSD.

Results: Results from the first analysis showed that the PTSD-MDD overlapping symptoms were no less specific than the symptoms unique to PTSD. Further, in both samples the PTSD-MDD overlapping symptoms were not more frequent in depressed patients compared to non-depressed patients. The total number of PTSD symptoms and total number of PTSD-MDD overlapping symptoms was also similar in the depressed and non-depressed patients.

Conclusions: These analyses suggest that the comorbidity of PTSD and MDD is not due to contamination by overlapping symptoms but due to true comorbidity between the disorders. Other possible explanations for PTSD-MDD comorbidity and implications for these finding on diagnosis and treatment of PTSD are discussed.

NR632 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Obsessive-Compulsive Symptoms in Patients with Panic Disorder

Albina R. Torres, *Department of Psychiatry, FMB UNESP, Rubiao JR, Botucatu, SP 18618-970, Brazil*; Andre M. Dedomenico, Andre L. Crepaldi

Summary:

Comorbidity studies show an important association between panic disorder (PD) and obsessive-compulsive disorder (OCD). This partial clinical overlap can be due to common biological and

psychological mechanisms. In OCD, panic attacks may occur secondarily to the feared stimuli and, in PD, superstitious behaviors can occur as an attempt to "control" the unpredictable attacks. The aim of this study was to systematically evaluate the occurrence of OC symptoms and OCD in patients with PD (DSM-IV criteria) from Bolucatu Medical School-UNESP, São Paulo, Brazil. The instrument used was the Yale-Brown Obsessive-Compulsive Scale. From the 30 patients that were evaluated (15 men and 15 women) 26.6% (N = 8) had subclinical OC symptoms (YBOCS score < 8) and 26.6% (N = 8) had comorbid OCD. Among those with PD only, some still had OC symptoms (particularly aggressive obsessions) but only during the panic attacks. In conclusion, it is important to evaluate the co-occurrence of OC symptoms in every patient with PD and vice versa due to the important symptomatologic overlap found. As panic symptoms are usually the main complaint, many times OC symptoms are found only when directly investigated, and this may have implications for the treatment and prognosis of the cases.

NR633 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Efficacy and Tolerability of Paroxetine for Long-Term Treatment of GAD

Fabrizio Stocchi, M.D., *S. Raffaele Hospital, Vicolo Sciarra 61, Roma 00187, Italy*; Giampietro Nordera, Rita Jokinen, Ulla M. Lepola, M.D.

Summary:

Paroxetine has demonstrated efficacy in the treatment of depression and anxiety disorders, including GAD. In order to further assess the efficacy and safety of paroxetine in the treatment of GAD, a long-term study was undertaken that evaluated the maintained efficacy of paroxetine in the treatment of GAD, by assessing the potential for relapse after discontinuation of medication. A total of 652 adult patients with DSM-IV GAD and a CGI Severity of Illness score of 4–7 (moderately to extremely ill) received paroxetine (20–50 mg/day) for eight weeks. Patients whose CGI severity of illness score had decreased by at least two points to a score of 3 or less at the week 8 visit were then randomized to double-blind treatment with either paroxetine (n = 278) or placebo (n = 288) for a further 24 weeks. The primary efficacy parameter was the proportion of patients relapsing during double-blind therapy (defined as either an increase in CGI severity of illness score of at least two points to a score of 4 or more or withdrawal due to lack of efficacy). The results of this study clearly demonstrate the maintained efficacy of paroxetine for the prevention of relapse of GAD. Significantly fewer paroxetine- than placebo-treated patients relapsed during the 24 weeks of double-blind therapy (10.9% versus 39.9%, respectively; $p < 0.001$). Statistical significance in favor of paroxetine was also demonstrated for all secondary efficacy parameters. Paroxetine was well tolerated, with no unexpected adverse events reported during this eight-month study.

NR634 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

The Effectiveness and Safety of Combined Treatment with Paroxetine and Clonazepam Compared with Paroxetine Alone for Panic Disorder

Mark H. Pollack, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC-812, Boston, MA 02114*; Naomi M. Simon, M.D., Michael W. Otto, Ph.D., John J. Worthington III, M.D., Fany S. Toshkov, B.A.

Summary:

Background: The serotonin selective reuptake inhibitors (SSRIs) have become first-line pharmacotherapy for panic disorder. Although many patients receiving SSRIs and other antidepressants for panic disorder are concomitantly prescribed benzodiazepines, there has been relatively little systematic assessment of the safety and effectiveness of this strategy. Previous studies suggested faster onset of efficacy with combined treatment, though rapid benzodiazepine taper resulted in withdrawal difficulties. No studies to date have examined the relative efficacy of continued combined treatment.

Method: The study is a double-blind, randomized, placebo-controlled, three-arm, 12-week trial comparing the efficacy of paroxetine 40 mg/d) combined with clonazepam (2 mg/d), to paroxetine plus placebo in patients with panic disorder. The clonazepam was administered either (1) acutely over five weeks and then tapered, or (2) maintained during the 12-week trial. The study also examined the safety of these treatment strategies including emergence of withdrawal symptomatology in patients tapering the benzodiazepine.

Results: Eighty patients were screened and 61 randomized to treatment. Preliminary analysis suggests equivalent and significant improvement in all three groups by 12 weeks with more rapid effects in the combined treatment groups. Withdrawal symptomatology was not prominent during or after the conservative taper schedule.

Conclusions: Combined paroxetine-clonazepam therapy compared with the SSRI alone seems to accelerate response during the acute phase of treatment; maintaining combined therapy over time may not accrue additional benefit.

NR635 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Effect of the Novel Selective Noradrenaline Reuptake Inhibitor Reboxetine on Anxiety

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Summary:

Objectives: The selective NRI reboxetine has proven to be an effective and well tolerated treatment for MDD. The efficacy of reboxetine in the treatment of other affective disorders, particularly anxiety and panic disorder, has also been examined.

Methods: The effect of reboxetine treatment on anxiety associated with MDD was assessed in an eight-week, double-blind, randomized, placebo-controlled trial in adults. Patients were randomized to receive reboxetine (8 mg/day; n = 126), fluoxetine (20–40 mg/day; n = 127) or placebo (n = 128). Aggregate scores on the HAM-D anxiety items 10 and 11 at last assessment were compared with baseline.

Results: Reboxetine proved at least as effective as fluoxetine in reducing anxiety related to depression, and significantly more effective than placebo ($p < 0.01$). In a separate study, the efficacy of reboxetine in the treatment of panic disorder was examined. Adult patients with panic disorder (DSM-IV) were randomized to receive reboxetine (6–8 mg/day) or placebo for up to eight weeks. Reboxetine proved significantly more effective than placebo in reducing the number of major panic attacks ($p < 0.001$) and in reducing phobic symptomatology ($p = 0.004$).

Conclusions: These results suggest that reboxetine may be a favorable choice in the treatment of anxiety associated with MDD and in the management of panic disorder.

NR636 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Augmentation of SSRI Response in Refractory OCD Using Adjunct Olanzapine: A Placebo-Controlled Trial

Alexander Bystritsky, M.D., *Department of Psychiatry, University of California at Los Angeles, 300 UCLA Medical*

Plaza, #2340, Los Angeles, CA 90095; Deborah L. Ackerman, Ph.D., Richard M. Rosen, M.D., Tanya Vapnik, Ph.D., Eda Gorbis, Karron M. Maidment, R.N., Sanjaya Saxena, M.D.

Summary:

Twenty-six patients meeting DSM-IV criteria for OCD, who had not responded to SRIs, were treated for six weeks in a double-blind, placebo-controlled augmentation study with either olanzapine (up to 20 mg/day) or placebo. Severity of illness was assessed bi-weekly by the Yale-Brown OCD Scale (Y-BOCS) and by Clinical Global Impressions/Improvement (CGI). Linear regression was used to compare improvement on the Y-BOCS. Logistic regression was used for dichotomous outcomes, which were defined as at least a 25% or 35% improvement on the Y-BOCS, or a CGI rating of much improved. Outcome was assessed for all patients using the last observation carried forward. The subjects in the olanzapine group had a mean decrease of 4.7 (s.d. = 2.2) in Y-BOCS compared with a mean increase of 0.54 (s.d. = 0.36) in the placebo group ($p = 0.05$). Six subjects (46%) in the olanzapine group showed a 25% or greater improvement in Y-BOCS score: five improved at least 35%, and four of these were much improved on the CGI. None in the placebo group met any criteria for response. The results indicate the efficacy of adding olanzapine to SRIs in treatment-resistant OCD.

NR637 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

GAD in Primary Care

William J. Korotitsch, M.A., *Department of Psychiatry, Brown University, Box G-BH Duncan Building, Providence, RI 02912*; Risa Weisberg, Ph.D., Jason Machan, M.A., Larry Culpepper, M.D., Martin B. Keller, M.D.

Summary:

Features of generalized anxiety disorder (GAD) are examined in primary care patients who were sampled from 15 general medical practices. Of the 474 participants meeting criteria for one of seven anxiety disorders assessed with the SCID-IV, 130 (27%) were diagnosed with GAD. Compared with primary care patients with other anxiety disorders, patients with GAD reported more negative perceptions of their overall mental health, and evidenced high rates of comorbid anxiety disorders. 62% of the patients with GAD had at least one coexisting anxiety disorder as opposed to 46% of those participants with other anxiety disorders (Chi-square = 9.19, $p < .01$). Additionally, GAD patients had a significantly greater number of coexisting psychiatric disorders ($z = 2.09$, $p < .05$). The age of onset for GAD was highly variable with an average of 22.7 years. When a comorbid anxiety or depressive disorder was present, GAD typically had an earlier onset. These findings indicate that primary care patients with GAD may evidence greater levels of overall psychopathology as compared with patients with other anxiety disorders. Implications of these findings for detection and intervention within primary care settings will be discussed.

PCAP is funded through an unrestricted grant from Pfizer Pharmaceuticals.

NR638 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Cognitive-Behavioral Therapy in Panic Disorder: A PET Study

Martin A. Katzman, M.D., *Anxiety Clinic, Clarke Institute-CAMH, 250 College Street, Toronto, ON M5T 1R8, Canada*; Joanna C. Jeffers, M.A., Karyn E. Hood, M.Ed., Richard P. Swinson, M.D., Martin M. Antony, Ph.D., Gregory M. Brown, M.D., Doug Hussey, B.S.C.

Summary:

Introduction: Functional imaging studies have demonstrated correlations between regional cerebral blood flow (rCBF) and anticipatory anxiety. Meyer et al. (1998) examined brain serotonin activity in major depression and panic disorder with agoraphobia (PDA) using [^{15}O]—H_2O positron emission tomography (PET) before and after intravenous (IV) administration of d-fenfluramine. At baseline, subjects with PDA showed relatively increased rCBF in the right posterior temporal lobe associated with scanner anxiety alone. Javanmard et al. (1999) found increased rCBF in the anterior cingulate associated with the expectation of a potentially uncomfortable experience.

Objective: This study examines changes over time on PET in PDA patients receiving cognitive behavioral therapy (CBT). We examined 1) whether a site of altered brain function could be visualized, and 2) whether this change would be normalized by treatment.

Method: We compared rCBF using PET in seven female outpatients with DSM-IV criteria for PDA before and after 16 weeks of CBT: PET data was analyzed using statistical parametric mapping (SPM) and was coregistered with individual MRIs.

Results: Caudate rCBF was significantly reduced in treated PDA patients compared to non-treated PDA patients.

Conclusions: Data suggest functional involvement of the bilateral caudate in PDA. This study was funded by the Medical Research Council.

NR639 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Social Anxiety Symptoms and the Blushing Response in Social Phobias and Healthy Controls

Martin A. Katzman, M.D., *Anxiety Clinic, Clarke Institute-CAMH, 250 College Street, Toronto, ON M5T 1R8, Canada*; Monica Vermani, M.A., Bronwen Hughes, B.A., Aimee M. Coonerty-Femiano, B.A., Sylvie Turenne, M.A., Brian M. Ross, Ph.D.

Summary:

Elevated vasodilatatory response (blushing) to social situations is a pathomnemonic feature of social phobia. A relatively unexplored basis for this phenomenon is an alteration in the underlying vasodilatory mechanisms. To investigate this possibility, we evaluated the vasodilatory response induced by methyl nicotinate, the methyl ester derivative of niacin, in patients with social phobia ($n = 20$) and in matched healthy controls ($n = 31$). A patch impregnated with 0, 0.1, 0.5, 1, or 10 mM methyl nicotinate was applied to the subjects forearm or face for one minute, followed by a 20-minute period during which blood flow was monitored using a laser Doppler spectroscope. The extent of stimulation of blood flow induced by 0.5 and 10 mM methyl nicotinate was significantly (2-way ANOVA; $P < 0.01$) reduced in patients with social phobia by 31% and 18%, respectively. Moreover, induced blood flow was negatively and significantly ($P < 0.05$) correlated with Leibovitz social phobia scores (Spearman correlation coefficient = –0.61) at the 10 mM dose, with a trend for correlation ($r = -0.43$) using the 1 mM dose. Furthermore, the maximal rate of change of the vasodilatatory reaction, as assessed using non-linear curve fitting, was highly correlated with symptom scores at both the 10 mM ($r = -0.79$) and 1 mM ($r = -0.71$) doses. Preliminary experiments have also suggested that induced increases in arm blood flow correlates with that recorded on the subjects face, suggesting that the more conveniently studied arm response is indicative of the face, the major location of social stress associated blushing. Our data suggest that patients with social phobia vasodilatate less when challenged topically with methylnicotinate, and that this effect is most pronounced in the most severely ill subjects. Although the mechanism underlying this effect is unclear, a desensitisation of vasodilatation is suggested.

NR640 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Efficacy of Venlafaxine Extended Release in Treating the Somatic Symptoms of GAD

David Hackett, M.S.C., *CNS, Wyeth Ayerst, 80 Avenue du General de Gaulle, Paris La Defense 92031, France*; Jill G.C. Rasmussen, M.D., Paolo Meoni, Ph.D.

Summary:

Somatic and psychic symptoms of anxiety have been suggested to have different sensitivities to pharmacotherapy. The efficacy of venlafaxine XR in treating the somatic symptoms of GAD in patients with mainly somatic symptoms at baseline was assessed in this analysis using the somatic factor of the HAM-A.[1]

At baseline 83.6% of the 1,841 patients from five double-blind (two with long-term extensions), multicenter, placebo-controlled studies of venlafaxine XR efficacy in GAD[2] had a somatic/psychic factor scores ratio ≤1. After 8 weeks of treatment, "somatizers" (somatic/psychic factors ratio >1) did not show any difference in response rates (≤50% from baseline) to venlafaxine XR on the somatic or psychic factors (54% and 58% non-somatizers and 63% and 58% somatizers were somatic and psychic responders, respectively). In the two 6-month study extensions, analysis of 767 participating patients indicated a somatic and psychic response rate increase with venlafaxine XR in patients with mainly somatic symptoms (65% and 64% non-somatizers and 77% and 75% somatizers were somatic and psychic factor responders, respectively).

The present study supports the efficacy of venlafaxine XR in GAD, including those patients with predominantly somatic symptomatology.

NR641 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

PTSD and Quality of Life: Results Across 64 Weeks of Sertraline Treatment

Mark H. Rapaport, M.D., *Department of Psychiatry, UCSD School of Medicine, 8950 Villa La Jolla Dr, #2243, La Jolla, CA 92037*; Jean Endicott, Ph.D., Cathryn M. Clary, M.D.

Summary:

Objective: To determine the quality of life outcome for patients receiving long-term treatment with sertraline for moderate-to-severe PTSD.

Design: Improvements in quality of life (QOL)/psychosocial functioning were analyzed across 64 weeks (a 12-week double-blind acute phase, a 24-weeks open-label continuation phase, and a 28-week double-blind relapse prevention phase of flexible-dose sertraline treatment (50–200 mg/day). Assessments included the Quality of Life Enjoyment and Satisfaction Questionnaire (Q-LES-Q), factors from the Medical Outcomes Study (MOS) SF-36, as well as the occupational and social functioning items on the CAPS-2 scale. The impact of comorbidity, gender, and other correlates of quality of life at baseline were also examined using logistic regression.

Results: QOL was significantly impaired at baseline. By the end of the initial 12-weeks, sertraline treatment resulted in significant improvements in all QOL/functional outcomes, with 72% of sertraline-treated patients achieving within 10% of community norms on the Q-LES-Q total score compared to 31% treated with placebo. Baseline CAPS-2 severity (partial $R^2 = 0.248$) was the most significant determinant of QOL impairment, although the severity of QOL/functional impairment at acute baseline was not associated with reduced treatment response at 12 weeks. Progressive but modest improvements occurred across the later phases of treatment. Severity of residual QOL/functional impairment did not predict increased risk of relapse during final 28 weeks of placebo-controlled treatment.

NR642 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Elevated Serum Cholesterol Levels in OCD Patients Compared with Phobic Patients and Normal Controls

Helmut Peter, M.D., *Department of Psychiatry, University of Hamburg, Martinistrasse 52, Hamburg 20246, Germany*; Fritz Hohagen, M.D., Almut Koenig, M.D.

Summary:

Objective: Serum cholesterol levels in panic disorder patients are reported to be elevated. There is some evidence that also patients with GAD and agoraphobia have increased serum cholesterol levels. So far, there have been only two reports on cholesterol levels of OCD patients, giving controversial results.

Method: Serum cholesterol levels of OCD patients, phobic patients (mainly agoraphobia with or without panic disorder) and normal control subjects were compared with each other (N = 60 in each group). Serum cholesterol were measured in each subject. Subjects of the three groups were matched by age and gender.

Results: 1. Patients with OCD had elevated cholesterol levels compared to normal control subjects. 2. Cholesterol levels in OCD patients were comparable to those in phobic patients.

Conclusion: Our data support the assumption that elevation in cholesterol level is not a specific feature of panic disorder as mostly assumed but is more generally associated with anxiety disorders. Increased cholesterol levels in patients with OCD and phobic disorders may be of clinical relevance. Yet, it is not clear whether cholesterol elevation in anxiety disorder patients is a state or a trait factor.

NR643 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Expressed Emotion and Spouse Interaction Predicting Outcome of Exposure in Vivo in Female Agoraphobic Patients

Helmut Peter, M.D., *Department of Psychiatry, University of Hamburg, Martinistrasse 52, Hamburg 20246, Germany*; Grazyna Kaiser, Ph.D., Iver E. Hand, M.D.

Summary:

Research regarding the influence of marital problems on the course of agoraphobia has produced controversial results, possibly due to problems in assessing a relationship.

Method: We applied the Camberwell Family Interview to measure expressed emotion and additionally an assessor rating of spouse interaction in 33 female agoraphobic patients with or without panic disorder. We compared these data with the results of marital self-rating questionnaires. Patients were treated with exposure in vivo.

Results: High expressed emotion (HEE) at pretreatment, mainly the criticism of the patients, and patients' interaction style, particularly rejective behavior, were associated with non-response at follow-up. Marital self-ratings did not correlate with treatment results. If both patients and spouses scored high on criticism, positive treatment response occurred only in patients where marital patterns changed significantly (e.g., separation) during treatment or follow-up.

Discussion: Our data support the assumptions that marital problems are involved in the maintenance of agoraphobia and that marital self-ratings fail to show this association. Treatment response of patients in HEE-couples require a change in marital patterns. However, surprisingly 50% of HEE couples solved their marital problems after exposure without any specific intervention. The experience in mastering their agoraphobic anxieties may have encouraged these patients to successfully tackle their marital conflicts.

This study was supported by the "Deutsche Forschungsgemeinschaft"

NR644 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Paroxetine Treatment of PTSD: Effects on Cortisol, Physiologic Reactivity, and Emotional Symptoms

Phebe M. Tucker, M.D., *Department of Psychiatry, University of Oklahoma, 920 Stanton Young Boulevard, WP3440, Oklahoma City, OK 73190*; Kurt L. Smith, M.A., Mangalore N. Pai, M.D., Dan E. Jones, Ph.D., Dorothy B. Wyatt, R.N., Katherine L. Beebe, Ph.D., Gary K. Borrell, M.D.

Summary:

Objective: Effects of paroxetine treatment of PTSD on psychometrics, autonomic reactivity, and cortisol were examined.

Method: Twenty-five outpatients with PTSD (CAPS-1, score ≥50), 15 depressed outpatients, and 16 traumatized, mentally healthy control subjects were recruited by advertisements. All were healthy and not taking psychotropic or cardiovascular medications. SCID-P assessed axis I diagnoses. Baseline measures of PTSD (CAPS-1), depression (BDI), 8 a.m. and 4 p.m. salivary cortisol levels, and heart rate and blood pressure responses (Lablink) to taped trauma scripts were obtained for all. Twenty-two PTSD patients received open-label paroxetine treatment, 20–50 mg/day for 10 weeks, with all assessments repeated. Three subjects discontinued.

Results: PTSD patients did not differ from control subjects in baseline a.m. or p.m. cortisol level. PTSD patients lacked diurnal cortisol variation (difference between AM and PM, $p = 0.191$, N.S.), whereas depressed ($p < 0.0001$) and traumatized control subjects ($p = 0.001$) had significant differences.

After medication, PTSD patients improved significantly in PTSD (CAPS totals, $p < 0.0001$) and three cluster subscales ($p < 0.0001$), depression ($p < 0.0001$) and sleep ($p = 0.001$). Heart rate ($p < 0.0001$) and systolic ($p < 0.0001$) and diastolic ($p = 0.005$) blood pressure reactivity decreased. Treated PTSD patients did not acquire diurnal cortisol variation ($p = 0.163$). However, among biological measures, change in diurnal variation was most predictive of improvement with treatment (Pearson's correlation coefficient: $r = 0.6986$, $p = 0.008$; multiple regression analysis: multiple $R = 0.708$, $t = 2.8$, $p = 0.02$).

Conclusion: Open-label paroxetine treatment improved subjective and objective (autonomic) PTSD measures. Neuroendocrine changes may occur more slowly with treatment of PTSD or may be independent of autonomic reactivity and emotional symptoms in PTSD's pathophysiology.

NR645 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

SSRIs Versus Tricyclic Antidepressants in the Treatment of Panic Disorder: A Meta-Analysis

Abraham Bakker, M.D., *Department of Psychiatry, St Lucas Hospital, Jan Tooropstraat 164, Amsterdam 1061-AE, Netherlands*; Anton J.L.M. Van Balkom, M.D., Philip Spinhoven, Ph.D.

Summary:

Objective: To compare the short-term efficacy of SSRIs versus TCAs in the pharmacological treatment of panic disorder, a meta-analysis was conducted.

Method: Included were 43 studies, pertaining to 53 treatment conditions, 2,367 patients at pretest and 1,804 at post-test. Outcome was measured with the proportion of patients becoming panic free, and with pre/post Cohen's *d* effect sizes, calculated for four clinical variables: panic, agoraphobia, depression, and general anxiety.

Results: There were no differences between SSRIs and TCAs on any of the effect sizes, indicating that both groups of antidepressants are equally effective in reducing panic symptoms, agoraphobic avoidance, depressive symptomatology, and general anxiety. Also the percentage of patients free of panic attacks at posttest did not differ. The number of dropouts, however, was significantly lower in the group of patients treated with SSRIs (18%, versus TCAs 31%).

Conclusion: Compared with TCAs, SSRIs are the first choice in the treatment of panic disorder.

NR646 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

A Description of Skin Picking in an OCD Population

Margaret A. Richter, M.D., *Anxiety Clinic, CAMH-Clarke Division, 250 College Street, Room 1148, Toronto, ON M5T 1R8, Canada*; Joanna C. Jeffers, M.A., Laura J. Summerfeldt, Ph.D.

Summary:

Compulsive skin picking (SP), also known as neurotic excoriation, has been identified as a common comorbid condition in individuals with obsessive-compulsive disorder (OCD); however all published descriptions of skin pickers have ascertained subjects via dermatology and general hospital clinics. To examine the clinical phenomenology of patients both with OCD and skin picking behavior, 22 outpatients meeting. DSM-IV criteria for OCD were identified with clinically significant SP. SP subjects had a mean +/– SD age of onset of 12.5 years +/– 7.3. The most frequent sites of picking were face (21%), hands and cuticles (16%), and feet (11%); 50% of subjects reporting picking at more than one site. Rates of comorbidity were high. The most common concurrent Axis I disorders were social anxiety disorder (55%), body dysmorphic disorder (32%), and specific phobia (27%). However, when subclinical and life-time diagnoses were included, there was significant comorbidity with tic disorders (45%). OCD participants with comorbid SP appeared comparable to primary skin pickers described in the literature. However, unlike previous studies, a significant overlap with tic disorders was identified, providing support for conceptualization of this condition as one of the OCD spectrum disorders. The implications of these findings will be discussed further.

NR647 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

The Y-Aminobutyric Acid Type A (GAMA a-y2) Receptor Gene in OCD

Margaret A. Richter, M.D., *Anxiety Clinic, CAMH-Clarke Division, 250 College Street, Room 1148, Toronto, ON M5T 1R8, Canada*; Emanuela Mundo, M.D., Fariba Sam, B.S.C., Richard P. Swinson, M.D., James L. Kennedy, M.D.

Summary:

Objective: The γ-aminobutyric acid type A ($GABA_A$) system is implicated in obsessive-compulsive disorder (OCD), based on its major role in modulation of anxiety and its function as the principal inhibitory neurotransmitter system in the cortex. The $GABA_A$-γ2 receptor may also be in linkage disequilibrium with the HLA region. Thus, in light of recent interest in autoimmune mechanisms in OCD, the $GABA_A$-γ2 is a candidate gene for this disorder by virtue of its function and proximity to HLA.

Method: A total of 118 probands meeting DSM-IV criteria for OCD and their living parents were recruited for participation in this study and informed consent was obtained. A Neil restriction site polymorphism in the second intron was genotyped and data analyzed using the Transmission Disequilibrium Test (TDT).

Results: In total, 61 of the participating families were informative (ie, with at least one heterozygous parent). No biases were observed in the transmission of either of the two alleles ($\chi^2 = 0.276$, $df = 1$, $p = 0.599$) to the affected probands.

Discussion: While these results do not provide support for a major role for the $GABA_A$-γ2 receptor in OCD, further investiga-

tions with alternative phenotypes (early-onset, streptococcal-related) are-warranted.

This work was funded by the Ontario Mental Health Foundation.

NR648 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Comparison of the Efficiency of Two Treatment Outcome Instruments in Panic Disorder

Vladan Starcevic, M.D., *Hunter Mental Health Service, James Fletcher Hospital, 29 Smith Street, Charlestown 2290 NSW, Australia*; Milan Latas, M.D., Dusan Kolar, M.D., Goran Bogojevic, M.D.

Summary:

Objective: The assessment of the outcome of treatment of panic disorder (PD) has recently been improved by introduction of the Panic and Agoraphobia Scale (PAS) and Panic Disorder Severity Scale (PDSS). The goal of this study was to compare the efficiency of these instruments for measuring the outcome of treatment of PD.

Method: A total of 96 patients with PD were treated with cognitive-behavior therapy (CBT) and pharmacotherapy. CBT was performed over the course of 16 sessions, followed by "booster" sessions once a month. Pharmacotherapy involved an eight-month course with an SSRI plus a six-week initial treatment with a high-potency benzodiazepine. The scores on the PAS and PDSS were obtained at baseline and after eight months of treatment.

Results: Patients showed a significant improvement on both the PAS and PDSS scores. However, the magnitude of the improvement ($p = 0.002$) was greater when the differences between the PAS scores at baseline and post-treatment were compared with the differences between the PDSS scores at baseline and post-treatment ($p = 0.03$). The improvement demonstrated by the PAS correlated more closely with clinical observations.

Conclusions: The difference between the efficiency of PAS and PDSS as treatment outcome measure in PD may be a consequence of their different structure. The PAS and PDSS do not measure the same components of PD, and components specifically measured by the PAS (e.g., worries about health) appear more indicative of a therapeutically significant change and/or may be more amenable to such a change than some components of PD measured by the PDSS (e.g., phobic avoidance of physical sensations).

NR649 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Platelet 5HT Concentration in PTSD

Marina Sagud, M.D., *Department of Psychiatry, University Hospital, Rebro-Kispaticeva 12, Zagreb 10000, Croatia*; Miro Jakovljevic, Ph.D., Nela Pivac, Ph.D., Dorotea Mueck-Seler, Ph.D., Alma Mihaljevic-Peles, Ph.D.

Summary:

Posttraumatic stress disorder (PTSD) is associated with alterations in various neurobiological systems, including serotonergic. The present study included male subjects: 48 war veterans with combat-related PTSD, 48 age-matched healthy controls, 48 non-psychotic depressed patients, 14 war veterans without PTSD, and 25 war veterans with PTSD who were prisoners of war (POWs), and focused on platelet serotonin (5-HT) concentration in PTSD subject and its relationship with different clusters of depressive symptoms determined by 19-item Hamilton rating scale for depression. There was a significant difference ($F = 3.63$, $df = 4,178$: $p < 0.007$, one way ANOVA) in platelet 5-HT concentration between these groups, with higher ($p < 0.05$, Newman-Keuls test) platelet 5-HT in PTSD subjects and POWs than in depressed patients. Platelet 5-HT concentrations was significantly different in PTSD subjects with severe loss of appetite ($F = 3.65$; $df = 3,76$; $p = 0.016$), weight loss ($F = 3.45$; $df = 3,76$; $p = 0.021$), and exposed to additional severe acute stress ($F = 3.53$; $df = 3.78$; $p = 0.019$), when compared with control subjects, but did not differ significantly in PTSD subjects divided by the occurrence of other symptoms like insomnia, anxiety, and suicidality. These results show that war veterans and POWs with PTSD have higher platelet 5-HT concentration, and that platelet 5-HT contentration was increased in PTSD subjects with severe symptoms of appetite and weight loss and exposed to additional stress. Our findings suggest that platelet 5-HT might indicate the severity of depressive symptoms that occur in PTSD, or that some of these symptoms are linked to the alterations in 5-HT function.

NR650 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

The Psychopharmacological Treatment of Panic Disorder in a Naturalistic Setting

Calvin Fones, M.D., *Department of Psychological Medicine, National University of Singapore, 5 Lower Kent Ridge Road, 119074, Singapore*

Summary:

Naturalistic treatment outcome data is an important supplement to findings from therapeutic drug trials, which are restrictive in patient selection and treatment flexibility. We report on 100 outpatients with a principal diagnosis of panic disorder (PD) (DSM-IV), with/without agoraphobia as ascertained by the Structured Clinical Interview for DSM-IV (SCID) who were treated at the National University Hospital, Singapore.

A treatment algorithm for PD was adhered to. An SSRI antidepressant (AD) or high-potency benzodiazepine (HPBZ) (clonazepam or alprazolam) were used as first-line agents, alone or in combination.

Sixty patients completed at least 12 weeks of treatment. About 60% were prescribed a combination of both HPBZ and AD. HPBZ alone or in combination with AD provided rapid relief of panic symptoms within two to four weeks on the Clinical Global Impression of Improvement (CGI-I) scale. 53.3% of patients were panic-free at four to six weeks; 70% at eight to ten weeks; and 83.3% are completely well at 12 weeks. Daytime sedation or cognitive deficits were major adverse effects. AD had a therapeutic lag phase of at least four weeks when used alone. Poor initial symptom relief or adverse side effects, especially jitterness, often led to drug discontinuation or alternative help-seeking early on. Combination of AD with HPBZ helped to alleviate some AD-related side effects.

NR651 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

A New Cognitive Behavioral Approach to Self-Harm Behavior

Maria E. Ridolfi, M.D., *Department of Psychosocial, McLean Hospital, 115 Mill Street, Belmont, MA 02478*; John G. Gunderson, M.D.

Summary:

Objective: This study examines the effect of short-term Manual-Assisted Cognitive Therapy (MACT), developed in England to reduce deliberate self-harm behavior (Tyrer and Davidson, 2000). It is a brief, six-session treatment including some skills training components of DBT, reinforced with a set of treatment booklets. This study tests the effectiveness of MACT on patients with borderline personality disorder (BPD) who cut themselves.

Method: MACT was offered to seven female BPD patients, between the age of 18–45, with recent history of cutting behaviors. All were receiving psychotropic medications, and six of them were in therapy. Outcome was assessed by changes in the severity

and frequency of their self-harm behavior as measured by two standardized instruments.

Results: The average number of cutting episodes before treatment was 20, 16 during the prior 6 months. During the roughly 3 months of active MACT, this was reduced to an average of two.

Conclusions: The results suggest that MACT can be as effective with BPD patients who cut themselves as in the English study that included a wide range of diagnostic types and self-harm behaviors. These results set the stage for a more definitive evaluation of MACT.

NR652 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Valproate Levels and Behaviors in Dementia Patients Switched to Depakote Extended Release

Leonard F. Ditmanson, M.D., *Kino Hospital, 2800 East Ajo Way, Tucson, AZ 85713*; Marie Gardner, Pharm.D., Leila Akhund, M.D.

Summary:

Objective: To compare serum levels of valproate and behaviors in dementia patients receiving delayed-release divalproex when switched to extended-release divalproex.

Background: Valproate is used to treat dementia-related aggressive behaviors, including verbal abuse, physical aggression towards self and others, irritability, and paranoid ideation.

Methods: This study evaluated 10 residents of a long-term facility who were being treated with delayed-release divalproex for dementia-related behavioral problems. They were selected because they were behaviorally stable and were receiving 1500 mg/day or less of delayed-release divalproex. A serum valproate level was drawn before the switch, and two levels were drawn after the switch. Target behaviors were continually monitored, and the patients were switched to an equivalent dose of extended-release divalproex administered at bedtime.

Results: All 10 patients tolerated the switch without problems. No adverse reactions were noted. Serum valproate levels averaged 54.11 mcg/ml with extended-release divalproex. After conversion to extended-release divalproex, serum valproate levels averaged 52.33 mcg/ml at week 1 and 52.97 mcg/ml at week 4. Behavior counts remained stable, and no patient decompensated.

Conclusions: Extended-release divalproex was as clinically effective as delayed-release divalproex in treating dementia-related behavioral problems and is potentially more cost-effective and convenient with once daily dosing.

NR653 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Safety and Pharmacokinetics Profile of Concurrent Donepezil HCl and Levodopa/Carbidopa

Chukwuemeka S. Okereke, Ph.D., *Eisai Incorporated, 500 Frank W. Burr Boulevard, Teaneck, NJ 07666-6741*; Dinesh Kumar, M.S., Edward I. Cullen, Ph.D., Raymond D. Pratt, Ph.D. William F. Hahne, Ph.D.

Summary:

Objective: This randomized, double-blind, crossover study investigated the safety of, and possible drug-drug interaction between donepezil HCl and levodopa/carbidopa in Parkinson's disease (PD) patients.

Methods: 25 PD patients taking physician-optimized doses of levodopa/carbidopa were administered once-daily doses of either donepezil HCl (5 mg) or placebo for 15 days, in two treatment periods, separated by a washout of at least 2 weeks. 26 healthy matched control subjects received open-label donepezil HCl only for a single 15-day period.

Results: After 15 days of treatment, donepezil pharmacokinetics (PK) remained unchanged in PD patients when compared with healthy control subjects who received donepezil HCl only. Carbidopa PK were also unchanged by administration of donepezil HCl when compared with PD patients who received placebo. Eight hours after donepezil HCl administration, levodopa C_{max} was slightly higher (+27%) and t_{max} was slightly shorter (−40%) compared with the placebo period. These changes did not result in any clinical effect. The incidence of adverse events attributed to cholinergic effects of donepezil was not different between PD patients and healthy volunteers who received donepezil HCl only. There were no significant differences in UPDRS motor examination parameters between PD patients taking donepezil HCl and those taking placebo.

Conclusions: No clinically significant drug-drug interactions between donepezil HCl and carbidopa/levodopa were observed at steady state. The small changes in the PK of levodopa did not result in any significant change in motor activity.

Supported by: Eisai Inc

NR654 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Pharmacokinetics of Donepezil with Concomitant Sertraline, Risperidone, or Thioridazine

Josephine F. Reyes, D.M., *Eisai Incorporated, 500 Frank W. Burr Boulevard, Teaneck, NJ 07666-6741*; Christa F. Nagy, Ph.D., Miroslav Ravic, Ph.D., Edward I. Cullen, Ph.D., Carlos A. Perdomo, M.S., Raymond D. Pratt, Ph.D.

Summary:

Objective: To establish the pharmacokinetics (PK) and safety of donepezil HCl (DON) co-administered with sertraline HCl (SERT), thioridazine (THIO), or risperidone (RISP).

Methods: Three open-label trials evaluating the PK of DON are reviewed: 1) single- and multiple-dose DON 5 mg/day during concurrent administration with SERT 50–100 mg/day in healthy volunteers (N = 16); 2) multiple-dose DON 5 mg/day co-administered with steady-state RISP 1–4 mg b.i.d. in male subjects with schizophrenia (N = 16) versus healthy matched control subjects receiving DON alone (N = 15); 3) the effect of DON 5 mg/day at steady state on single doses of THIO 50 mg in healthy volunteers (N = 12).

Results: 1) Steady-state PK of DON were unaltered by co-administration with SERT, and no clinically significant changes were observed after a single dose of SERT. Co-administration of single or multiple doses of DON did not alter SERT PK. 2) DON PK were similar between subjects taking DON + RISP and control subjects taking DON alone. RISP PK were unaltered in schizophrenic subjects after 7 days of DON. 3) Steady state DON had no clinically relevant effects on THIO PK, compared with THIO alone. DON was well tolerated in all three studies. There were no significant increases (relative to DON alone) in the incidence of adverse events during combination treatments, with no clinically relevant changes in ECGs or vital signs.

Conclusions: These results are in line with previous studies demonstrating the low potential of DON for PK interactions and show that DON can be co-administered with other psychotropic agents without any safety concerns.

Supported by: Eisai Inc

NR655 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Tolerability, Ease of Use, and Efficacy of Donepezil and Rivastigmine in Alzheimer's Disease Patients

Felix C.V. Potocnik, M.B., *Department of Psychiatry, University of Stellenbosch Medical School, P.O. Box 19063, Tygerberg 7505, South Africa*; Robert Smith, Peter Passmore, Christoph Hock, David Wilkinson, Catherine M. Maud, M.D., Steven Hopker

Summary:

Objective: To explore the tolerability, ease of use, and cognitive effects of donepezil and rivastigmine in Alzheimer's disease (AD) patients in a 12-week, multinational, randomized study.

Methods: 111 AD patients were randomly assigned to receive open-label rivastigmine (up to 6 mg twice daily) or donepezil (up to 10 mg once daily) for 12 weeks, according to approved product labeling. Physicians and caregivers rated ease of use and satisfaction with assigned treatment. Cognition was assessed using the ADAS-cog by trained independent raters blinded to assigned medication.

Results: 89.3% donepezil- (N = 55) compared with 69.1% rivastigmine-treated patients (N = 56) completed ($p = 0.009$). 10.7% and 21.8% of patients, respectively, discontinued due to AEs. Nausea and vomiting were experienced by fewer donepezil-treated patients (10.7% and 7.1%) than with rivastigmine-treated patients (41.8% and 23.6%), respectively. 98.2% and 60.0% of donepezil- and rivastigmine-treated patients, respectively, reached the maximum effective dose. 87.5% of the donepezil-treated patients compared to 47.3% of the rivastigmine-treated patients, respectively, remained at the maximum dose until the final visit. Both groups showed comparable improvements from baseline ADAS-cog assessments. Both physicians and caregivers reported significantly higher satisfaction with donepezil compared with rivastigmine at Weeks 4 ($p < 0.0001$) and 12 ($p < 0.05$).

Conclusions: Donepezil was better tolerated in comparison with rivastigmine, although both agents improved cognition to a similar extent. Physicians and caregivers reported significantly higher overall satisfaction and ease of use with donepezil than with rivastigmine.

NR656 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Childhood Separation Anxiety and Substance Use Disorders

Isabelle R. Bailly-Lambin, M.D., *Department of Child Psychiatry, USN B, 6 Rue du Professeur Laguesse, Lille 59037, France*; Daniel D. Bailly, M.D.

Summary:

Objective: To investigate the prevalence rate of childhood separation anxiety disorder (SAD) in patients with substance use disorders (SUD) and its role in the comorbidity between SUD and affective disorders.

Method: Subjects included 127 patients with SUD (DSM-III-R criteria) who were consecutive admissions to an inpatient unit for addictive behaviors. They were assessed with two structured psychiatric diagnostic interviews (the SADS-LA and the SCID) and with a self-report questionnaire (the SCL-90-R). In addition, the traumatic events during the first 15 years of life were collected as described by Faravelli.

Results: 35 patients (27.5%) had a history of childhood SAD (mean age at onset: 6.0 +/- 2.7 years). The lifetime prevalence of comorbid anxiety disorders (panic disorder/agoraphobia) and suicide attempts was found to be significantly higher in these patients than in patients without childhood SAD. Patients with childhood SAD also had a general psychopathology profile that was significantly more severely affected. They experienced significantly more early stressful life events (somatic diseases or physical/sexual abuse).

Conclusions: Our findings suggest that childhood SAD may predispose to SUD and may be associated with specific clinical characteristics. These data need to be taken into account in prevention and treatment programs.

NR657 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Carbohydrate-Deficient Transferrin Tri-TIA (%CDTri-TIA) Versus ChronAlcol.D. in the Diagnosis of Excessive Alcohol Use

Aleksander Korzec, M.D., *Department of Psychiatry, St. Lucas Hospital, Jan Tooropstraat 164, Amsterdam, Netherlands*; Torsten Arndt, Marij Bar, Maarten W.J. Koeter, Ph.D.

Background: Carbohydrate-deficient transferrin (CDT) is used for laboratory diagnosis of chronic excessive alcohol use. CDT tests with differing analytical specificity (including or excluding trisialotransferrin) are available. We wanted to assess whether this difference affects the diagnostic accuracy of CDT.

Methods: Subjects in this study were 24 controls (alcohol intake ≤280 g/week, no alcoholism diagnosis), 17 hazardous drinkers (alcohol intake >280 g/week, no alcoholism diagnosis), and 53 alcoholics (alcohol intake >280 g/week and alcoholism diagnosis). Alcohol use disorder (AUD, alcoholism) was diagnosed with the Composite International Diagnostic Interview (CIDI); Time Line Follow Back (TLFB) were used to measure alcohol intake. Serum CDT was measured by %CDTri-TIA test (including trisialotransferrin in CDT) and ChronAlcol.D. (excluding this isoform).

Results: There was no significant difference in specificity between %CDTri-TIA and the ChronAlcol.D. test. In the alcoholics group, ChronAlcol.D. showed a significantly higher sensitivity (71,1%) than %CDTri-TIA (52.8%). The accuracy of ChronAlcol.D. was also significantly better than %CDTri-TIA. In the hazardous drinkers group only sensitivity of ChronAlcol.D. was significantly better.

Conclusions: ChronAlcol.D. is a more accurate test than %CDTri-TIA in alcoholics in the diagnosis of chronic excessive alcohol intake.

NR658 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Clinical Utility of Life Measure in Dual-Diagnosis Patients

Ihsan M. Salloum, M.D., *Department of Psychiatry, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213*; Juan E. Mezzich, M.D., Dennis C. Daley, Ph.D., Levent Kirsci, Ph.D., Crystal Spotts, M.Ed.

Summary:

Objectives: The aim of this study is to explore the utility of a brief, culturally informed, self-rated, quality-of-life scale (the Quality of Life Index, Mezzich & Cohen, 2000) in comorbid psychiatric and substance use disorders.

Method: The Quality of Life Index (QLI) inquires about 10 dimensions of health ranging from physical well being to spiritual fulfillment. Sixty-two consecutively admitted patients to an integrated ambulatory dual-diagnosis program completed the QLI. The sample consisted of 27 males (43.5%) and 34 females (56.5%) with an average age of 35.5 years. Twenty-seven were African Americans (47%), and 28 were Caucasians (48%). We assessed the reliability and construct validity of the QLI and we then tested whether the QLI predicts treatment adherence over a three month period.

Results: The results revealed that the QLI had good reliability (item-total correlation ranged between .48 and .77 and Cronbach's alpha = .89). Principal component factor analysis revealed that the first factor explained 53.4% of the variance, which indicated the unidimensionality of the instrument. There were no gender and ethnic differences; older age, however, correlated with poorer social and emotional support ($p = -.280$, p (2-tailed) = .03). Logistic regression analysis, controlling for age, revealed that both the interpersonal functioning and the availability of social and emotional support significantly predicted treatment adherence (odds ratio = 1.42, $p = .03$, and odds ratio = .65, $p = .01$, respectively).

Conclusions: These results suggest that the Quality of Life Index may be a useful instrument in regular clinical care of dually diagnosed patients.

Supported in part by NIAAA (AA-10523), NIAAA (AA-11929), and NIDA (DA-09421).

NR659 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

A New Approach to Diagnosis and Treatment of Alcoholism

Marc A. Lindberg, Ph.D., *Department of Psychology, Marshall University, 1600 Hal Greer Boulevard, Huntington, WV 25755-2672*; Stuart Thomas, Ph.D., Beth Chitty, Mary Aldred, Amy Lefler

Summary:

Objective: The attachment relationships and personality characteristics of alcoholics were examined in two studies. The first study examined 27 patients in residential treatment centers compared with 118 controls selected from a larger study who matched on age, socioeconomic status, and sex. A second study replication study was performed with 51 patients in the initial detoxification phase of their treatment who were compared with 211 similarly matched controls.

Method: Patients completed the Attachment and Personality Dynamics Questionnaire, a new instrument with fake scales and extensive validity tests with an average alpha of .79 over the 29 different scales measuring secure, avoidant, ambivalent, and preoccupied attachments to mother, father, and partner, and other scales measuring sexual relations, anxiety, shame, denial, abusiveness, withdrawal, mistrust, and family of origin dynamics.

Results: A Stepwise Discriminant Function analysis found that the shame, anxiety, and preoccupied mother and partner scales served as the best discriminates between the two groups F (4, 129) = 11.43, $p < .0001$. Further tests revealed that the groups also significantly differed on 17 of the 29 scales in predictable fashions. Study two replicated these results.

Conclusion: The results showed clear differences for alcoholics in terms of relationship functioning and related personality measures agreeing with the predictions from several attachment researchers (Cassidy & Shaver, 1999). The standard deviation and scale data, however, suggested that the researcher and clinician must consider individual differences in the above insecurities (with alcoholics scoring higher and lower on many of the scales) in any diagnostic evaluation and treatment approach.

Funding source: Marshall University.

NR660 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Alcohol Use and Cognitive Decline After 11.5 Years

Iracema Leroi, M.D., *Department of Psychiatry, Johns Hopkins University, 600 North Wolfe Street, Olser 320, Baltimore, MD 21287-5371*; Jeannine-Marie Sheppard, B.S.C., Constanine G. Lyketsos, M.D.

Summary:

Objective: To examine the relationship between cognitive decline and alcohol use or abuse over an 11.5-year period.

Method: The 1,488 participants of the Baltimore arm of the Epidemiologic Catchment Area Study who completed the Mini-Mental State Examination (MMSE) at three time points in 1981, 1982, and 1993–1996 were divided into five groups based on amount and frequency of alcohol intake. The relation between level of alcohol use and MMSE score change between waves 2 and 3 of the study was examined using analysis of variance, which was then adjusted for the effects of age, race, and education. DSM-III-R diagnosis of alcohol intake was also examined.

Results: When compared to non-drinkers in the entire study group, alcohol users had significantly less cognitive decline. When adjusted for age, education, and race, a trend toward significantly *less* cognitive decline was seen in women drinkers but not in men. There were no significant differences in cognitive decline among men in different alcohol use categories. In contrast, among female users, there was a trend toward *less* cognitive decline in women who used alcohol habitually as compared to those who were non-users or heavy users. Alcohol abuse or dependence was not associated with cognitive decline.

Conclusion: Over long time periods, alcohol use is *not* associated with cognitive decline. In women, alcohol use may be associated with *less* decline in cognitive performance after 11.5 years.

NR661 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

The Pharmacokinetics of Methadone Following Lamivudine/Zidovudine Administration

Elinore F. McCance-Katz, M.D., *Department of Psychiatry, Montefiore, 111 East 210th Street, Rosenthal 169, Bronx, NY 10467*; Petrie M. Rainey, M.D., Peter Jatlow, M.D., Gerald H. Friedland, M.D., Susan Mitchell, Mary K. Murphy, Jerry W. Snidow, Pharm.D.

Summary:

Objective: To determine whether the antiretroviral theraputic lamivudine/zidovudine affects methadone pharmacokinetics.

Method: An open-label, within-subject, pharmacokinetics study was conducted in 16 methadone-maintained, non-HIV-infected subjects. On study Day 1, subjects received their usual dose of methadone, and 24 hours later (Day 2) they received their methadone dose concurrently with one lamivudine 150-mg/zidovudine 300-mg combination tablet. Methadone serum concentrations were determined over 24 hours.

Results: Comparison of the pharmacokinetic parameters of methadone in the absence and presence of coadministered lamivudine/zidovudine revealed no significant differences in mean area under the serum concentration-time curve (AUC). No clinical evidence of opiate withdrawal or toxicity was observed.

	M	M+lamivudine/zidovudine
$AUC_{0\text{-}24h}$	8641 ± 4431	8753 ± 4280 μg-h/L
Oral clearance(CL/F)	9.9 ± 4.9	10.3 ± 5.5 L/h
Oral volume of distribution(Vd/F)	647 ± 465	481 ± 305 L
Maximum serum concentration (Cmax)	514 ± 223	510 ± 237 μg/L
Terminal elimination half-life ($t_{1/2}$)	55.3 ± 61.0	35.0 ± 17.5 h

Conclusion: A change in methadone dose is not likely to be necessary when treatment with lamivudine/zidovudine occurs concurrently with methadone maintenance therapy in opioid-dependent patients with HIV disease.

Supported by Glaxo Wellcome

NR662 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Effect of Methadone or LAAM on Nelfinavir Pharmacokinetics

Elinore F. McCance-Katz, M.D., *Department of Psychiatry, Montefiore, 111 East 210th Street, Rosenthal 169, Bronx, NY 10467*; Patrick F. Smith, Pharm.D., Brent M. Booker, Pharm.D., Robin Difrancesco, M.B.A., Eugene D. Morse, Pharm.D., Peter F. Cottone, B.A., Mary K. Murphy

Summary:

Objective: Nelfinavir (NFV), a frequently prescribed protease inhibitor, is often co-administered with M or L in HIV-positive, opioid-dependent patients. M effect on pharmacokinetics (PK) of NFV and its M8 metabolite have not been prospectively evaluated.

We determined PK of NFV and M8 in combination with M or L in a non-crossover design.

Method: Healthy, non-HIV infected, volunteers maintained on M (40-120 mg/d) (n = 16) or L (50-140 mg twice weekly, 65-190 mg once weekly) (n = 10) or non-opioid dependent controls (CTL) (n = 15) received NFV (1250mg BID) for five days followed by steady-state PK evaluation over 24 h and HPLC assay for NFV and M8. PK parameters determined by standard non-compartmental methods were compared with CTL by non-parametric ANOVA.

Results: Median NFV 12-hr troughs were higher (3.3 vs. 1.2 uM, $p < 0.05$) in the M group, and did not differ with L. The metabolic AUC ratio (M8:NFV) for CTL was 0.38, and was significantly higher with L (0.51), and lower with M (0.24), both $p < 0.05$.

Conclusions: NFV exposure was higher, and M8 significantly lower when co-administered with M; the opposite trend was evident with L. M effects may be consistent with inhibition of conversion of NFV to M8; L may increase the conversion rate of NVF to M8.

Supported by NIDA RO1 DA 13004 (EMK) and NIH MO1RR12248 (Albert Einstein College of Medicine GCRC)

NR663 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Cocaine and Alcohol Abuse: Gender Effects

Elinore F. McCance-Katz, M.D., *Department of Psychiatry, Montefiore, 111 East 210th Street, Rosenthal 169, Bronx, NY 10467*; Beth K. Boyarsky, M.D., Carl L. Hart, Ph.D., Julie Sarlo, B.A., Corinne M. Rogers, M.S., Mary K. Murphy, Peter Jatlow, M.D.

Summary:

Objective: To examine effects of binge use of cocaine and/or alcohol in humans.

Method: A randomized, double-blind, placebo-controlled, within-subject study with three, eight-hour sessions in 17 (eight women) with three regimens: four doses of intranasal cocaine (1 mg/kg every 30 min) with alcohol (1 g/kg) following cocaine and a second drink (120 mg/kg) at 60 min; four doses of cocaine/placebo alcohol; four doses of placebo cocaine/alcohol. Area under the curve values representing responses to successive doses of cocaine and alcohol were analyzed using a two-factor ANOVA. $p \leq .05$ (two-tailed) was significant.

Results: Blood pressure increased during cocaine-alcohol and cocaine relative to alcohol, but without gender differences. Pulse increased during cocaine-alcohol vs. cocaine or alcohol. Women had greater increases in pulse during alcohol, but similar increases relative to men for cocaine-alcohol and cocaine. Increased "high" occurred during cocaine-alcohol vs. cocaine or alcohol without gender effects. "Feel good" was greater for cocaine-alcohol vs. cocaine or alcohol. Women reported increased "feel good" during cocaine and alcohol administration. No gender differences for cocaine, alcohol, or cocaethylene plasma concentrations occurred.

Conclusion: Enhanced "feel good" effects for women during binge drug use may produce increased vulnerability to adverse events due to a reduction in internal cues to curtail consumption.

Supported by NIDA grants K20-DA00216, P50-DA09250, and R29-DA09573 Psychiatrists and other physicians, alcohol and drug counselors, mental health providers, nurses

NR664 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

The Influence of Mother's Alcoholism on Son's Drinking

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

Summary:

Objective: This 30-year, prospective, high-risk study of sons of alcoholic and nonalcoholic fathers explored the influence of mothers' alcoholism on her son's drinking, on the presence of other psychiatric disorders, and psychosocial functioning at age 30.

Methods: In the late 1970s, all identified fathers (8,446) of a large Copenhagen birth cohort (1956-1961) were submitted to the Danish central psychiatric register and local alcoholism clinics. All living sons of alcoholic fathers were identified. A carefully matched group of sons of fathers with no alcoholism diagnosis was selected as a control group. To the already existing large neonatal database, additional information was collected at a 20-year followup and at the 30-year followup that included an extensive review of parental drinking from the sons as well as a review of all mothers in the central psychiatric register and in the local alcoholism clinics. From these three sources, a global risk measure was used to create the following groups from the total 241 subjects who participated in the 30-year followup: neither parent alcoholic (N = 55); father only alcoholic (N = 144); mother only alcoholic (N = 3); both mother and father alcoholic (N = 39). Because of the high degree of assortative mating (i.e., 39 of the 42 alcoholic mothers married an alcoholic man), the sons of the three alcoholic mothers who did not marry an alcoholic father were dropped from the analyses.

Results: Mothers' alcoholism, in combination with fathers' alcoholism, predicted greater alcoholism severity and more alcohol abuse/dependence than fathers' alcoholism alone or no parental alcoholism. A strong linear relationship existed between the three parental groups and measures of lifetime drinking problems as well as the diagnosis of alcohol dependence. A similar linear relationship was found for measures of psychosocial functioning. In contrast, rates of other psychiatric disorders were equally high in sons with fathers only alcoholic or both parents alcoholic, compared with sons with neither parent alcoholic where the prevalence of psychiatric disorders was the lowest. These findings suggest a step-wise "threshold" effect of parental alcoholism on psychiatric disorder but an additive effect on drinking severity.

Conclusion: Mother's alcoholism contributed significantly to the pathological drinking of their sons over a 30-year period.

NR665 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Impact of Comorbidity on the Hospital Length of Stay Among Cocaine-Dependent Patients

Ashok Jain, M.D., *Department of Psychiatry, MCHC, P O Box 726, Hazard, KY 41702*; Pedro Ruiz, M.D.

Summary:

Objective: During the last decade there has been, in the United States, a major emphasis on outpatient psychiatric care over inpatient care. This emphasis has resulted in much pressure being applied for early hospital discharge of psychiatric patients, including substance abuse patients. Unfortunately, this is happening without attention given to the comorbidity status of the patients, leading to inappropriate decision making. In our study, the objective has been to emphasize and review the impact of psychiatric comorbidity among cocaine dependent patients hospital length of stay.

Methods: The sample of patients of our study emanated from a metropolitan/urban state hospital. In total, we examined 1,244 admissions of patients with the discharged diagnosis of cocaine dependence. All diagnoses were made in accordance to DSM-IV. These data were analyzed according to standard statistican P values.

Results: In total, 38% of the patients sample also had an additional comorbidity diagnosis in addition to cocaine dependence,

with the most frequent comorbidity diagnosis being drug and alcohol dependence (24%). Mood disorders as a comorbidity diagnosis only represented 6% and psychotic disorders only represented 5% of the overall patient sample. With respect to the hospital length of stay, patients with psychotic comorbidity diagnosis tended to stay in the hospital much longer. In general, patients with another substance abuse comorbidity disorder tended to have a shorter hospital length of stay. In many instances, drop out from treatment was a major factor in these patients. In terms of alcoholism comorbidity, patients tended to drop out from treatment during the third week of hospitalization. Patients with cocaine dependence comorbidity dropped out of treatment more often during the second week of hospital stay. Mood disorders comorbidity led patients to drop out more often during the first week of hospital stay. Finally, psychosis comorbidity kept the patients in the hospital for longer than four weeks.

Conclusion: This study reports significant drop out among psychiatric inpatients with a cocaine dependent diagnosis during initial treatment phase. In contrast to previous studies there is significantly less psychiatric comorbidity found among cocaine dependents. Hopefully, this study will stimulate further research among patients with substance abuse comorbidity who are admitted to hospitals as part of their required care.

NR666 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Comorbidity in Tobacco Use

Isabel Gonzalez, M.D., *Department of Psychiatry, University of Chile, Av La Paz 1003, Santiago, Chile*; Jorge Gaete, M.D., Ricardo Araya, M.D., Rosemarie Fritsch, M.D., Graciela Rojas, M.D.

Summary:

Objective: To study tobacco use in relation with psychiatric morbidity and illegal drug use among adults in Santiago.

Method: A cross-sectional study through a household survey with a probabilistic sampling design was done (N = 3,237,286). To determine psychiatric morbidity CIS-R was used and a structured questionnaire applied.

Results: Sample = 3,870. 52.2% were women, 47.8% were men, median age was 34 years. Income per cápita was US $120.

13.3% of smokers used marijuana (men = 19.2%, women = 6.4%), 2.5% used cocaine (men = 3.5%, women = 1.4%), and 1.9% used paste (men = 2.4%, women = 1.2%). Smokers were 5.9 times (95% CI = 5.83–5.96) likelier to use marijuana, 5.7 (95% CI = 5.56–5.85) times likelier to use cocaine, and 4.9 (95% CI = 4.74–5.01) times likelier to use paste. Among people that met the criteria for psychiatric disorder, 47.1% smoked, they were at 1.23 times greater risk (95% CI = 1.23–1.24) of smoking than people without a psychiatric disorder (p = 0.00). For women with a psychiatric disorder, the risk of smoking was 1.39 (95% CI = 1.39–1.40; p = 0.00) and for men it was 1.28 (95% CI = 1.27–1.28; p = 0.00) compared to women and men without a psychiatric disorder, respectively.

Conclusions: There is a positive association between smoking and psychiatric disorders.

This study was funded by FONDECYT 1961075 and the European Community

NR667 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Psychiatric Disorders and Their Influence in Long-Term Methadone Maintenance Treatment (MMT) Outcomes

Juan M. Fernandez, M.D., *Department of Psychiatry, University of Oviedo, Julian Claveria 6-3, Oviedo 33006, Spain*; Maria P. Gonzalez, Ph.D., Pilar A. Saiz, Ph.D., Eduardo Gutierrez, M.D., Julio B. Bobes, Ph.D.

Summary:

Objectives: To discover the psychiatric disorders of a heroin-dependent population undergoing MMT and the influence of such on the outcomes of treatment.

Patients/Method: A total of 132 opiate-dependent subjects from a drug addiction treatment Unit (Spain) were followed-up over six years. At the beginning and after six years of treatment an ad hoc protocol (sociodemographic and clinical variables) was administered. Analyses of HIV and urine (opiates, cocaine, and benzodiacepines) were made. The IPDE was also administered.

Results: The effectiveness of MMT was high, with evident social and clinical improvement. Disorders diagnosed: affective (29.7%), anxiety (19.1%), psychotic (11.8%), and personality (PD) (51.1%). Anxiety and affective disorders were related with heroin and benzodiacepine use, and being HIV+. PD were more prevalent in older addicts, unemployed, patients with court cases pending, and those with cocaine and benzodiacepine use. Methadone dose was not related with psychiatric disorders.

Conclusions: Psychiatric disorders (affective, anxiety and PD) were frequent and linked to worse treatment outcomes (drug use, criminal activities). In some patients, there was a HIV-depression-drug use relationship. These patients clearly needed a specific psychosocial intervention. For MMT programmes to be more effective greater attention needs to be paid to their mental health problems.

NR668 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Personality Disorders, Consumption Habits, and Viral Infections in Opiate Addictions

Eduardo Gutierrez, M.D., *Department of Psychiatry, University of Oviedo, Julian Claveria No 6-3, Ovideo 33006, Spain*; Pilar A. Saiz, Ph.D., Maria P. Gonzalez, Ph.D., Juan M. Fernandez, M.D., Julio B. Bobes, Ph.D.

Summary:

Objectives: To analyze the existing relationship among personality disorders (PD), consumption habits, and HIV, HBV, and HCV infections in opiate addicts.

Patients and Methods: Patients were recruited over a six-month period. Inclusion criteria: over 18 years of age, opiate dependence (DSM-IV), informed consent. Evaluation: EuropASI, IPDE.

Results: One hundred and fifty patients [mean age (SD): 27.33 (5.93); 84% males]: methadone maintenence program (MMT) 53 (35.3%), naltrexone maintenance program (NMP) 97 (64.7%). PD-67.3%; antisocial 30% (most frequent). HIV- less prevalent in paranoid subtype (41.7%; p = .04). HBV- more prevalent in PD (82.9%; p = .01), less prevalent in paranoid (31.7%; p = .01), borderline (36.6%, p = .03), and avoidance subtypes (36.6%, p = .01). HCV- less prevalent in paranoid (28.4%, p = .006), and antisocial (40.3%, p = .01). Parenteral route in the last six months-lower in paranoid (26.9%, p = .02), and narcissistic (9%, p = .03), and higher in antisocial (62.2%, p = .004). Parenteral route in the last month-lower in narcissistic (9%, p = .03) and higher in antisocial (60%, p = .01).

Conclusions: Paranoid subtype suffer from fewer viral infections, probably due to their personality disorder. Antisocial subtype continue their consumption habits, which lead to a greater frequency of problems from viral infection.

NR669 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Value of Personality Tests in Differentiating Transsexuals from Transvestites

Thierry Gallarda, M.D., *Shu Pr Loo, Ch Sainte-Anne, 1 Rue Cabanis, Paris 75674, France*; Sandrine Coussinoux, Ph.D.,

Bernard Cordier, M.D., Marie-Chantal Bourdel, Jean-Pierre Olie, M.D.

Summary:

Background: An increasing number of patients are seeking a sex change in France. Sex changes are only approved in cases of primary transsexualism, which is a very rare condition. The main difficulty for the psychiatrist is to differentiate primary M-F transsexualism (M-Fs) from some forms of transvestic fetishism. From a theoretical point of view, transvestic fetishism occurs in bisexual or heterosexual men who cross-dress for the purpose of sexual excitement, whereas M-Fs refers to an early and persistent cross-gender identification. However, a history of transvestic fetishism is often reported in the childhood of M-Fs, and the percentage of transsexually inclined transvestites wondering whether to have transsexual surgery is increasing.

Objective: To inform the therapeutic choice by evaluating the gender identification of M-Fs and transvestites by using two psychometric variables (Masculinity/Feminity (M/F) score on the MMPI and card III of the Rorschach).

Methods: M-Fs (N = 28) and transvestites (N = 15) were individually administered the MMPI and the Rorschach test and were compared to each other and to a male control group (N = 10).

Results: Regarding frequency of cross-gender responses on card III, M-Fs and transvestites were indistinguishable and differed from the male controls. When the M/F score was calculated by genetic sex, M-Fs and transvestites scored higher than the mean and differed from the male controls. When calculated by desired sex, M-Fs scored within the norms, similar to female controls, whereas transvestites scores remained pathological.

Discussion: When using Rorschach card III, the gender identification of transvestites was virtually indistinguishable from that of M-Fs. However, the M/F score on the MMPI could be a more useful indicator for discriminating between these two groups.

NR670 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Gender Differences and Cognition: Do Preassigned Female to Male Transsexuals (F-Ms) Perform According to Their Biological or Desired Sex?

Thierry Gallarda, M.D., *Shu Pr Loo, Ch Sainte-Anne, 1 Rue Cabanis, Paris 75674, France*; Isabelle Amado-Boccara, Ph.D., Sandrine Coussinoux, Ph.D., Jean-Pierre Luton, M.D., Bernard Cordier, M.D., Marie-Chantal Bourdel, Jean-Pierre Olie, M.D.

Summary:

Background: Neuropsychological research has shown cognitive differences between men and women are probably based on hormonal effects on the organization of the brain in the womb, in early infancy, and in puberty. Transsexualism is defined as a discrepancy between biological sex and experienced core-gender identity. Transsexuals therefore represent an interesting population for investigating sex-differentiated cognitive abilities. Do preassigned transsexuals show a cognitive pattern that is more similar to their genetic sex or their experienced gender identity?

Methods: 17 pre-reassigned F-Ms (without any hormonal treatment) were administered cognitive tasks that have shown sex-differentiated performance differences and were compared to 12 male and 13 female control subjects (matched for educational level). Male favoring tasks were three-dimensional rotated figures and mathematical problem solving whereas female favoring tasks were verbal fluency, word spelling, perceptual speed, and fine motor skills.

Results: The results showed that pre-reassigned F-Ms obtained comparable scores to female control subjects and, when compared to male controls, exhibited better performance in fine motor skills and lower performance in the three-dimensional rotated figures task.

Discussion: These results were clearly in accordance with other studies that argued that pre-reassigned F-Ms exhibited cognitive abilities within the same range as adult women.

NR671 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Gender Differences in Pathological Gambling

Angela Ibanez-Cuadrado, M.D., *Department of Psychiatry, Hospital Ramon Y Cajal-Alcala Universit, Crt. Colmenar, km. 9,1, Madrid 28034, Spain*; Carlos Blanco-Jerez, M.D., Paula Moreyra, M.A., Jeronimo Saiz-Ruiz, M.D.

Summary:

Objective: To determine the differences in clinical presentation, gambling behavior, and psychiatric comorbidity of male and female treatment-seeking pathological gamblers.

Method: Sixty-nine consecutive pathological gamblers applying to a specialized outpatient treatment program were evaluated with structured interviews, self-report questionnaires and psychological scales.

Results: Male and female pathological gamblers had similar gambling severity and rates of psychiatric comorbidity. Sixty-seven percent of males versus 25% of females had been exposed to gambling in adolescence ($\chi^2 = 9.2$, df = 1, p = .002). Females had a later age of first bet and a faster evolution of the disorder. Male pathological gamblers had higher rates of substance abuse and antisocial personality disorder. Females had higher rates of affective disorders and history of abuse. Female pathological gamblers placed less importance than men in the immediacy and monetary aspects of the reward, but stressed more other aspects such as the social setting where the gambling took place (all p < .05).

Conclusions: There are significant gender differences in the clinical presentation and comorbidity of pathological gambling. These genders differences should be incorporated in the treatment selection and planning of pathological gamblers.

NR672 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Sildenafil Citrate in a Double-Blind, Placebo-Controlled Study with Extension for SRI-Associated Sexual Dysfunction: Open-Label Results

H. George Nurnberg, M.D., *Department of Psychiatry, University of New Mexico, 2600 Marble Avenue, NE, Albuquerque, NM 87131*; Alan J. Gelenberg, M.D., Maurizio Fava, M.D., Paula L. Hensley, M.D., John Lauriello, M.D., Susan Paine, M.D.

Summary:

Objective: In a double-blind, placebo-controlled design, sildenafil citrate demonstrated highly significant efficacy for all aspects of sexual dysfunction (SD) associated with serotonergic reuptake inhibitor (SRI) antidepressant treatment. This report presents the results of an open-label continuation study in double-blind nonresponders.

Method: Ninety men with clinically recovered major depression and SRI-associated SD received either sildenafil (50 or 100 mg) or placebo in a double-blind fashion for six weeks. Blinded nonresponders (CGI-SF ≥2; sildenafil, 14/50 [28%]; placebo, 27/40 [68%]) continued to open-label sildenafil for 17 weeks. Subjects had to remain in remission (HAM-D/A scores <10) and on a stable SRI dose. SD measures were determined using ASEX/MGH/SFI/IIEF and CGI-SF.

Results: Of the initial double-blind nonresponders, 96.3% (26/27) and 92.9% (13/14) from the placebo and sildenafil groups, respectively, achieved a score of "much/very much improved" with open-label sildenafil using the CGI-SF as primary measure (sildenafil: 3.85 ± 3.6 to 1.86 ± 0.95; placebo: 4.11 ± 0.51 to

1.59 ± 0.80; $P = 0.0001$). Placebo nonresponders (n = 27) showed greater improvements than sildenafil nonresponders (n = 14) using ASEX/MGH measures (sildenafil: 19.0 ± 4.4/18.2 ± 3.1 to 16.1 ± 4.7/13.2 ± 3.3; placebo: 20.1 ± 4.7/21.7 ± 4.0 to 13.3 ± 3.2/ 11.8 ± 3.7; $P = 0.003$–0.009), respectively.

Conclusions: Sildenafil was highly effective (>90%) in reversing SRI-associated SD in combined double-blind and open-label continuation treatment. This confirms earlier reports of sildenafil efficacy for first-line treatment of SRI-associated SD.

NR673 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

The Sexual Function Inventory: A Screening Instrument for Antidepressant-Associated Sexual Dysfunction

H. George Nurnberg, M.D., *Department of Psychiatry, University of New Mexico, 2600 Marble Avenue, NE, Albuquerque, NM 87131*; Alan J. Gelenberg, M.D., Maurizio Fava, M.D., Paula L. Hensley, M.D., John Lauriello, M.D., Susan Paine, M.D.

Summary:

Objective: The Sexual Function Inventory (SFI) is a hybrid of similar instruments (ASEX, MGH, IIEF, etc.) designed to be an effective screening measure for clinical practice. It is intended to be gender neutral and easily administered by both patients and health care providers.

Method: The SFI was developed in clinical trials investigating antidepressant-associated sexual dysfunction (SD). The design of these studies involved several validated research sexual function questionnaires, some self-administered (IIEF, ASEX), others clinician-rated (MGH, CGI-SF). The SFI was constructed to structurally reflect those instruments, to provide measures of reliability and concurrent validity, and to screen patients in clinical settings for potential study enrollment.

Results: The correlations between the SFI and CGI-SF were highly significant for total, active, and placebo subjects (P values <0.005), and equal or greater than corresponding correlations for ASEX, MGH, and IIEF (total and domain). Intercorrelations between instruments after double-blind treatment are shown below:

	CGI-SF	SFI	MGH	ASEX
SFI	0.78	—		
MGH	0.81	0.92	—	
ASEX	0.72	0.97	0.85	—
IIEF	0.76	0.85	0.84	0.78

Conclusions: The SFI is an easily administered instrument that appears to be useful in identifying patients with antidepressant-associated SD. Further ongoing studies in other settings are necessary to refine validation and generalizability.

NR674 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Dual Diagnosis: Prevalence and Treatment

Chandresh Shah, M.D., *VA Outpatient Clinic, University of Southern CA, 351 East Temple Street, # 116 A, Los Angeles, CA 90012*

Summary:

Dual diagnosis (DD) of mental illness (MI) and substance abuse (SA) poses a challenge for long-term recovery and creates an economic pressure of increased cost of its treatment. To assess the prevalence of DD and its treatment, records of patients enrolled into SA treatment programs for a minimum of 120 days were reviewed. There were 58 patients with a diagnosis of alcohol abuse/dependence (A), 38 with cocaine abuse/dependence (C), and 118 with opioid dependence (H). A total of 58.62% of A had major MI as compared with 39.47% of C ($p < 0.05$), and 28.81% of H ($p < 0.001$). C were younger (47.80 ± 6.35 years) and H were older (51.12 ± 6.28 years) in age, as compared with A (48.91 ± 8.68); though the differences were nonsignificant. The MI was treated with different psychotropic drugs, including anxiolytics (AX), antidepressants (DP), neuroleptics (NP) and mood stabilizers (MS) Most of the patients received one or two classes of drugs. But 29.41% of H received three different classes of drugs as compared with 14.71% of A ($p < 0.005$) and only 6/64% of C ($p < 0.001$). This may reflect more severity and/or complexity of MI among H. Review of classes of drugs used revealed that DP was widely and commonly used. The use of DP among C was at 100% as compared with that of other drugs ($p < 0.001$), and at 88.24% among A and H. A total of 55.88% of A received AX as compared with 20.00% of C ($p < 0.001$). On the contrary, only 14.71% of A received MS as compared with 33.33% of C ($p < 0.05$). These data show that DD is quite prevalent, and hence needs to be assessed and addressed. In addition, it also reflects heterogeneity of diagnosis and its treatment among patients with DD.

NR675 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Identification of Trauma PTSD in Substance Abusers During an Emergency Room Visit

Leo J. Bastiaens, M.D., *Department of Psychiatry, St. Francis Medical Center, 400 45th Street, Pittsburgh, PA 15201*; Jacob Kendrick, B.S.

Summary:

Objective: To improve the identification of trauma and PTSD in a substance abusing population during an emergency room evaluation.

Method: 172 study patients with a substance use disorder (SUD) were evaluated with the Mini International Neuro-psychiatric Interview (MINI), while 150 control patients with an SUD were evaluated with an unstructured clinical interview.

Results: In the study group, 24% reported a significant trauma as defined by DSM-IV, while only 7% in the control group did ($\chi^2 = 16.8$, df = 1, $p < 0.001$). In the study group, 57% of the traumatized patients reported PTSD symptoms, while 45% in the control group did. However, among patients who reported symptoms, only 21% in the study group and 40% in the control group received an axis I diagnosis of PTSD in the medical record.

Conclusion: The use of a structured assessment improved the identification of trauma, but not the diagnosis of PTSD, among SUD patients. The identification of trauma and PTSD in SUD patients is important to improve retention and outcome in rehabilitation. Systems that rely on an emergency evaluation to refer patients to appropriate programs may want to include a structured interview in their assessment. Psychiatrists need to incorporate the results of structured interviews in their differential diagnostic thinking.

NR676 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Eating and Weight Concerns in Men and Women Recovering from Substance Abuse

Tamara D. Jackson, Ph.D., *Department of Psychiatry, Yale University, P O Box 208098, New Haven, CT 06520-8098*; Carlos M. Grilo, Ph.D.

Summary:

Objective: The goal was to conduct a descriptive, exploratory examination of eating and weight concerns in a racially diverse

sample of low-income men and women seeking treatment for substance abuse.

Procedure: Subjects were 37 women and 44 men who were in recovery from substance abuse and were recruited from an urban substance abuse treatment facility. Participants reported that they were not actively using substances, and they exhibited no acute symptoms of alcohol or substance withdrawal. Subjects completed the following psychometrically established self-report measures: the Questionnaire on Eating and Weight Patterns—Revised (QEWP-R), the Eating Disorder Examination-Questionnaire (EDE-Q), and the Body Shape Questionnaire (BSQ).

Results: Sixty percent of men and 69% of women were overweight (body mass index (BMI) ≥ 25). BMI was also examined within ethnic groups. Among African-American subjects, 14 of the 25 (56%) men and 27 of the 39 (69%) women were overweight. Among Caucasian subjects, eight of the 12 (67%) men and four of the seven (36%) women were overweight. Among Hispanic subjects, four of the seven (57%) men and two of the three (67%) women were overweight. For weight cycling history, approximately 50% of men and women reported weight fluctuations of 20 pounds or more at least once, with 36% of men and 23% of women reporting such weight fluctuations on at least three separate occasions. Regarding the frequency of binge eating and inappropriate compensatory behavior (e.g., vomiting, laxative use, excessive exercise), 9% of men and 16% of women reported binge eating at least one day per week, and 14% of men and 12% of women reported engaging in some form of inappropriate compensatory behavior.

Discussion: Our findings suggest that the level of weight and eating concerns among recovering substance abusers may warrant additional clinical attention and intervention during the treatment process.

NR677 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Eating and Weight Issues in a Community Sample of African-American Women

Tamara D. Jackson, Ph.D., *Department of Psychiatry, Yale University, P O Box 208098, New Haven, CT 06520-8098*; Carlos M. Grilo, Ph.D.

Summary:

Objective: The primary goal was to examine body mass index (BMI), body dissatisfaction, eating-related psychopathology, and depression in a community sample of African-American (AA) women.

Procedures: Subjects were 49 AA female adults who were recruited via flyers seeking women interested in completing a survey on health behaviors distributed in an urban community. Subjects completed the following psychometrically established self-report measures: the Questionnaire on Eating and Weight Patterns—Revised (QEWP-R), the Eating Disorder Examination-Questionnaire (EDE-Q), the Body Shape Questionnaire (BSQ), and the Beck Depression Inventory (BDI).

Results: Independent sample t-tests compared obese (n = 25; BMI ≥ 30) and non-obese women (n = 24; BMI < 30) on the variables of interest. Obese women displayed significantly higher body dissatisfaction than non-obese women ($t = -3.57$, $p = .00$). Obese women reported greater binge frequency ($t = -2.26$, $p = .03$) and higher eating concerns ($t = -3.99$, $p = .00$), shape concerns ($t = -3.72$, $p = .00$), weight concerns ($t = -5.12$, $p = .00$), and dietary restraint ($t = -2.20$, $p = .03$) on the EDE-Q than non-obese women. No significant group differences were found in level of depression ($t = -.40$, $p = .69$). Hierarchical multiple regression analysis was conducted to examine the main and interaction effects of BDI and BMI on predicting BSQ. In block 1, BMI significantly predicted BSQ ($R = 3.64$, $p = .01$). In block 2, BDI significantly contributed to the overall equation ($\Delta R^2 = .26$, $p = .00$). In block 3, the interaction of BMI and BDI was also a significant predictor ($\Delta R^2 = .06$, $p = .03$). Examination of the interaction effect revealed that while higher depression was significantly associated with higher body dissatisfaction in both obese and non-obese women, the association was particularly strong in the obese women and predicted clinically elevated levels of body dissatisfaction (M = 139.17).

Discussion: Our findings suggest the potential importance of depression in predicting body dissatisfaction in AA women.

NR678 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Polysubstance Use Among Cocaine Abusers

Ashwin A. Patkar, M.D., *Department of Psychiatry, T. Jefferson University, 833 Chestnut Street, Suite 210E, Philadelphia, PA 19107*; Raman N. Gopalakrishnan, M.D., Stephen P. Weinstein, Ph.D., Allan Lundy, Ph.D., Muhammad I. Raja, M.D.

Summary:

Objective: Studies have indicated that dependence on more than one drug worsens prognosis, with polysubstance abuse linked to poor outcome. As a part of a large study investigating biological and clinical correlates of treatment outcome, we employed standardized instruments to diagnose current and lifetime substance use disorders among cocaine-dependent patients.

Method: Consecutive admissions to an intensive outpatient substance abuse treatment program affiliated to a university hospital in Philadelphia were studied. Inclusion criteria included cocaine as the primary drug. Subjects with comorbid bipolar disorders, schizophrenia, or current major depression, were excluded from the study. Consenting patients underwent the Structured Clinical Interview (SCID) for DSM-IV and current and lifetime diagnoses of substance use disorders were recorded. Chi square tests and tests of correlation were used for data analyses.

Results: Eighty-eight African-American subjects (74% men, mean age 35.5) with a primary diagnosis of cocaine dependence were studied. Only 12.5% of subjects have a current diagnosis of cocaine dependence alone (excluding nicotine dependence). 55.7% had a current diagnosis, and 56.8% had a lifetime diagnosis of alcohol abuse or dependence. About 76% had a lifetime diagnosis of nicotine dependence. Nearly 24% had current and 55.7% had lifetime diagnoses of cannabis abuse or dependence. About 5% were currently dependent on opiates and 11.4% had abused or were dependent on opiates in their lifetime. As expected, the number of lifetime and current substance abuse/dependence diagnoses were significantly correlated ($r = .421$, $p < 0.01$). About 13% had a current diagnosis of substance-induced mood or anxiety disorder and approximately 15% had a lifetime history of panic disorder or major depression, which was significantly correlated with the number of life-time diagnoses of substance use disorders ($r = .47$, $p < 0.01$).

Conclusion: The frequency of polysubstance abuse and dependence, especially alcohol, marijuana, and nicotine among cocaine-dependent patients seeking treatment is very high, at least in inner-city treatment settings. In fact, very few patients were "pure" cocaine abusers. These clinical syndromes may have implications for treatment and outcome.

Funded by NIDA grant # DA340-02.

NR679 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Longitudinal Study of Functional Status of Deinstitutionalization

Miklos F. Losonczy, M.D., *Department of Mental Health, VA NJ Health Care System, 151 Knollcroft Road, Lyons, NJ 07939*; Susan M. Essock, Ph.D., Robert A. Rosenheck, M.D., Thomas J.H. Craig, M.D., Mikaela Bachoe, B.A., David A. Smelson, Psy.D.

Summary:

Introduction: Despite large and rapid deinstitutionalization in the VA and public health care systems, there has been little systematic study of the quality of life of long-term hospitalized veterans. This study was undertaken to examine the effects of deinstitutionalization on veterans' quality of life at several NY/NJ VA hospitals.

Methods: Veterans with at least 90 consecutive days of psychiatric hospitalization were rated for 2 years following discharge to the community. Functional and psychiatric status was assessed using a 16-item scale rated by their clinician.

Results: Fifty-nine veterans were rated. Eighty-eight percent of the deinstitutionalized veterans had at least one rating within 6 months of discharge. Symptom severity was moderate in this group (mean CGI = 3.91). 10% were in nursing homes, while 62% were in supervised group homes. Employment of any type was low (10%). Most patients required a case manager (88%). Rehospitalization was low (10% within 30 days). Patient satisfaction with social setting was high (90%).

Discussion: Despite concerns about adverse consequences of deinstitutionalization, patients remain in treatment, have low short-term relapse rates, and remain generally satisfied with their quality of life. They do require case management, and improvements may be possible to provide greater autonomy in housing and employment.

NR680 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Impulsivity Testing Is a Predictor of Hospitalization Rates and Cue-Elicited Craving

John A. Williams, M.D., *Department of Mental Health, VA New Jersey, 151 Knollcroft, Lyons, NJ 07939*; Aron Starosta, Ph.D., David A. Smelson, Psy.D., Mikaela Bachoe, B.A., Douglas M. Ziedonis, M.D., Sarah M. Young, M.D., Miklos F. Losonczy, M.D.

Summary:

Introduction: There is increasing concern by clinicians about the effects of impulsivity in psychiatric disorders. Impulsive individuals tend to have greater psychiatric disturbance and are often challenging to clinicians. One type of psychiatric disorder that is frequently associated with impulsivity is substance abuse. Moreover, impulsive substance abusers have greater family discord, job loss, incarceration, and more difficulty maintaining sobriety. Perhaps related to impulsivity and important in maintaining the addiction is craving, particularly among cocaine-dependent patients. Because of the high incidence of impulsivity among substance abusing veterans, we were interested in studying its effect on both cocaine craving and hospitalizations.

Methods: Twenty hospitalized veterans previously diagnosed with cocaine dependence underwent cue-exposure to stimulate craving and completed the Eysenck impulsivity test. Hospitalization rates 2 years prior to admission were obtained retrospectively.

Results: Preliminary results suggest that the intensity of impulsivity predicted the amount of cue-elicited craving ($p = 0.005$) ($N = 20$). Furthermore, more impulsive individuals had significantly more admissions in the 2 two years ($p = 0.004$).

Discussion: Clinicians need to manage the spectrum of impulsive behaviors in psychiatric disorders, particularly cocaine addiction, which may reduce service utilization.

NR681 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Cue-Elicited Craving Among Individuals with Schizophrenia and Cocaine Dependence

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Summary:

Introduction: Cocaine abuse remains a serious public health problem in the United States among the psychiatric and non-psychiatric populations. In the psychiatric population, it is associated with increased hospitalizations, more relapses, and worse long-term outcomes. Because of the role of reinforcement in maintaining an addiction, we recently compared craving in schizophrenic and non-schizophrenic cocaine addicts. This study used a retrospective design and found that the cocaine-dependent schizophrenic subjects had significantly more craving than their non-schizophrenic counterparts (Carol et al, 2000). To extend this research, the present study used cue-exposure to stimulate craving and compare cue-elicited craving in cocaine-dependent schizophrenics subjects to non-schizophrenic cocaine addicts.

Methods: The sample consisted of eighty-nine schizophrenic and non-schizophrenic cocaine addicts who underwent a cue-exposure paradigm.

Results: The schizophrenic cocaine addicts ($N = 33$) had significantly more cue-elicited craving than non-schizophrenic cocaine addicts ($N = 56$) (mean = −13.2 [SD = 8.5] versus 0.42 [SD = 12.3]; $t = 5.6$, $df = 87$, $p < 0.0001$). After dichotomizing the data into responders and non-responders, 97% of the cocaine-dependent schizophrenic subjects were cue-reactive compared to 43% of the non-schizophrenic cocaine addicts ($\chi^2 = 23.7$ $df = 1$, $P < 0.0001$). Other data will also be reported in the poster.

Discussion: Future research should focus on targeting craving while treating the dual disorders.

NR682 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Prevalence of Inhalant Use Among Turkish High School Students

Kultegin Ogel, M.D., *Bakirkoy Akil Hastanesi, Umatem, Istanbul, Turkey*; Turkay Demir, M.D., Cuneyt Evren, M.D., Defne Tamar, M.D., Aytekin Sir, M.D., Berna D. Ulug, M.D., Demet E. Demir, M.D.

Summary:

Objective: There are limited studies on inhalant use among high school students in Turkey. It is believed that inhalant use is prevalent only among street children. In order to examine this opinion we conducted a research study on prevalence of inhalant use among high school students.

Method: The study was done in 15 different cities in Turkey. These cities were selected from different regions of Turkey. A detailed questionnaire was administered to 20,245 high school students between ages 15–17.

Results: Lifetime prevalence for inhalant use was 8.8%. Prevalence rate for the last 12 months was 4.5% and for the last month 3.1%. There were no gender differences. 24.2% of inhalant users used these substances for the first time when they were 16 years old. Inhalants were the most used drugs among friends of the students. Inhalants were the most available substances after beer, and 24% of students stated that they could find volatiles easily.

Conclusion: Inhalant use has been increasing in recent years in Turkey. These substances are very cheap and easily available. This study suggests that inhalant use is quite common among high school students, and it is not a specific drug for street children as it is believed.

NR683 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

The Journey to Quit Smoking by Patients with Severe Mental Illness and Addicted to Nicotine

Lisa B. Dixon, M.D., *Department of Psychiatry, University of Maryland, 701 West Pratt Street, Room 476, Baltimore, MD 21201*; Colleen McGuire, M.A., Letitia T. Postrado, Ph.D.

Summary:

Objective: Addiction to nicotine is a major health problem for persons with severe mental illness (SMI) who smoke at twice the rate of the general population. This study assessed smoking history, quit attempts, and stages of behavioral change among smokers with SMI.

Methods: 120 consenting randomly selected smokers with SMI (mean age = 42.2 years; 63% were men, 80% was African American) receiving services at a community mental health center and rehabilitation program completed a 30-minute interview focused on their smoking habits.

Results: Most patients (59%) were in the precomtemplation phase, 21% were in contemplation, and only 10% were in the preparation phase. Precontemplaters had higher Fagerstrom scores ($p < 0.05$). 72% of patients expressed at least some desire to quit smoking. Patients reported an average of 2.1 past serious attempts. The most common quit methods were "gradually cutting down" (79%) and going "cold turkey" (73%); a minority of patients used nicorette gum (28%), self-help manuals (12%), stop smoking programs (7%), support groups (7%), or hypnosis (4%).

Discussion: Despite the expressed desire for most smokers with SMI in this study to quit, the range of techniques they have used in the past suggests that health services are not being utilized. Although the neurobiological barriers to quitting for smokers with SMI are formidable, this study suggests the great need for service systems to provide tobacco cessation programs.

NR684 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Very Low Dose Naltrexone Pretreatment Attenuates Opiate Withdrawal in Rats

Paolo Mannelli, *Department of Psychiatry, Jefferson University, 833 Chestnut East, Suite 210E, Philadelphia, PA 19107*; Edward Gottheil, M.D., Wolfgang H. Vogel, Ph.D., Elisabeth J. Van Bockstaele, Ph.D.

Summary:

Objective: Acute administration of antagonists to shorten opiate detoxification causes intense withdrawal. Heavy pharmacological sedation is then routinely performed to control the symptoms; however, serious complications often occur. On the other hand, experimental evidence of increased opiate analgesia and reduced dependence by very low doses of antagonists points to alternative strategies in detoxification. To verify this possibility, we examined the effects of very low-dose naltrexone pretreatment on behavior and on immediate early gene (c-fos) expression in brain during opiate withdrawal in rats.

Method: Twelve rodents implanted subcutaneously with morphine (150 mg) or placebo pellets were injected on the ninth day of treatment with either saline or naltrexone (100 mg/kg i.p.) and observed for withdrawal. Eight of them had received naltrexone in drinking water (5mg/l), from day 3 on, without showing discomfort.

Results: Compared with the non-pretreated condition, naltrexone pretreatment attenuated the withdrawal behaviors that were rated. The pretreated rats showed also reduced c-fos activation, as measured by quantitative analysis in the nuclei of the solitary tract, paragigantocellularis, rostral and caudal ventrolateral medulla, which mediate autonomic expressions of withdrawal. C-fos induction in other brain nuclei is under evaluation, and will be presented.

Conclusions: Very-low naltrexone dosing may attenuate withdrawal intensity by decreasing withdrawal-induced neuronal activation.

NR685 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Curriculum Infusion: Impact of AOD Education on Emergency Room Health Care Providers

Ernesto A. Amaranto, M.D., *Department of Psychiatry, New Jersey Medical School, 30 Bergen Street, ADMC 1514, Newark, NJ 07107-3000*; Barbara B. Caldwell, M.S.N., Edward J. Flynn, Ph.D.

Summary:

Substance-abusing individuals are overrepresented in emergency room utilization. Studies show an increase (30%) in the probability that a chronic drug abuser will use an ER compared with nondrug-users. These studies suggest ER settings are useful in identifying drug-related problems. An empirical examination of documentation and referral of drug use on medical history was conducted. Date were collected from an inner city health sciences university hospital emergency department. A probability sample (N-200) was randomly drawn from ER medical records. Curriculum infusion was used to obtain qualitative information from ER personnel. Curriculum infusion consisted of substance abuse grand rounds and post-presentation discussion with ER director, staff, and hospital administration. Analysis suggests that professional disciplines vary in documentation and referral of substance abusing ER patients. In the case of alcohol, less than half (45.3%) of the medical records documented use. When documented over 88% of patients were users. Of the patients sent for referral (41.5%) only 12% were referred to a substance abuse treatment facility.

Conclusions: Qualitative information gathered indicated high substance abuse problems among ER patients that medical records failed to document. Although when documented supported the high level of use. However, referral for substance abuse treatment was less than referrals for other medical conditions.

NR686 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Higher Transferrin Receptors (TfR) and Lower Clara Cell Protein (CC16) Serum Levels in Medicated Bipolar Mania

Sy-Jye C. Leu, Ph.D., *Graduate Institute of Cell & Molecular Biology, Taipei Medical University, 250 Wu-Hsing Street, Taipei 110, Taiwan*; Shang-Ying Tsai, M.D., Chao-Hsien Lee, Ph.D., Chiao-Chicy Chen, Ph.D., Yi-Yuan Yang, Ph.D., Hsin-Chien Lee, M.D.

Summary:

Objective: Our prior works found that immune modulators [e.g., soluble interleukin-2 receptor (sIL-2R) and sIL-6R] of bipolar mania might differ from those of schizophrenia and major depression [1, 2]. The serum levels of soluble transferrin receptor (TfR) and Clara Cell protein (CC16) in bipolar mania have not been well examined.

Method: The subjects were 36 physically healthy bipolar patients (DSM-IV) with Young Mania Rating Scales scores ≥26 who were age 17 to 45 and 36 age-matched normal control subjects. Seven patients were free from any psychotropic drugs, and the rest of the patients were treated with mood stablizers alone or with typical antipsychotics.

Results: The serum TfR levels were significantly higher in medicated manic patients than in drug-free ones or normal control subject ($F = 3.43$, $p < 0.04$). The serum CC16 levels of medicated manic patients were lower than those of drug-free ones and normal control subjects with marginally statistical significance ($F = 2.62$,

p = 0.08). Neither types of mood stabilizer nor combination of antipsychotics showed any influence on serum TfR or CC16 levels.

Conclusions: The immuno-modulation mechanism of drug-free bipolar manic patients may differ from those of major depression and schizophrenia. However, the effects of psychotropic agent on TfR and CC16 in bipolar mania may resemble those in schizophrenia and major depression.

NR687 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Fluoxetine Versus Placebo in PTSD

Ferenc Martenyi, M.D., *Department of Neuroscience, Lilly Area Medical, Barichgasse 40–42, Vienna A-1030, Austria*; Eileen Brown, Ph.D., Harry Zhang, Ph.D., Apurva Prakash, M.S., Stephanie Koke, M.S.

Summary:

Objective: This study was designed to address the efficacy and tolerability of fluoxetine in patients with PTSD. The patient population included both civilians and combat veterans.

Methods: This was a double-blind, randomized, placebo-controlled study conducted in Europe and South Africa. 81% of the patients were male, with 48% exposed to a combat-related traumatic episode. Patients were randomly assigned to 12 weeks of acute treatment with fluoxetine (N = 226) or placebo (N = 75). Dosage could be increased from 20 mg to 80 mg at fixed intervals based on response. The primary efficacy measurement was the mean change from baseline in the Treatment Outcome PTSD rating scale (TOP-8) total score. Secondary assessments included the Clinician-Administered PTSD Scale (CAPS), Davidson Trauma Scale (DTS), MADRS, HAMA, CGI-Severity, CGI-Improvement, and SCL-90-R. Safety measures included comparison of treatment-emergent adverse events, vital signs, and laboratory measures.

Results: Fluoxetine was associated with a greater improvement from baseline in total TOP-8 score than was placebo. This difference was statistically significant by week 6 of treatment through the end of the acute phase of the study (week 12). Compared to placebo, fluoxetine was also associated with statistically greater improvement in CAPS total score, intrusive and hyperarousal subscores, HAMA, MADRS, CGI-Severity, and CGI Improvement. The mean fluoxetine dose at endpoint was 57 mg/day. There was no statistically significant difference between treatment groups in the incidence of any individual adverse event nor was there any difference in dropout rate due to adverse events.

Conclusion: Fluoxetine is effective and well-tolerated in the treatment of PTSD.

Research funded by Eli Lilly and Company, Indianapolis, Indiana 46285.

NR688 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

The Effects of Stress on Memory Consolidation

Bernet M. Elzinga, M.S.C., *Department of Psychology, University of Amsterdam, Roetersstraat 15, Amsterdam 1018 WB, Netherlands*; Abraham Bakker, M.D., J. Douglas Bremmer, M.D.

Summary:

One of the most intriguing findings in the field of stress and memory is that occasionally people may develop memory impairments after having experienced traumatic events, so that large parts of the traumatic memory are lost (APA, 1994). Only a few studies have demonstrated that exposure to a stress-inducing task may result in immediate memory dysfunctions (Lupien et al., 1997). Long-term declarative memory for information learned under stressful circumstances has not been studied before. In this study we investigated the effects of stress, and the stress-hormone cortisol, on memory consolidation in healthy subjects. Sixteen participants were presented neutral and emotional material (words and paragraphs) before and after a stress challenge. Recall of the information was tested 24-hours later. Heart rate, blood pressure, and cortisol levels significantly increased as a result of the challenge. Recall of paragraphs and words learned after the stress challenge was significantly impaired compared to information encoded before the challenge. Memory impairments did not correlate with changes in cortisol, however. This shows that consolidation of information can be disrupted after exposure to a stressful event. More research is needed to study the psychophysiological mechanisms involved in these impairments.

NR689 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Reducing Violence in Psychosis: The Effect of Intensive Case Management

Elizabeth M. Walsh, M.D., *Division of Psychological Medicine, Institute of Psychiatry, de Crespigny Park SE5 8AF, England*; Catherine M. Gilvarry, B.S., Chiara Samele, Ph.D., Francis Creed, M.D., Peter Tyrer, M.D., Thomas J. Fahy, M.D., Robin M. Murray, M.B.

Summary:

Objective: To establish whether intensive case management (ICM) reduces the prevalence of violence in the severely mentally ill compared to standard care and to identify predictors of violent behavior.

Method: 708 individuals with established psychotic illness were randomly assigned to receive either ICM (caseload 10–15 per case manager) or standard care (30+ patients per case manager). The 2-year prevalence of physical assault, measured from multiple data sources, was compared between the groups. Possible predictors measured at baseline were identified in a regression model.

Results: No significant effect on violence was found in the intensive case management versus the standard care group (22.7% vs 21.9%, respectively; p = 0.86). Predictors of violence included drug abuse (p = 0.003), special education (p = 0.02), multiple recent psychiatric admissions (0.04), and a previous history of violence (p = 0.02).

Conclusions: Increasing the intensity of community treatment did not reduce the prevalence of violence in the severely mentally ill compared to standard care in the first randomized controlled trial conducted to examine this issue.

NR690 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Significant Levels of Anxiety: An Effect of War on Children

Ruby C. Castilla Puentes, M.D., *Department of Epidemiology, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213*; Ivan Gomez, M.D., Sandra Castilla, M.D., Wilma Castilla, M.D., Douglas Williamson, Ph.D., Miguel Habeych, M.D., Boris Birmaher, M.D.

Summary:

Objective: To examine symptoms of anxiety in children living in rural areas of Colombia, South America, exposed to the stress of civil war.

Methods: A total of 300 school-aged children/adolescents from a stratified, random sample of schools in a rural area in Belen, Boyacá, Colombia, were ascertained. Children and their parents were assessed with the Screen for Child Anxiety Related Emotional Disorders (SCARED).

Results: The overall response rate was 97.6%, consisting of 183 girls and 11 boys with a mean age of 12.3 years (range 10–18 years). Among all of the children, 239 (81.56%) reported a total score of >25, which is the cut-off score for anxiety disorders.

Of the girls, 169 (91.84%) had a total score of >25, and 70 (64.22%) of the boys had total scores of >25.

Conclusions: Our results suggest that these children exposed to dangerous and violent situations in their environment are experiencing higher levels of anxiety symptoms, particularly among girls. The anxiety symptom scores in our rural population is higher than those reported in similar studies using the SCARED in children and adolescents not exposed to the stress and violence associated with a civil war.

NR691 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Trauma and Psychopathology in Rural Mississippi

Maurice Preter, M.D., *Department of Psychiatry, The University of MS Medical Center, 6295 Old Canton Road, 9A, Jackson, MS 39211*; Sabina E. Preter, M.D.

Summary:

Objective: To identify and characterize exposure to traumatic experiences in a poor rural county near the Mississippi Delta.

Method: The first 138 consecutive patients presenting over the last year to a new neuropsychiatry and child psychiatry satellite of the University of Mississippi received a comprehensive psychiatric evaluation that included an extensive trauma history.

Results: There were 45 female and 32 male adult patients from aged 18 to 84 (mean age = 33.1, SD = 10.1,). 61% had experienced psychologically devastating traumatic events. There were 28 girls and 43 boys aged 1 to 18 (mean = 9.2, SD = 3.1), 66% of whom were traumatized. Experiencing a traumatic event was the presenting complaint in less than 5% of traumatized patients. Events elicited included witnessing of suicides, homicides, and fatal car accidents; sexual abuse; and in young children, abandonment and neglect. Only 10% of the total sample had full PTSD. Partial PTSD, chronic adjustment disorders, depression with chronic suicidality, and conduct disorder were prevalent. Results are presented separately for children.

Conclusion: Severe trauma, although rarely the presenting complaint, was highly prevalent and was associated in this sample with high levels of psychopathology and dysfunction. PTSD diagnostic criteria may significantly underestimate community rates of trauma.

NR692 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Peritraumatic Dissociation and Traumatic Stress: A Three-Month Prospective Study

Philippe J.R. Birmes, M.D., *Department of Psychiatry, Chu de Toulouse, Place Baylac, Toulouse 31059, France*; Didier Carreras, M.D., Jean-Paul Charlet, M.D., Barbara A. Warner, M.D., Dominique Lauque, M.D., Laurent J. Schmitt, M.D.

Summary:

Objective: This study compared the relations between peritraumatic dissociation, acute stress, and development of PTSD in victims of violent assault.

Method: 88 subjects were assessed within 24 hours of the trauma with the Peritraumatic Dissociative Experiences Questionnaire-Self-Report Version (PDEQ-SRV). 27 were followed longitudinally to assess acute stress (2 weeks after the assault) with the Stanford Acute Stress Reaction Questionnaire (SASRQ) and posttraumatic stress 3 months after with the Clinician-Administrated PTSD Scale (CAPS) and the Impact of Event Scale (IES).

Results: Of the 27 victims, nine (33.3%) were diagnosed with PTSD at 3 months. Among PTSD subjects mean PDEQ scores were significantly higher (3.3, SD = 10.9) than in those without PTSD (2.3, SD = 0.7) (t = 3, df = 25, p = 0.006). Among PTSD subjects mean SASRQ scores were significantly higher (95.4, SD-24.3) than in those without PTSD (55.3, SD = 28.5) (t = 3.6, df = 25, p =.001).

Conclusions: High levels of peritraumatic dissociation and acute stress following violent assault are risk factors for PTSD at 3 months. Identification of acute reexperiencing can help the clinician identify subjects at highest risk.

NR693 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Acute Stress and PTSD with Comorbid Depression

Philippe J.R. Birmes, M.D., *Department of Psychiatry, Chu de Toulouse, Place Baylac, Toulouse 31059, France*; Jean-Paul Charlet, M.D., Laurent J. Schmitt, M.D.

Summary:

Objective: Study of the relation between acute stress and development of PTSD with comorbid depression in victims of violent assault.

Method: A total of 49 subjects were assessed two weeks after the trauma with the Stanford Acute Stress Reaction Questionnaire (SASRQ). Twenty-seven were followed to assess posttraumatic stress and depression three months after with the Clinician-Administrated PTSD Scale (CAPS), the Impact of Event Scale (IES), and the Beck Depression Inventory-13 items.

Results: Of the 27 victims, four (14.8%) were diagnosed with PTSD and depression at three month (PTSD/MDD). Among PTSD/MDD subjects mean SASRQ scores were significantly higher (102 ± 24.6) than in those without PTSD and depression (62.9 ± 31) (t = 2.3 df = 25 p = 0.024).

Conclusions: High levels of acute stress following violent assault are risk factors for PTSD with comorbid depression at three month. Identification of acute anxiety or increased arousal can help the clinician identify subjects at highest risk.

NR694 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Efficacy of Divalproex Sodium Treatment of Incarcerated Violent Offenders

Richard A. Greer, M.D., *Department of Psychiatry, University of Florida Health Center, Box 100256, Gainesville, FL 32610-0256*; Michael J. Herkov, Ph.D., Pamela Kenworthy, M.D., Jerry G. Newman, M.D., Robert A. Stetson, M.D.

Summary:

Intermittent explosive disorder, as listed in the DSM-IV, is an ill-defined mental disorder with no standard psychopharmacological therapy. Incarcerated violent offenders have a high rate of emotional lability and verbal/physical outbursts. Medications, which ameliorate these characteristics, have significant public health implications. Previous open-label studies using divalproex sodium with adolescents have shown some efficacy in this area. This treatment modality was compared with traditional forms of medication management in an institutionalized forensic setting.

Violent offenders, who met criteria for intermittent explosive disorder, received four weeks of divalproex treatment and four weeks of treatment with either antipsychotic, antidepressant, or non-benzodiazepine tranquilizing medication. At the end of four weeks, individuals in the divalproex group were switched to one of the other medications and vice versa. Independent evaluators, blind to group assignment, assessed response at the end of each time period. Patients with significant medical problems, mental retardation, major depression, head trauma, or bipolar disorder were excluded. For diagnosis, a forensic psychiatrist using the structured clinical interview for DSM-IV, with supplemental questions for intermittent explosive disorder, was used. Outcome at the end of each phase was measured by an independent evaluator, administering six items from the anger—hostility subscale SCL90 and the Modified Overt Aggression scale, used to assess impul-

sive/aggressive behavior in adults with personality disorders. Results indicate incarcerated violent offenders obtain a significant response, demonstrating divalproex is an effective treatment for explosive temper and mood labiality. Furthermore, divalproex appears to be well tolerated, without significant side effects or the potential for abuse.

NR695 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Universal and Distinct Features in Survivors of Different Types of Trauma

Jaime H. Carcamo, Psy.D., *Columbia University, 1051 Riverside Drive, Unit 69, New York, NY 10032*; Randall D. Marshall, M.D.

Summary:

The official DSM-IV diagnosis of PTSD does not fully capture the range of posttraumatic problems that many patients experience. Furthermore, there is a dearth of research that examines the unique features that are specific to different types of traumas (e.g., sexual abuse, physical assault, or accidents).

Methods: The history of each individual (N = 43) was reviewed by two clinicians in order to determine the primary trauma linked to PTSD symptoms. The group was divided into three trauma categories: 1) sexual abuse/assault, 2) physical assault, and 3) other (primarily accidents). Group rates were then compared on selected variables.

Results: Significant differences were found among the three trauma groups on selected SCID I disorders ($F = 4.06$, $df = 2$, $p < 0.025$). A trend was also observed when the three trauma groups were compared on SCID II disorders ($F = 3.05$, $df = 2$, $p = 0.059$). Post hoc pairwise comparisons revealed that the sexual abuse/assault group had higher rates of SCID I and SCID II disorders than the other two trauma groups. These results suggest that type of trauma may be associated with clinically meaningful differences within the diagnosis of PTSD. Comorbidity and associated features may be important to consider in future descriptive and treatment outcome studies.

Funding: By a grant from the Lowenstein Foundation.

NR696 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Effectiveness of Paroxetine in Low-Income African-American Women with MDD

Joyce Y. Chung, M.D., *Department of Psychiatry, Georgetown University Medical School, 3800 Reservoir Road, NW, Washington, DC 20007*; Juned Siddique, M.S., Katherine L. Beebe, Ph.D., Erica Wetherhold, B.S.N., Jeanne Miranda, Ph.D.

Summary:

Objective: We examined the effectiveness of paroxetine versus usual care in depressed low-income African American women.

Methods: Subjects were screened for depression from community-based clinics providing services such as family planning or WIC. Women with MDD were randomly assigned to one of three conditions (antidepressants, CBT, or usual care). We report on 9-week outcomes for 18 African American subjects who received paroxetine compared to 18 matched control subjects assigned to usual care. Demographic characteristics: mean age = 28.9; married = 19%; mean number of children = 2.3; uninsured = 39%, Medicaid = 28%. Eighty-one percent had at least one anxiety disorder; 33% had two or more anxiety disorders. PTSD was the most common comorbid disorder (61%) followed by GAD (37%).

Results: Baseline HAM-D scores: medication group = 19.6, usual care group = 16.3 (n.s.). Mean paroxetine dose: 30 mg. Mean change in HAM-D scores after 9 weeks: paroxetine group = 10.1, usual care group = 3.6 ($p < 0.02$). Six-month change in HAM-D/HAM-A scores for paroxetine subjects was 12.0/10.8 and for usual care was 6.5/4.2 ($p < 0.09/0.06$).

Conclusions: After 9 weeks of treatment there were significant effects of paroxetine compared to usual care in subjects with MDD and high rates of comorbid anxiety disorders. Our findings provide support for the effectiveness of paroxetine in low-income African American women.

Research funded by National Institute of Mental Health and SmithKline Beecham

NR697 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Treatment Outcomes in Low-Income Depressed Women With and Without PTSD

Joyce Y. Chung, M.D., *Department of Psychiatry, Georgetown University Medical School, 3800 Reservior Road, NW, Washington, DC 20007*; Juned Siddique, M.S., Bonnie Green, Ph.D., Katherine L. Beebe, Ph.D., Erica Wetherhold, B.S.N., Jeanne Miranda, Ph.D.

Summary:

Objective: We evaluated treatment outcomes in low-income depressed women with and without comorbid PTSD to determine whether comorbidity effects treatment response.

Methods: The WECare study is a treatment intervention study that focuses on low-income mostly minority women with MDD. We report clinical outcomes for the first 38 subjects treated with either CBT or paroxetine. Fifty-five percent had both MDD and PTSD at the time of study enrollment. Ethnic representation: African American 67%, Hispanic 24%, and white 9%. Demographic characteristics: mean age-29.7; mean number of children-2.4; 38% were married; uninsured-58%, Medicaid-19%. Baseline HAM-D/HAM-A scores were as follows: MDD alone: 16.6/16.3, MDD+PTSD: 19.2/17.7. Mean paroxetine dose: 30 mg.

Results: CBT subjects' 6-month mean change in HAM-D scores: 7.3 (MDD) and 11.0 (MDD+PTSD). Paroxetine subjects' 6-month mean change in HAM-D scores: 8.4 (MDD) and 12.9 (MDD+PTSD). Six-month mean change in HAM-A scores for CBT subjects: 6.8 (MDD) and 7.0 (MDD+PTSD). Six-month mean change in HAM-A scores for paroxetine subjects: 8.1 (MDD) and 12.8 (MDD+PTSD). SF-36 summary scores improved for all subjects.

Conclusions: Subjects with MDD and comorbid PTSD treated with either CBT or paroxetine did as well, if not better, than subjects with MDD alone. Our findings support the effectiveness of standard treatments for depression in low-income women with complex psychiatric profiles.

Research funded by National Institute of Mental Health and SmithKline Beecham

NR698 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Interchange Ability: Brand Versus Generic Clozapine

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Summary:

Background: Recent lay press publications and one published abstract have questioned the interchangeability of generic clozapine (Zenith Goldline (ZGP)/IVAX Pharmaceuticals) and Novartis brand Clozaril® on a clinical and pharmacological basis. This poster will provide information derived from the ZGP Clozapine patient registry database to address whether patients can be converted between these two clozapine formulations without the necessity of dose changes. Although the primary goal of a clozapine

registry is to monitor WBC counts, for many patients, dosage values are also reported. To be considered interchangeable on a milligram to milligram basis, one could expect the frequency of dose changes after conversion from brand to generic to be no more than what one would expect after a new patient achieves therapeutic stability at any particular dose.

Methods: The ZGP database included 14,726 patients with dosage information. For these, patients stabilized on generic drug (6 months of continuous use) were compared to those who were newly "switched" between formulations. Patient data was analyzed for changed doses during the 2-week-follow-up blood draws.

Results: Analysis revealed that of the patients new or converting to ZGP clozapine, with available dosage information greater than 90% did not require dose adjustments. Of the patients who required a change (increase or decrease) there was no statistically significant difference ($p > 0.05$) between converted and new patients.

Dose changes on new versus converted clozapine patients[1]

	New Patients[2] (n=1,018)	Converted Patients[3] (n=13,708)
No. with increase in dose	60 (5.9%)	655 (4.8%)
No. with decrease in dose	47 (4.6%)	481 (3.5%)
No. with no change in dose	911 (89.5%)	12,572 (91.7%)

1) Dose changes (increase or decrease) are similar for patients who are switched compared to patients who start on generic with over 6 months of continuous therapy. The difference is not significant ($p>0.5$) between the two groups with respect to relative increases or decreases in dosage.
2) The dose comparison for new patients was performed on those with at least 6 months of continuous treatment on ZGP Clozapine (evidenced by WBC count reports received by the ZGP patient registry). The first data point was the first WBC report received by the registry after 6 months of continuous treatment. The second data point was the next available dose not greater than 21 days from the first data point (mode=14).
3) The dose comparison for converted patients was performed on those with at least 6 months history of using Clozaril® evidenced by a having a bi-weekly WBC monitoring frequency at the time of registration. The first data point was the first WBC report received by the registry after registration. The second data was derived as above.

Conclusions: These data support interchangeability (i.e., the AB rating) because significant number of patients have been converted from brand to generic on a milligram-to-milligram basis and have required no additional dosage adjustments. The data also support the concept that patient registries can offer health care professionals valuable opportunities to explore complex patient/dose/time course data in ways previously unexplored.

NR699 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Detained Youth: Who Needs Mental Health Services?

Bonnie T. Zima, M.D., *Department of Psychiatry, UCLA-NPI, 10920 Wilshire Boulevard, #300, Los Angeles, CA 90024*; Gregory Lecklitner, Ph.D., Denise M. McDermott, M.D., Mary Ann Schaepper, M.D., Diana Liao, M.S., Douglas Wiegand, M.A.

Summary:

Objective: To describe the number of mental health problems among detailed youth and to examine their relationship to sociodemographic factors, service use, and criminal history.

Method: A two-stage screening procedure was used to interview 251 youth ages 11–17 years entering one of three large juvenile halls. The main outcome measures were the Massachusetts Youth Screening Instrument (MAYSI-2), Voice Diagnostic Interview Schedule for Children (V-DISC-IV), Kaufman Brief Intelligence Test (K-BIT), and the Child and Adolescent Functional Assessment Scale (CAFAS).

Results: Almost one-third (32%) of the youth screened positive for at least one serious mental health problem. Of these, 75% met diagnostic criteria for at least one psychiatric disorder, 55% had below average intelligence scores, and 75% had marked or severe functional impairment. Youth were likely to be at risk for mental health problems if they had a prior history of mental health service use ($p = 0.0002$), school failure ($p = 0.009$), juvenile hall entry ($p = 0.018$), or homelessness ($p = 0.002$) but not if they had been charged with a serious violent offense ($p = 0.681$).

Conclusions: Detained youth are at high risk for serious mental health problems. Mental health interventions should be targeted toward those with a history of prior mental health service use, school failure, and recidivism.

NR700 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Treatment of Depression in Nursing Homes: Second-Generation Issues

Catherine J. Datto, M.D., *Department of Psychiatry, University of Pennsylvania, 3600 Market Street, 7th floor, Philadelphia, PA 19104*; Stephen M. Scheinthal, D.O., David W. Olsin, M.D., Joel E. Streim, M.D., Suzanne D. DiFilippo, R.N., Deborah L. Rooney, R.N., Ira R. Katz, M.D.

Summary:

The undertreatment of depression was one of the issues that drove nursing home reform and federal regulations over the last decade. Recently, however, HCFA reported that 25% of nursing home residents nationwide are receiving antidepressant medications, suggesting that there have been significant changes in clinical practice. To begin to characterize current care, we evaluated medication use and cognitive status (MMSE) in 653 residents from five community nursing homes. 200 residents had MMSE scores >12 and completed the Geriatric Depression Scale (GDS). Overall, 47.2% of residents were receiving an antidepressant. Among those with MMSE score >12, 34.% had GDS >10 and were considered depressed, and 47.6% were receiving an antidepressant. Crosstabulation showed that 14.7% of the more intact residents were depressed without current treatment, 22.0% were depressed in spite of current antidepressant treatment, and 25.6% were taking antidepressants without current symptoms. This suggests that failure to treat depression remains a significant problem. However, it also suggests that there are new "second-generation" problems including inadequate prescribing and that there is a need for algorithms to guide decision-making about continuous/maintenance treatment. Although there have been improvements in care over the past decade, the need for mental health services research in nursing homes remains apparent.

NR701 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Reliability in Reporting Diabetes-Related Health Information Among Adults with Serious Mental Illness (SMI)

Richard W. Goldberg, Ph.D., *Department of Psychiatry, University of Maryland, 685 West Baltimore Street, MSTF Room 300, Baltimore, MD 21201*; Karen A. Wohlheiter, M.S., Janine C. Delahanty, M.A., Faith Dickerson, Ph.D., Lisa B. Dixon, M.D., Anthony F. Lehman, M.D., Alan S. Bellack, Ph.D.

Summary:

Objective: To evaluate test/re-test reliability on a diabetes-related assessment for a sample of people with serious mental illness (SMI) and diabetes.

Methods: Using a two-week retest, correlation coefficients and percent agreement scores were calculated on questions about diabetes-related health behaviors, service utilization, and health beliefs for 18 adults with SMI and diabetes and 17 adults with diabetes but no history of mental health treatment.

Results: Reliability scores were generally comparable across the two groups. Percent agreement scores for reports of health

status (e.g., age of onset, medications used) and use of diabetes-related medical services were almost all above 90%. Agreement scores on diabetes-related health problems (e.g., kidney problems) were over 80% for both groups, as were scores on items regarding the receipt of health-related cues (e.g., advice regarding diet and exercise). Consistency on health belief items was not as strong (agreement scores ranged from 29% to 69%).

Conclusion: People with SMI are able to consistently report information about their health status and related behaviors. As these data are part of a larger study, future reports will be able to reliably discuss how people with schizophrenia and other serious mental illnesses access and utilize adequate medical care.

NR702 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Health Care Utilization and Costs in Schizophrenic Patients Taking Risperidone Versus Olanzapine in a Veterans Administration Population

Matthew A. Fuller, Pharm.D., *Department of Veterans Affairs, Medical Center, 10000 Brecksville Road, Brecksville, MD 44141*; Kenneth M. Shermock, Pharm.D., Michelle Secic, M.S., Jonathan S. Laich, B.S., Michael B. Durkin, M.S.

Summary:

Objective: To compare the change in health care utilization and costs over the one-year period before and after starting risperidone versus olanzapine.

Methods: A retrospective analysis was conducted in schizophrenic patients comparing risperidone (R) and olanzapine (O). The change in number and costs of inpatient hospitalizations, outpatient clinic visits, medications, and total health care were compared using analysis of covariance.

Results: The olanzapine group (n = 304) had more inpatient admissions (O: 0.09 vs. R: −0.24, p = 0.026), longer inpatient lengths of stay (O: 4.3 days vs. R: −4.2 days, p = 0.004), and higher costs of inpatient admissions (O: $2,735 vs. R: −$3,226, p = 0.003) as compared with decreases in the risperidone group (n = 344). The olanzapine group were slightly older (O: 53.3 vs. R: 51.1, p = 0.02) and had more Caucasians (O: 64.8% vs. R: 51.2%, p = 0.001). The risperidone group had significantly lower total costs in the year after starting risperidone as compared with increased total costs in the olanzapine group (O: $5,665 vs. R: −$1,167, p < 0.001).

Conclusions: Patients receiving risperidone had significantly less service utilization and lower costs compared to the year prior to risperidone therapy, whereas olanzapine patients had significantly greater utilization of medical services and costs as compared with prior to starting olanzapine.

NR703 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Risperidone and Olanzapine Utilization and Expenditures Within the Texas Medicaid Program

Michal Johnsrud, Ph.D., *Department of Pharmacoeconomic Studies, University of Texas at Austin, 2409 University Avenue, Room 3210E, Austin, TX 78712*; Lynn Crimson, Pharm.D., Ann Thompson, B.S.N., Amy L. Grogg, Ph.D.

Summary:

Objective: Describe trends in the use and expenditures of risperidone and olanzapine within the Texas Medicaid Program.

Methods: A retrospective cohort analysis utilizing 21 months of Texas Medicaid pharmacy claims data that included 37,528 risperidone and 20,340 olanzapine patients.

Results: The mean age for risperidone patients was (52.7 years vs. 50.7 years, (p < 0.001)). Use within children and geriatric patients was higher for risperidone. Analyses were conducted between risperidone and olanzapine patient groups, respectively, for all patients: (1) mean cost per day ($4.56 vs. $8.62 (p < 0.001)), (2) mean dose per day (2.52 mg vs. 10.65 mg), (3) mean length of treatment (221.3 days vs. 239.2 days (p = 0.001)), (4) mean medication possession ratio (62.5% vs. 64.6% (p < 0.001)), (5) mean cost per patient for concomitant medications utilized during the study ($833.77 vs. $933.33 (p < 0.001)), (6) rate of switching to the other study agent (7.8% vs. 10.3%). Additionally, mean risperidone cost per day was significantly lower across all patient age groups.

Conclusions: Relative differences in treatment measurements are not clinically notable. Based on mean cost per day, olanzapine was 89% more expensive than risperidone. Thus, significantly lower costs per day for risperidone, as compared with olanzapine patients, would suggest greater cost-effectiveness with risperidone.

NR704 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Medicaid Eligibility: Former Supplemental Security Income (SSI) Recipients with Drug Abuse and Alcoholism (DA & A) Disability

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Summary:

As of 1/1/97, Supplemental Security Income (SSI) recipients who were disabled due to drug abuse or alcoholism (DA&A) were no longer eligible for SSI and began to be eliminated from receiving this benefit. This endangered related benefits, notably Medicaid. The study purpose was: (1) to determine baseline hospital use as an indicator of medical need among those affected by the policy change, and (2) to examine the relationship of baseline medical need to their subsequent eligibility for Medicaid due to psychiatric and medical disability.

Design: Longitudinal cohort study of 11,740 Chicago residents who were eligible for SSI and Medicaid due to DA&A disability from 1995 to 1996.

Measures: Medicaid and state records for hospital use in 1995 and Medicaid eligibility files (1997–1998).

Results: A total of 26% were hospitalized in 1995 (N = 3,098), including 535 for psychiatric problems, primarily psychotic disorders, 72% (N = 384). A year after the policy change (12/31/97), 42% had lost Medicaid eligibility as well as SSI (N = 4,911). Psychiatric hospitalization in 1995 was a significant predictor, p < .005 of receiving Medicaid one year after the policy change (12/97). However, 38% of those previously hospitalized with psychotic disorders were no longer eligible for Medicaid (N = 144), including 27% of schizophrenics.

Discussion: This policy change threatened access to Medicaid in a highly vulnerable population. Baseline hospital use suggested very high levels of medical need among SSI recipients whose disability status, DA&A, no longer qualified them for Medicaid after 1/97. Over one-fourth were hospitalized in 1995, which is about three times the rate in the general population of adults under age 65. Although those with psychiatric hospitalizations were more likely to retain Medicaid eligibility, substantial proportions of persons with serious psychiatric disorders lost their Medicaid benefit.

NR705 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Comparison of Crisis Intervention Programs in a Military Population

Gail Manos, M.D., *Department of Psychiatry, Navel Medical Center, Portsmouth, VA 23708*; Janis R. Carlton, M.D., Juan C. Arguello, D.O., Belina R. Alfonso, M.D.

Summary:

We describe transition from an inpatient psychiatric crisis intervention model to an outpatient program with a review of 600 records. Demographics, clinical outcomes, and cost analysis are presented. The outpatient program consisted of a five-day structured protocol, total contact time 25 hr/patient. Average length of inpatient stay was 5.35 days. Time on the unit was 127.7 hours, direct contact time was 18.7 hours; 84% of inpatients and 57% of outpatients reported suicidal ideation. Rate of suicide attempts was similar (15% inpatients; 13% outpatients). Primary stressors were occupational and relational for both groups. Discharge diagnoses were similar. 58% inpatients and 17% outpatients were recommended for separation from the military for personality disorder or inability to adjust. Cost of inpatient treatment was $764/day compared with $54/day for outpatients. During FY97 there were 606 admissions for crisis intervention with a total cost of $3,102,723. During FY98 there were 1,794 patients who completed the outpatient program for a total cost $98,329. Beck scores and customer satisfaction scores were not available for inpatients. Beck scores for outpatients showed a seven-point improvement. Patient satisfaction ratings were high. Not only was the outpatient program much more cost effective, but it appeared to have superior clinical results.

The views expressed in this article are those of the authors and do not reflect the official policy or position of the Department of the Navy, Department of Defense, or the United States Government.

NR706 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Neurosteroids in an Endocrine Model for Postpartum Mood Disorders

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Summary:

Background: Neuroactive metabolites of gonadal steroids (neurosteroids) are potent neuromodulators implicated in both the pathophysiology of depression and the mechanism of action of antidepressants. Neurosteroids could play a role in postpartum depression (PPD).

Methods: We employed a blinded "scaled down" endocrine model of pregnancy. First, hypogonadism was induced in euthymic women with the gonadotropin-releasing hormone agonist leuprolide acetate. Second, supraphysiologic doses of estradiol and progesterone for were added back for 8 weeks. Finally, both steroids were acutely withdrawn. Samples for neurosteroid assays (using gas chromatography-mass spectroscopy) were obtained at 6, 8, and 10 weeks, approximating mid- and late pregnancy and early postpartum, respectively. Data were analyzed using ANOVA-R and Spearman's rho.

Results: Seven women with PPD and seven without a history of PPD were studied. Significant increases in depressive symptoms were observed in the PPD women only, both during hormonal replacement and after hormone withdrawal. No significant diagnostic group differences in neurosteroid levels were observed. At the end of addback, changes in allopregnanolone levels were significantly and inversely correlated with Beck Depression Inventory score ($r = -0.93$, $p = 0.01$) and Edinburgh Postnatal Depression score ($r = -0.80$, $p = 0.04$).

Conclusions: In women with PPD, lower allopregnanolone levels during late pregnancy may contribute to the susceptibility to affective dysregulation.

NR707 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Nicotine, Caffeine, and Alcohol Use in Bipolar Disorder and MDD

Constance Guille, B.A., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114*; Jordan W. Smoller, M.D., Michael W. Otto, Ph.D., Maurizio Fava, M.D., Gary S. Sachs, M.D., Jerrold F. Rosenbaum, M.D.

Summary:

Objective: To compare use of nicotine, caffeine, and alcohol in BD versus MDD.

Method: Clinical data were collected from all individuals with mood disorders (MDD = 93, BD = 112) participating in a genetic study. SCID-IV interview was used to establish current and lifetime diagnoses. A self-report questionnaire was used to quantify caffeine, nicotine, and alcohol use.

Results: Multivariate analyses indicate that lifetime diagnosis of BD doubles the likelihood of ever smoking compared with MDD (OR = 1.9;95% CI:1.03–3.59). Subjects meeting criteria for a current mood episode were more likely to be current smokers than subjects in remission (OR = 2.13;95%CI:1.06–4.22). Controlling for mood disorder diagnosis (BD vs. MDD), those in a current depressive episode were 5.26 (95% CI:1.04–26.59) times more likely to be current smokers than were those in a hypomanic/manic episode. Individuals meeting criteria for current hypomania/mania were less likely to drink caffeine than currently depressed (OR = 0.28; 95% CI:0.09–0.83) or remitted individuals (OR = 0.29; 95% CI 0.09–0.91) and had a significantly lower amount of daily caffeine intake ($p < 0.05$). Neither diagnosis nor presence of current mood episode appeared to influence current alcohol consumption.

Conclusions: These results suggest that patterns of substance use differ between BD and MDD and are influenced by the presence and polarity of mood episodes. Depressive episodes were associated with increased risk of smoking while hypomania/mania was associated with decreased caffeine use.

Sponsor: Millennium Pharmaceuticals, Inc.

NR708 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Evaluation and Intervention of Prodromal Symptoms of Bipolar I Disorder

Mohammad Z. Hussain, M.D., *2727 2nd Avenue West, Prince Albert, SK S6V 5E5, Canada*; Zubaida Chaudhry, M.D., Seema Hussain, M.D.

Summary:

Often bipolar mood disorder emerges in childhood or adolescence, but the average interval between prodromal symptoms and diagnosis is 10 or more years. To allow early intervention, we need to define the early symptoms that predate the full syndrome and identify youth during that phase.

Twenty-six children were diagnosed with bipolar I prodrome state. They had positive family history, episodic mood, and energy symptom fluctuation with anger dyscontrol, irritability, defiance, demanding behavior, conduct problems, sleep disturbance, anxiety, tension, worrying, stubborness, and somatic complaints. A 25-item, four-point prodrome scale was created with items relevant to youth from DSM-IV criteria, Hamilton Depression, and Young Mania scales. The scale reflects the atypical presentation of bipolar disorder in childhood. Comorbidities were recognized that add another dimension to evaluation. The group of 16 male and 10 female subjects were a mean age of 11 years (range 7–16). All received mainstay treatment of topiramate in a dose range 25–100 mg at bedtime, with some subjects requiring adjunctive treatment. Five discontinued treatment secondary to adverse effects and poor response. They were rated at baseline and at 1, 2, 3, 6, 9,

and 12-month intervals. Twenty-one subjects responded with 65% to 87% symptom reduction on consecutive assessments. Topiramate is an effective treatment in prodromal bipolar disorder.

NR709 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Potential Utility of the 5HT/Norepinephrine Reuptake Inhibitor Duloxetine in Persistent Pain

Smriti Iyengar, Ph.D., *Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Rosa M.A. Simmons, M.S., Dominic L. Li, M.S., Doo H. Lee, Ph.D.

Summary:

Serotonin (5HT) and norepinephrine (NE) are implicated in enhancing endogenous analgesic mechanisms via descending inhibitory pain pathways in the brain and spinal cord. Duloxetine, a potent and balanced 5HT/NE reuptake inhibitor, currently in phase III clinical trials for depression was evaluated for effects in rat models of persistent pain at doses consistent with 5HT and NE reuptake blockade *in vivo*. Intraperitoneal or oral administration of duloxetine significantly attenuated formalin-induced late-phase paw-licking behavior (a model of persistent pain) in a dose-dependent manner. Duloxetine (p.o.) also significantly reversed mechanical allodynia behavior in two models of neuropathic pain: 1) partial sciatic nerve ligation (Seltzer model), and 2) L5/L6 spinal nerve ligation (Chung model). Moreover, there were no decreases in the effects of duloxetine after subchronic administration in both neuropathic pain models. The effects of duloxetine occurred in the absence of neuromuscular dysfunction as measured by performance in the rotorod test. Thus, in addition to depression, duloxetine may also have utility in the treatment of persistent pain.

NR710 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Risperidone in Reducing Tardive Dyskinesia: A Double-Blind, Placebo-Controlled Study

Ya-Mei Pai, M.D., *Department of Psychiatry, Yu-Li Veterans Hospital, No. 91 Shin-Shin Street, Yu-Li, Hua-Lian 981, Taiwan*; Shun-Chief Yu, M.D., Chao-Cheng Lin, M.D.

Summary:

Objective: Tardive dyskinesia (TD) is a severe side effect of classical antipsychotics. We designed a double-blind, placebo-controlled study to evaluate the effect of risperidone on reducing the severit of TD.

Method: Fifty patients with schizophrenia with severe TD were included. Their original antipsychotic dosage was less than 200 mg/day of chlorpromazine equivalents. All the antipsychotics were withdrawn for 4 weeks, then the patients were randomly assigned to receive risperidone or placebo. Risperidone, 6 mg/day and an identical-looking placebo were prescribed to each group for 12 weeks. The TD condition was evaluated blindly by a psychiatrist with the Abnormal Involuntary Movement Scale (AIMS) every 2 weeks.

Result: Eight patients dropped out due to unstable psychiatric or medical conditions. The final sample consisted of 22 cases in the risperidone group and 20 cases in the control group. The baseline AIMS score of all patients was 16.4 $\pm$ 4.1. Sixteen patients (72.7%) in the risperidone group and five patients (20%) in the control group had significant reductions in TD (Fisher's exact $p = 0.005$). The final average AIMS score was 9.9 (SD = 4.3) for the risperidone group and 15.3 (SD = 5.7) for the control group ($t = -3.517$, $df = 40$, $p = 0.001$).

Conclusion: For patients with severe TD, changing to risperidone can decrease TD more significantly than neuroleptic withdrawal.

NR711 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Comorbidity, Impairment, and Suicidality in Subthreshhold PTSD

Randall D. Marshall, M.D., *Anxiety Disorders, NY State Psychiatric Institute- Columbia Univ, 1051 Riverside Drive, Unit 69, New York, NY 10032*; Mark Olfson, M.D., Fred Hellman, B.S., Carlos Blanco-Jerez, M.D., Mary T. Guardino, B.A., Elmer Struening, Ph.D.

Summary:

Reliance on the categorical model of disorder has led to neglected study of posttraumatic sequellae that fall short of full criteria. Significant disability and suicidal risk have been associated with subthreshold PTSD, but the relationships between disability, suicidality, comorbid disorders, and severity of subthreshold PTSD have not been studied.

Methods: On National Anxiety Disorders Screening Day 1997, 2,608 out of 9,358 individuals screened for affective and anxiety disorders at 1,521 sites across the U.S. reported at least one PTSD symptom of at least one month's duration.

Results: 27.9% of subjects reported at least one PTSD symptom persisting > one month after a traumatic event, and the current prevalence rate of screen-positive PTSD was 8.6%. Increasing number of subthreshold PTSD symptoms was associated with incremental increases in the following: (1) degree of impairment, (2) number of comorbid anxiety disorders, (2) rate of major depressive disorder, and (4) rate of current suicidal ideation (odds ratio 1.73) even after controlling for the presence of MDD.

From a public health perspective, the use of only full PTSD to examine the degree of posttraumatic disability in the general population has resulted in substantial underestimation, since disability and suicidality are also strongly associated with subthreshold symptoms.

Funding: NIMH Grant MH01412 and the Lowenstein Foundation

NR712 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

A Comparison of Clinical and Demographic Factors in Early-Onset and Late-Onset Pathological Gamblers

Robert Breen, Ph.D., *Department of Psychiatry, Brown School of Medicine, 235 Plain Street, Suite 501, Providence, RI 02905*; Mark Zimmerman, M.D.

Summary:

Objective: Although pathological gambling (PG) is classified as an impulse-control disorder, the DSM-IV criteria for PG were modeled on the alcohol/substance disorder criteria, and many people conceptualize PG as an addictive disorder. There is an extensive body of work in the alcoholism literature that has identified and investigated potentially important subtypes of alcoholics based on age of onset, chronicity, comorbidity, and genetic and other biological markers. If an addictive model of PG is valid, similar typologies might be observed in PGs. This study compared late-onset PGs to early-onset PGs on the characteristics of their gambling activity, demographic features, and comorbid psychiatric disorders.

Methods: Treatment-seeking PGs (N = 48) were subdivided into early-onset and late-onset groups and compared on gambling behavior, demographic variables, and current and lifetime psychiatric diagnoses.

Results: Compared with late-onset PGs, early-onset PGs were younger, more often male, less frequently had a problem with machine gambling, and had a higher lifetime frequency of substance disorders. In patients who had experienced a major depressive episode, the first episode almost always followed the onset of PG in the early-onset group, whereas it usually preceded the onset of PG in the late onset group.

Conclusion: The results are supportive of a simple method of subtyping of PGs that could have important theoretical and clinical applications. The chronic course of early-onset PG with high comorbidity of addictive disorders may argue for an abstinence-based approach to treatment (e.g., GA) and/or pharmacological treatment with opioid-antagonists such as Naltrexone. Late-onset PG, briefer in duration and usually secondary to depression, may be amenable to motivational interviewing or other brief psychosocial interventions, or may be treated pharmacologically with SSRIs.

NR713 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Diagnosing Malingering Using Visuo-Spatial Paradigms

Amy L. Funes, *Department of Psychiatry, Beth Israel Medical Center, First Avenue at 16th Street, 6 Karpas, New York, NY 10003*; Sarosh Cooper, Enid C. Gertmenian-King, B.A., Carrie J. Weaver, M.A., Pamela G. McGeoch, M.A., Lisa J. Cohen, Ph.D., Igor I. Galynker, M.D.

Summary:

Background: Presently, there exist few sensitive and specific tests for identification of individuals malingering psychiatric disorders. The purpose of this ongoing study is to develop a visiospacial test that can identify malingering without being confounded by language and education.

Method: A drawing test consisting of three simple geometric figures, was developed and administered to three groups: 64 normal controls, 108 psychiatric patients, and 85 subjects instructed to malinger. A multi-item score sheet was developed in order to quantify criteria for figure reproduction by healthy controls, psychiatric patients, and malingerers. The scoring as well as "gestalt recognition" data were analyzed using a general linear and regression model.

Results: The cumulated item score correctly identified 68.8% of control subjects, 82.5% of psychiatric patients, and the 47% of malingering subjects. The "gestalt recognition" correctly identified 82.8% of controls, 78.1% of psychiatric patients, and 56.5% of malingerers. A cut-off score of 3 on the malingering scale identified malingerers with 97.2% specificity and 52.4% sensitivity.

Conclusion: An easy-to-administer paper and pencil drawing test, which is relatively irrelevant to subjects' education and cultural background, identified simulated malingerers of psychiatric illness with very high specificity though low sensitivity. Further studies on elaboration of current design and scoring system are needed to improve the test sensitivity and are in progress.

NR714 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

GW320659 Treatment of Adult ADHD

Joseph De Veaugh-Geiss, M.D., *N & P Clinical Development, GlaxoSmithKline, Five Moore Drive, Research Triangle, NC 27709-3398*; Joseph Biederman, M.D., C. Keith Conners, Ph.D., Laurence L. Greenhill, M.D., Antonio Laurenza, M.D., Christopher Webster, B.S., Mahnaz Asgharnejad, Ph.D.

Summary:

Objective: To assess the efficacy and tolerability of four doses of GW320659 in the treatment of adults with attention-deficit/hyperactivity disorder (ADHD).

Methods: This was a randomized, double blind, placebo-controlled, six-week treatment study. Study medication was administered twice daily for a total daily dose of GW320659 of 2.5mg, 5mg, 10mg, or 15mg.

Results: Two hundred seventy-nine adult patients were randomized and 225 completed the study. More subjects receiving GW320659 5mg per day responded to treatment compared with placebo at Weeks 1 through 6 with onset of efficacy noted at Week 1. The efficacy rates at Weeks 1 through 6 for GW320659 5mg per day were 15%, 25%, 38%, 50%, 46%, and 46% versus placebo at 2%, 7%, 15%, 13%, 24%, and 22%, respectively, ($p = 0.014$, $p = 0.024$, $p = 0.011$, $p < 0.001$, $p = 0.036$, and $p = 0.008$). At the one-week post-treatment visit, the 5mg group was no different than placebo (15% for both 5mg and placebo).

Twenty-one patients experienced adverse events that led to their premature discontinuation. The percentage of subjects who prematurely discontinued due to adverse events in the GW320659 active treatment groups were identical to or less than the percentages in the placebo group.

Conclusions: GW320659 5mg per day was efficacious and well tolerated in the treatment of ADHD in adults.

NR715 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Effect of Mirtazapine on Ejaculation: A Comparative Study with Paroxetine

Marcel D. Waldinger, M.D., *Department of Psychiatry, Leyenburg Hospital, Leyweg 275, The Hague CH-2545, Netherlands*; Aeilko H. Zwinderman, Ph.D., Berend Olivier, Ph.D.

Summary:

Background: Depression is a common cause of sexual dysfunction, but also antidepressant medication (e.g., paroxetine) is often associated with sexual side effects. Mirtazapine is associated with less sexual dysfunction than SSRIs. This is probably related to its pronounced antagonistic activity at the 5-HT_{2c} receptor.

Objective: To compare the influence of mirtazapine versus paroxetine in delaying ejaculation in patients with primary premature ejaculation.

Method: In this study mentally, physically, and sexually healthy men with lifelong rapid ejaculation and their female partners were selected. After one month baseline measurement of men's intravaginal ejaculation latency time (IELT) at home using a stopwatch, those men with an IELT of less than one minute were randomized in a double-blind manner into two groups using paroxetine 20 mg/day ($N = 12$) or mirtazapine 30 mg/day ($N = 12$) for a period of five weeks, after taking half the dosage in the first week.

Results: Mirtazapine and paroxetine differed significantly ($p < 0.01$) among each other in affecting ejaculation, mirtazapine having no effect on ejaculation.

Conclusions: This is the first study into the effects of mirtazapine on ejaculation time. The results confirm (1) previous findings showing that paroxetine produces a serious delay of ejaculation and (2) are in line with the low rate of sexual side effects reported with mirtazapine.

Educational grant from Organon.

NR716 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Effects of Paroxetine on Declarative Memory and the Hippocampus in PTSD

Eric Vermetten, M.D., *Department of Psychiatry, Emory University, 1256 Briarcliff Road, NE, Atlanta, GA 30306*; Meena Vythilingam, M.D., Heather Douglas-Palumberi, M.S., Steven M. Southwick, M.D., Dennis S. Charney, M.D., J. Douglas Bremner, M.D.

Summary:

Background: Stress is associated with damage to the hippocampus and related memory dysfunction. Studies reported deficits in hippocampal-based declarative verbal memory and hippocampal atrophy in patients with posttraumatic stress disorder (PTSD). Preclinical evidence suggests that selective serotonergic reuptake inhibitors (SSRI) can stimulate neurogenesis and contribute to the reversibility of hippocampal atrophy.

Objective: The purpose of this study was to assess the effects of paroxetine, an SSRI, on declarative memory performance and hippocampal volume in PTSD patients.

Methods: A total of 27 adult outpatients with chronic PTSD underwent six to nine months of treatment with 10–50 mg of paroxetine. Hippocampal function was assessed before and after treatment with measures of verbal and visuospatial declarative memory. Hippocampal volume was assessed with MRI.

Results: A significant reduction in PTSD symptoms was observed in the mean changes on the Clinician Administrated PTSD Symptom Scale (CAPS) total score among the 23 study completers ($p = 0.0001$). Treatment resulted in significant improvements in verbal declarative memory ($p = 0.01$) and percent retention ($p = 0.02$). Data on hippocampal volume will be presented.

Conclusion: The findings suggest that paroxetine may be associated with reversibility of hippocampal-related declarative verbal memory deficits in PTSD. These findings have implications for understanding neurobiological effects of SSRIs on hippocampal-mediated memory function and possibly by extension hippocampal structure.

NR717 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Decreased Serum S100-Beta-Protein in Drug-Free Social Phobic Patients

Flavio Kapczinski, Ph.D., *Department of Psychiatry, Bioquimica ICBS, Ramiro Barcelos 2600 Anexo, Porto Alegre, RS 90035-003, Brazil*; Rodrigo Machado-Vieira, M.D., Daniela Z. Knijnik, M.D., Diogo R. Lara, Ph.D., Regina Margis, M.D., Eduardo Chachamouich, M.D., Diogo O. Souza, Ph.D.

Summary:

Background: The purpose of the present study is to assess whether S100B, an astrocytic brain trophic factor, whose expression is influenced by serotonergic activity, is reduced in social phobia.

Method: Serum S100B levels of 21 drug-free social phobic patients and age/gender-matched controls were compared.

Results: Serum levels of S100B protein were significantly reduced in social phobic patients.

Conclusions: These results may reflect decreased serotonergic activity in social phobia. Decreased S100B levels in social phobia also point out astrocytes as candidate cells to be further investigated in anxiety disorders.

NR718 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Functional Responsivity of the Brain During Medication

Jin Pyo Hong, M.D., *Department of Psychiatry, Asan Medical Center, 388-1 Pungnap-Dong Songpa-Gu, Seoul 138-736, Korea*; Jeong-Soo Kim, M.D., H. K. Lee, Chang-Yoon Kim, M.D., Chul Lee, M.D.

Summary:

Objective: During meditation deep physiological relaxation occurs in a context of wakefulness. Subjective reports of meditators typically describe marked anxiety reduction during this state. Functional magnetic resonance imaging was used to study brain response during meditation.

Method: Seven trainers who have trained Guksun-do (Traditional Korean Tae-ji) more than 15 years participated as paid subjects. They were scanned in a 1.5T scanner during two courses of rest and meditation period. Functional images were acquired in twenty 3 mm contiguous axial slices spanning entire brain using an EPI Blood oxygen level-dependent(BOLD) sequence. Statistic Parametric Mapping (SPM) 99b(Wellcome Dept. Cogn. Neurol) was used for image processing and analysis. Individual and conjunctional brain maps were inspected for foci of significant activation($p < 0.05$, corrected).

Results: All individual fMRI data showed significant activation within both prefrontal and left parietooccipital cortex consistently. Right superior temporal gyrus and both amygdala were activated in some of subjects. However, conjunctional analysis indicated significant right amygdala activation.

Conclusions: These findings suggest that several cortical areas including prefrontal association area be related with meditation and right amygdala mediate the meditation effects.

NR719 Wednesday, May 9, 3:00 p.m.-5:00 p.m.

Parental Psychopathology, Parenting Behavior, and Offspring Psychopathology

Jeffrey G. Johnson, Ph.D., *Department of Psychiatry, Columbia University, Box 60 NYSPI, 1051 Riverside Drive, New York, NY 10032*; Patricia R. Cohen, Ph.D.

Summary:

Objective: A longitudinal study was conducted to investigate the role of maladaptive parental behavior in the association between parent and offspring psychopathology.

Method: A representative community sample of 593 biological parents and their offspring were interviewed in 1975, 1983, 1985–86, and 1991–93. In 1975, the offspring were a mean of 6 years of age.

Results: Maladaptive parental behavior mediated a significant association between parental and offspring psychiatric symptoms. Parents with psychiatric disorders had higher levels of maladaptive behavior in the household than did parents without psychiatric disorders. Maladaptive parental behavior was associated with increased offspring risk for psychiatric disorders during adolescence and early adulthood. Most youths that experienced high levels of maladaptive parental behavior during childhood had psychiatric disorders during adolescence or early adulthood, whether or not their parents had psychiatric disorders. The offspring of parents with psychiatric disorders were not at increased risk for psychiatric disorders unless there was a history of maladaptive parental behavior.

Conclusions: Maladaptive parental behavior is associated with increased risk for the development of psychiatric disorders among the offspring of parents with and without psychiatric disorders. Maladaptive parental behavior appears to be an important mediator of the association between parental and offspring psychiatric symptoms.

Funding Sources: National Institute of Mental Health. National Institute on Drug Abuse

NR720 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Chrono-Record Software for Daily Self-Reporting of Mood: A New Clinical Tool for Bipolar Disorder

Michael Bauer, M.D., *Department of Psychiatry, UCLA, 300 UCLA Medical Plaza, Suite 2330, Los Angeles, CA 90024*; Laszlo Gyulai, M.D., Tasha Glenn, Ph.D., Peter C. Whybrow, M.D.

Summary:

Objective: Daily self-reporting of mood and sleep is an established tool for the assessment and longitudinal treatment of bipolar disorder. This study investigates whether patients with bipolar disorder can use a software program on their home computer to accurately enter data on mood (visual analogue scale [VAS]), sleep, life events, psychiatric medications, weight, and, if female, menstrual data. The software (ChronoRecord) is an electronic version of an established paper-based form for daily self-reporting

(Chronosheet) and provides immediate longitudinal analysis of patient data.

Method: 30 patients with bipolar disorder (DSM-IV) were given the software and entered data daily on their home computer for a consecutive 3-month period. Patients returned the data by diskette or e-mail for evaluation. The validation analysis correlated VAS mood score the patient entered at home with scores of mood rating scales (Hamilton Rating Scale for Depression [HAMD]. Young Mania Rating Scale [YMRS], and Beck Depression Inventory [BDI]) completed on the same date. Subjective patient evaluations of the software were also obtained during the study.

Results: Preliminary analysis with 12 patients who completed the study showed high correlation between HAMD ($r = -.762$; $p = 0.01$) and BDI ($r = -.763$; $p = 0.01$) scores and patient VAS mood ratings. Patient evaluations showed high acceptance of the software. Individual 3-month graphical reports will be presented as well as analysis of data from the entire study population.

Conclusion: Patient self-reported VAS mood scores on the ChronoRecord showed high correlation with clinician ratings of depression on the HAM-D and with paper-based self-rating on the BDI. With home computers becoming commonplace, ChronoRecord software is a promising clinical tool for longitudinal evaluation of bipolar disorder.

NR721 Thursday, May 10, 12:00 p.m.-2:00 p.m.

A Placebo-Controlled Trial of Fluoxetine in BDD

Katharine A. Phillips, M.D., *Butler Hospital/Brown University, 345 Blackstone Boulevard, Providence, RI 02906*; Ralph S. Albertini, M.D., Steven A. Rasmussen, M.D.

Summary:

Background: BDD, a distressing and/or impairing preoccupation with an imagined or slight defect in appearance, is a relatively common disorder that causes marked impairment in functioning. Although available data suggest that BDD responds to SRIs, no placebo-controlled treatment studies have been done.

Methods: Seventy-four patients with DSM-IV BDD or its delusional variant were enrolled and 67 were randomized into a placebo-controlled parallel group study. After one week of single-blind placebo, patients were randomized to 12 weeks of double-blind treatment with fluoxetine or placebo and were assessed at regular intervals with the BDD-YBOCS (the primary outcome measure) and other scales.

Results: Fluoxetine was significantly more effective than placebo, with a response rate on the BDD-YBOCS of 53% (18 of 34) to fluoxetine and 18% (6 of 33) to placebo (chi square = 8.8, df = 1, p = .003). Controlling for baseline group differences in BDD severity, fluoxetine was more effective than placebo ($F(1,64) = 16.5$, p = .000) beginning at week 8 and continuing at weeks 10 and 12. A medium to large effect size was found (F = 0.35). Among delusional patients, 50% (six of 12) responded to fluoxetine compared with 0% (0 of 15) to placebo (chi square = 9.6, df = 1, p = .002). Among nondelusional patients, 56% (11 of 20) responded to fluoxetine compared with 35% (6 of 17) to placebo (chi-square = 1.4, df = 1, p = .23). Delusional patients were as likely as nondelusional patients to respond to fluoxetine but were less likely than nondelusional patients to respond to placebo (chi square = 6.5, df = 1, p = .01). The mean time to fluoxetine response was 7.5 ± 3.7 weeks, and the mean dose of fluoxetine at endpoint was 77.7 ± 8.0 mg/day. Treatment response was not predicted by duration and severity of BDD or the presence of major depression, OCD, or a personality disorder. Fluoxetine was well tolerated.

Conclusion: Fluoxetine is well-tolerated and more effective than placebo in delusional and nondelusional BDD.

NR722 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Nefazodone Treatment of Somatization Disorder

Matthew A. Menza, M.D., *Department of Psychiatry, RWJ Medical School, 675 Hoes Lane, Room D207A, Piscataway, NJ 08854*; Lesley Allen, Ph.D., Javier I. Escobar, M.D., Marc Lauritano, B.A., Melissa Warman, Ph.D., Connie Hoyos-Nervi, Psy.D., Robert Hamer, Ph.D.

Summary:

Objective: Somatization disorder (SD) is commonly seen in medical clinics and is associated with significant impairment in functioning as well as increased utilization of health care. While antidepressants have been studied in some functional somatic syndromes such as fibromyalgia and chronic fatigue, there are few treatment studies of SD itself, a higher order syndrome that may include many subcategorical functional somatic syndromes. This trial examines the use of nefazodone in these SD patients.

Methods: A total of 15 patients with either full SD by structured clinical interview or "abridged somatization" by Escobar's criteria (four unexplained symptoms for men and six for women) were given nefazodone in a prospective, eight-week, open-label study. Patients were seen at two-week intervals and the primary outcomes included measures of physical symptom severity (visual analogue, VAS), functioning (MOS-36), depression (HAMD), and overall improvement (CGI-I).

Results: A total of 14 of the 15 patients achieved the target dose of 300 mg/day and completed the trial. The 15th completed two weeks of drug and was included in the LOCF analysis. Eleven of 15 patients (73%) patients were rated as improved on the CGI and 79% (11 of 14) improved on the self-rated VAS. Paired t-tests showed significant improvement for the whole group (pre-post) in HAMD, cognitive and somatic subscales of the HAMD, MOS-36 and the HAMA. Nine patients had a categorical depression diagnosis and of these five (55%) were rated as improved. Four of six (67%) of the non-depressed patients were rated as improved.

Conclusions: Nefazodone was well tolerated and effective in both the depressed and non-depressed patients with SD in this prospective, open-label trial. While these data need to be confirmed in a double-blind trial, they suggest that nefazodone may be a useful treatment for patients with SD. Further analyses will be discussed.

Bristol-Myers Squibb funded this study.

NR723 Thursday, May 10, 12:00 p.m.-2:00 p.m.

The Survey of a Virtual Psychiatric Clinic

Chao-Cheng Lin, M.D., *91, Hsing-Hsing Street, Hualien County, Yuli 981, Taiwan*; Ya-Mei Bai, Jen-Yeu Chen, Chen-Jee Hong, Chia-Yih Liu, M.D.

Summary:

Objective: This is a cross-sectional survey of subjects asking questions about mental problems in a virtual psychiatric clinic via World Wide Web.

Method: Subjects were recruited, view the purpose of the study, join the study voluntarily, and fill in the study form anonymously from the study website. The mental health professionals answered the problems and send it to the subjects by e-mail. We analyzed the data of subjects who complete the study between Sep-9-1998, to Jul-8-1999.

Results: There were 186 subjects. Most are female(69.9%,n = 130), single(77.3%,n = 143), with stable job(41.4%,n = 77), highly educated(mean education year:15.0 ± 1.9), and young(mean age:26.1 ± 5.8). Fifty-one percent of subjects(n = 95) never had a psychiatric visit. Of those ever having a psychiatric visit(n = 90), 42%(n = 38) had no psychiatric diagnosis, 13.3%(n = 112) didn't know their exact diagnosis, 15.6%(n = 14) had anxiety disorder,

and 11.1%(n = 10) had depressive disorder. The majority of reasons using virtual psychiatric service is convenience(49.5%,n = 92). Seventy-three percent of subjects(n = 136) used internet at home; 63%(n = 98) used internet less than three hours/week; and 57%(n = 103) didn't want their questions and answers to be published.

Conclusion: The young, single, well-educated, employed female used the majority of the virtual psychiatric service. Among the known diagnoses, anxiety disorder and major depressive disorder are the most prevalent diagnoses.

NR724 Thursday, May 10, 12:00 p.m.-2:00 p.m.

A Survey of PTSD Among School Children After the Earthquake in Taiwan

Rong-Rong Huang, M.D., *Kai-Suan Psychiatric Hospital, 130 Kai-Suan 2nd Road, Kaohsiung 802, Taiwan*; Wei-Tsuen Soong, M.D., Yu-Chun Lee, M.D., Wen-Che Tsai, M.D., Yong-Shing Chen

Summary:

Introductions & Purposes: An earthquake with magnitude of 7.3 on the Richter scale struck middle Taiwan on September 21, 1999. The purpose was to study the psychiatric morbidity of school children at Yu-Chi township, 3 and 6 months respectively after the quake.

Methods: A questionnaire of 20 yes/no questions (Score 1/0) was constructed to screen for PTSD. All the grade 2–6 students were asked to fill in the questionnaire. A school with 112 students was selected to study the cutoff point. 40 students (9 with scores of 0–8, 14 with scores of 9–11, and 17 who scored 12 and above) were subjected to the second-stage interview with the K-SADS-CM. Three child psychiatrists who were blind to the score conducted the diagnostic interview.

Results: The questionnaire has adequate test-retest reliability (ICC coefficient .675) and internal consistency (Cronbach alpha .842). In the first survey, 3 months after the earthquake, 1079 valid questionnaires were analyzed. When a cutoff point for the child psychiatrist's diagnosis of PTSD per DSM-IV criteria was set at 11/12, sensitivity was 0.85, and specificity was 0.66. It was estimated that 7.2% had DSM-IV PTSD. The students were surveyed 6 months after the earthquake. The prevalence of PTSD was calculated and compared with the first survey.

Conclusions: 1. The new questionnaire is adequate for screening PTSD associated with an earthquake. 2. The prevalence of DSM-IV PTSD 3 months after a severe earthquake was 7.2%. 3. The prevalence of PTSD 6 months after the earthquake will be reported during the conference.

NR725 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Interest of Zolpidem Test for Catatonia in Children

Laurent J. Lauwerier, M.D., *Department of Child Psychiatry, USN B, 6 Rue du Professeur Laguesse, Lille 59037, France*; Marie B. de Chouly, Daniel D. Bailly, M.D.

Summary:

Objective: To show the utility of a zolpidem test for catatonia in children.

Method: Case reports. Two children, one boy and one girl both 11 years of age, were admitted to our inpatient unit with a symptom profile that included mutism, rigidity, negativism, and posturing. Neither of them had a previous history of mental disorder. Neither of them had a fever or changes in blood and serum parameters. Electroencephalography and magnetic resonance imaging did not show any abnormalities. Because the diagnosis of catatonia was clinically suspected, a test dose of 10 mg of zolpidem was given orally to both of these patients.

Results: Both of these patients responded dramatically to the test and recovered from stupor within 40 minutes after the oral administration of zolpidem. They were then successfully treated with the benzodiazepine lorazepam. The catatonic syndrome was associated with a major depressive episode in the boy and with an acute stress disorder in the girl.

Conclusions: Catatonia is uncommon in young people and appears more frequently reported in children with an organic condition (epilepsy, encephalitis) or psychotic disorder. However, this syndrome has received little research attention, and data suggest that it may be underdiagnosed. These two consecutive cases highlight the utility of a zolpidem test in the diagnosis of this condition in children.

NR726 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Grey Level Index Abnormalities in the Brains of Autistic Patients

Manuel F. Casanova, M.D., *Department of Psychiatry, Medical College of Georgia, Downtown VA Medical Center, Augusta, GA 30904-6285*

Summary:

Objective: Although neuropathological studies have centered on a small sample, it has been accepted that brains of autistic individuals tend to be on average larger than normal: Knowledge regarding the cause of this macrocephaly is limited. Postmortem studies reveal little in terms of cortical dysplasia; a few of these studies suggest increased cell packing density in subcortical structures. These neuronomorphometric studies have been subjective or based on measures of neuronal density. Our study examined the possible presence of increased cell packing density by using the Grey Level Index (GLI) of Schleicher et al. (1986).

Method: Analyzed images included cortical areas 9, 21, and Tpt of nine autistic patients (seven males, two females, mean age of 12 years) and 11 normal controls (seven males, four females, mean age of 14 years).

Results: The overall multivariate test revealed significant differences between autistic patients and controls ($p = 0.001$) and between hemispheres ($p = 0.005$). Follow-up univariate tests showed significant diagnosis-dependent effects in feature distance D ($p = 0.005$), the standard deviation in distance SD_D ($p = 0.016$), and feature amplitude A ($p = 0.001$). The overall mean GLI was 19.4% in controls and 18.7% in autism ($p = 0.724$).

Conclusions: Our preliminary results indicate that minicolumns in autism are more closely packed together. The greater columnar density in autism, combined with fewer cells per column (evident from the lower amplitude), results in no global difference in neuronal density. The findings suggest a distinction in cortical circuitry possibly at the mini-columnar level.

NR727 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Variations in Child Emotional, Physical, and Sexual Abuse Rates Across the U.S.

Stephanie Hamarman, M.D., *Department of Psychiatry, New Jersey Medical School, 215 South Orange Avenue, UBHC B43, Newark, NJ 07103*; Kayla Pope, J.D., Sally J. Czaja, Ph.D.

Summary:

Objective: Emotional abuse, unlike physical and sexual abuses, has an intangibility that has led to a lack of uniform legal definitions. Thus, we hypothesized that states might vary more greatly in reporting child emotional abuse compared to other abuses.

Methods: Data were analyzed from the 1998 U.S. D.H.H.S. report: Child Maltreatment Reports from the States to NCANDS.

Results: Emotional abuse rates per 10,000 children varied widely across states from 0.37 (Pennsylvania) to 113.02 (Connect-

icut). For the entire U.S., mean rates of emotional, physical, and sexual abuse were 11.7, 29.1, and 15.1 per 10,000 children, with statistical variances of 451, 342, 89. Compared to other forms of child abuse, rates of emotional abuse were the least consistent from state to state. The Levene statistic for equality of variance revealed a significant difference in variances of emotional versus physical abuse ($p < 0.001$) and emotional versus sexual abuse ($p < 0.001$) but no difference between physical versus sexual abuse variances ($p = 0.80$).

Conclusion: Individual states varied significantly more in their rates of child emotional abuse; physical and sexual abuse rates were more consistent across states. Although true differences may exist, lack of uniform definitions and legal standards for emotional abuse may contribute to the variations identified.

NR728 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Computer Modeling of Excitation-Inhibition Defects in Autism

Daniel Buxhoeveden, Ph.D., *Department of Anthropology, University of South Carolina, 1512 Pendleton, Columbia, SC 29208*; Manuel F. Casanova, M.D.

Summary:

Objective: We hypothesized that some of the biological and behavioral features associated with autism may be explained by a disruption of the normal balance between excitation and inhibition, with a decrease in lateral inhibition being suspected as most responsible. The reasons for this include the efficacious effects of GABAergic drugs in the treatment of tuberous sclerosis children with autistic behavior and autistic children, the propensity for seizure disorders among autistic children difficulty in generalization, and behavioral traits.

Methods: We tested a computer model based on minicolumn organization. Our experiment involved minicolumns arranged on a grid with "Mexican hat" lateral connections: short-range inhibition and longer-range excitation. Segregates were defined by the radiation of thalamic input.

Results: A 1:1 ratio of excitatory to inhibitory synaptic strengths produced a sharp cutoff of activity when thalamic input ceased. At the other extreme of values considered, a ratio of 8:1 produced transitory activity persisting on the order of 10 time intervals (approx. 20 msec) after cessation of stimulus.

Conclusions: Minicolumns remain excitatory for a much longer period of time than they would normally because lateral inhibition is weak. By remaining active these minicolumns alter the way additional information can be processed. In fact, they temporally block the ability of the minicolumns to respond to new input. This appears consistent with the behavior of autistic children concerning repetitiveness and the failure to generalize.

NR729 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Psychiatric Profile of Children with Chronic Upper Respiratory Streptococcal Infection

Ahmed A.R. Mubarak, M.D., *Department of Neuropsychiatry, Tanta University, 25 Ibrahim El Desouky, Tanta GHR 31111, Egypt*; Uama Tolba, M.D.

Summary:

Objectives: Studying the psychiatric profile of the children with chronic group A beta hemolytic streptococcal (GABHS) sore throat infection and its relation to the related biological parameters (e.g., antistreptolysin O titer, c-reactive protein, and erythrocyte sedimentation rate [ESR]), may help in understanding the role of such infection in the pathogenesis of clinical psy syndromes.

Methods: The study was carried out on 86 children their age ranged from 6–12 years (mean = 8.08 years, SD = 1.76), 41 males and 45 females. These patients came to the pediatric department at Tanta University Hospital suffering from sore throat infection with GABHS between January 1st and June 31st 2000 and were sent for psychiatric evaluation that included semi-structured psychiatric interview as well as some rating sales (e.g., Y-BOCS and Connor's scale were used either to confirm diagnosis or to assess the severity of some specific symptoms). Laboratory analyses for antistreptolysin O titer and blood picture were performed. 20 healthy children matched by age and sex with the studied sample were used as control subjects for the lab and psychometric evaluation.

Results: Out of 86 children suffering from chronic GABHS, 20 had obsessive-compulsive symptoms, six of them fulfilled the criteria for pediatric autoimmune neuropsychiatric disorders associated with streptococcal infections (PANDAS), 21 showed excess motor activity, eight had irritable mood, and 2 showed had attentional problems. Chorea was found in 21 cases, motor tics in three cases. Correlating these symptoms with the biological variables related to GABHS showed that global obsessive compulsive symptoms were correlated with the presence of anemia, high antistreptolysyn O titer, high ESR, and positive c-reactive protein. Irritable mood was correlated with the presence of anemia and high ESR, while inattention and motor tics showed no correlation with such variables. Logistic regression analysis showed that a combination of the presence of chorea, positive c-reactive protein, and family history of rheumatic cardiac complications was highly predictive of obsessive compulsive symptoms and motor hyperactivity.

Conclusion: Significant psychiatric morbidity correlated with biochemical parameters of GABHS infection is unequivocal proof of its role in pathogenesis. For this reason, prophylactic measure with LA penicillin could be a cost-effective psychiatric prevention in this group of patients.

NR730 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Tic Disorders in Children and Adolescents with ADHD

Atilla Turgay, M.D., *Department of Psychiatry, Scarborough Hospital, 3040 Lawrence Avenue, East, Scarborough, ON M1P 2V5, Canada*; Verka Urdarevik, M.D., Rubaba Ansari, M.A., Ozlem Erman, M.D., Bedriye Oncu, M.D.

Summary:

Out of 880 subsequently evaluated children and adolescents with no history of stimulant medication use, 47 patients (5.34%) had combined ADHD and tic disorders. Age, gender, comorbidity, and ADHD subtype differences were compared between 47 unmedicated patients with combined ADHD and tic disorders and an age- and gender-matched comparison group with ADHD, without tic disorders.

Method: DSM-IV criteria, Offord and Boyle Child Health Study, and DuPaul ADHD scales were used in diagnosis.

Results: (1) The boys had a higher risk for tic disorders. (2) The risk for the development of Tourette's disorder in patients with ADHD was found to be 60 times more than the general population. (3) The risk for Tic disorders was more common in patients with ADHD Combined Type. (4) Patients with ADHD and tic disorders had more comorbid disorders and higher risk of having OCD and generalized anxiety disorder and a lower risk of conduct and Oppositional defiant disorders.

Conclusion: Tic disorders are common in ADHD before the use of stimulant medication. In cases of combined ADHD and tic disorders, the presence of anxiety, mood, and speech disorders should also be considered.

NR731 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Risperidone in Children with Disruptive Behavior Disorder and ADHD

Atilla Turgay, M.D., *Department of Psychiatry, Scarborough Hospital, 3040 Lawrence Avenue, East, Scarborough, ON M1P 2V5, Canada*; Michael Anan, Ph.D., Carin Binder

Summary:

Objective: Test the hypothesis that risperidone is effective in treating symptoms of ADHD in children with a concomitant diagnosis of ADHD associated with subaverage IQ and conduct disorder, oppositional defiant disorder, or disruptive behavior disorder-NOS.

Method: A total of 110 children, 5–12 years, IQ 36–84 with various disruptive behavior disorders were randomized in a six-week, double-blind trial to risperidone or placebo. Comorbid ADHD existed in 84/110 children treated with/without psychostimulants. Psychostimulants were initiated prior to trial entry and maintained at stable doses throughout the trial.

Results: Mean dose of risperidone was 0.033 mg/kg/day (mean daily dose was 0.98mg). The hyperactivity subscale of the Nisonger Child Behavior Rating Form (NCBRF) and hyperactivity/noncompliance subscale of the Aberrant Behavior Checklist both showed a significant decrease in children treated with risperidone. The effect was detected in the risperidone with/without psychostimulant groups when compared with placebo with/without psychostimulants indicating that the efficacy of risperidone is independent from concomitant use of psychostimulants. No unexpected adverse events or laboratory findings were noted in either group.

Conclusions: Risperidone is effective and safe in reducing symptoms of comorbid ADHD in children with sub-average IQ and various disruptive behavior disorders.

NR732 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Psychosocial Adjustment of International Adoptees and Biological Children of Adoptive Parents

Yee-Jin Shin, M.D., *Department of Psychiatry, Yonsei University, CPO Box 8044, Seoul, Korea*; Wun-Jung Kim, M.D., Jung-Hyun Lee, M.D., Michael P. Carey, Ph.D.

Summary:

Background: Among the many issues addressed, one consistent question about adoption is how adopted children eventually fare. In this study, we compared internationally adopted Korean children with biological children of adoptive parents who share the same environment with respect to psychosocial adjustment to understand the psychological and social adjustment of international adoptees who experienced early adoption in a foreign country.

Method: This study surveyed a community sample of Korean adoptees in the Denver metropolitan area where about 500 families adopted Korean children. The American families organized an active support group to help themselves and their children to learn Korean culture and support one another. They hold annual summer camps to promote such causes. The senior author was invited to speak to the group and formed a close tie with them. Participants were recruited during summer camp, and 73 Korean-American adoptees were compared with 17 biological children. Both parents were administered the Child Behavior Checklist-Parent Form (CBCL-P) and a structured survey form including demographic data, adoption information, medical information, and descriptions of post-adoption adjustment.

Results: On CBCl-P, the adoptees were generally doing well compared with normal American children. However, when compared with biological children, they showed significantly lower T scores in school competence and higher school-related problems, such as requiring special education, and having interpersonal, behavioral, and emotional problems in school. The Korean adoptees also had higher T scores in attention problems, somatic complaints, internalization, and total behavior problems than those of biological children of adoptive parents. Parents reported that 10 adoptees have suffered from mental illness, but none in their biological children.

Conclusions: The internationally-adopted Korean-American children have more problems in some aspects of psychosocial adjustment compared with the biological children of adoptive parents, although their general adaptation seemed to be good compared with the normal population.

NR733 Thursday, May 10, 12:00 p.m.-2:00 p.m.

An Open Trial of Quetiapine in Adolescents with Psychosis

Jon A. Shaw, M.D., *Department of Psychiatry, University of Miami School of Medicine, 1695 NW 9th Avenue, Room 1404A, Miami, FL 33136*; Shlomo Pascal, M.D., Rajiv P. Sharma, M.D., Rigoberto Rodriguez, M.D., J. Lewis, Ph.D., R. Guillen, M. Guillen

Summary:

Objective: To study the effectiveness, safety, and tolerability of quetiapine in psychotic adolescents.

Methods: This eight-week, open trial studied effectiveness, safety, and tolerability using quetiapine with 15 adolescents (aged 13–17 years; mean age 15.1 years), with a diagnosis of a psychotic disorder (11 had diagnoses of schizophrenia). Primary measures included the BPRS, CGI, SANS, SAPS, and the Barnes Akathisia Scale. Secondary measures included adverse events, clinical laboratory tests, vital signs, electrocardiograms, and ophthalmologic examinations.

Results: Quetiapine significantly reduced psychotic symptoms and psychological dysfunction as measured by the BPRS, PANSS, YMRS, and CGI-Severity of Illness scores. The average weight gain was 4.4 kg. There was a slight increase in cholesterol and TSH, and a reduction in T_4. Common adverse effects were somnolence, agitation, drowsiness, and headache. No significant findings were noted on repeat electrocardiograms, EPS measures, prolactin levels, or opthalmic examinations. The final average treatment dose was 467 mg/d.

Conclusions: Quetiapine is proved to be effective in psychotic adolescents and to have a favorable side-effect profile.

NR734 Thursday, May 10, 12:00 p.m.-2:00 p.m.

An OROS Formulation of Methylphenidate in the Treatment of ADHD

Joseph Biederman, M.D., *Department of Child Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC-725, Boston, MA 02114*

Summary:

Objective: To review the efficacy of a once-daily, extended-release tablet of methylphenidate HCL (MPH) for the treatment of children with attention deficit hyperactivity disorder (ADHD) as assessed in four studies.

Design/Methods: This formulation in two randomized, double-blind, single-center studies (N = 60 and 70) and a 4-week, randomized, double-blind, multicenter parallel-group study (N = 282) in children with ADHD have compared with MPH t.i.d. and placebo. In a subsequent multicenter, open-label study, over 300 children received the once-daily, extended release tablet of MPH for up to 12 months. In all four studies, efficacy was measured in multiple settings by parents and teachers using assessments of attention and behavior.

Results: In the randomized studies, the once-daily, extended-release tablet of MPH was superior to placebo and similar to MPH

t.i.d. in improving attention and behavior. Results were consistent across settings, raters, and assessments. In the open-label study, the effectiveness of treatment with the once-daily, extended release tablet of MPH was sustained through 12 months and was well tolerated in all studies.

Conclusions: Treatment with a once-daily, extended release tablet of MPH improved attention and behavior in children with ADHD and was significantly better than placebo.

Study supported by: ALZA Corporation, Mountain View, CA.

NR735 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Efficacy of OROS MPH in Adolescents with ADHD in a Community Setting

Ed Schnipper, M.D., *Alza Corporation, 1950 Charleston Road, Mountain View, CA 94043*

Summary:

Objective: To evaluate the efficacy of a once-daily, extended-release tablet of methylphenidate (MPH) for ADHD treatment in adolescents in a community setting.

Background: This formulation of MPH is a new, controlled-release, oral MPH tablet that provides a duration of effect through 12 hours with once-daily dosing.

Design/Methods: 1,083 participants aged ≥6 years with ADHD were enrolled at 118 centers in a 9-month, open-label, nonrandomized study. The adolescent group consisted of 263 patients aged 13 to 17 years. Participants received each morning one oral dose of extended-release MPH (18.36, or 54 mg). Treatment effectiveness was assessed at 0, 3, 6, and 9 months. Results were analyzed by age.

Results: In an interim 3-month analysis, 80.6% of adolescent patients were still taking pharmacologic treatment. 87.6% of parents/caregivers were satisfied, very satisfied, or extremely satisfied with treatment at final assessment. Investigator global assessment produced similar results. Treatment was generally well tolerated. A full analysis of data will be presented following study completion.

Conclusions: Effectiveness of a once-daily, extended-release tablet of MPH was rated highly by parents/caregivers and investigators in adolescents with ADHD in a community setting, and the drug was well tolerated.

Disclosure: Study funded by ALZA Corporation, Mountain View, CA.

NR736 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Fluoxetine for Maintenance of Recovery from Depression in Children and Adolescents: A Placebo-Controlled, Randomized Clinical Trial

Graham J. Emslie, M.D., *Department of Psychiatry, University of Texas at Southwestern Medical, 5323 Harry Hines Boulevard, MC 8589, Dallas, TX 75235-7200*; John H. Heiligenstein, M.D., Sharon L. Hoog, M.D., Daniel E. Ernest, B.A., Brian VanHooy, Eileen Brown, Ph.D., Jennie G. Jacobson, Ph.D.

Summary:

Objective: We describe the first placebo-controlled, double-blind, randomized clinical trial of fluoxetine use for maintenance of recovery from major depressive disorder (MDD) in children and adolescents.

Methods: Children and adolescents who had been initially diagnosed with MDD (DSM-IV) with CDRS-R scores >40 who had then responded to 15 weeks of fluoxetine treatment (CDRS-R scores ≤28) were randomly assigned to receive placebo (N = 20) or continue taking fluoxetine (N = 20). Time to relapse (CDRS-R total score >40 with a history of 2 weeks clinical deterioration or per physician perception) was the primary analysis.

Results: Censored time to relapse estimates were 71.2 days (SD = 9.5) for placebo- and 180.7 days (SD = 17.0) for fluoxetine-treated patients (p = 0.046). Fewer fluoxetine patients (34%) than placebo-treated patients (60%) met relapse criteria. At the endpoint of this 32-week study, there were no statistically significant differences between treatment groups in adverse events, mean changes in laboratory values, or most vital signs. There was a slight, but statistically significant difference in sitting systolic blood pressure (p = 0.048), which was not considered clinically significant. An analysis of covariance adjusting for baseline differences in blood pressure was not statistically significant (p = 0.246).

Conclusion: Fluoxetine is effective and well-tolerated for prevention of relapse of MDD in children and adolescents.

NR737 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Risperidone in Children with Significant Conduct Problems and Subaverage Intellectual Functioning

Robert L. Findling, M.D., *Department of Psychiatry, University Hospital, 11100 Euclid Avenue, Cleveland, OH 44106-5080*; Michael G. Aman, Ph.D., Goedele Desmedt, M.D., Albert T. Derivan, M.D.

Summary:

Background: The benefit of risperidone for severe conduct disorder in children with subaverage intellectual functioning was documented in a previous short-term (six weeks) multicenter, double-blind, placebo-controlled study. The current study assessed the long-term safety and efficacy of risperidone for conduct disorders in these children.

Methods: A 48-week, open-label study was conducted in 107 patients (aged 5–12 years) with subaverage intellectual functioning who had conduct disorder, oppositional defiant disorder, or disruptive behavior disorder not otherwise specified, and who had previously completed at least two weeks of the previous six-week study. The primary measure of efficacy was the Conduct Problem subscale of the Nisonger Child Behavior Rating Form (N-CBRF).

Results: All patients received open-label risperidone (0.02–0.06 mg/kg/d). After 48 weeks, significant improvements were seen on the Conduct Problem subscale (p 0.001); improvements were also seen on all other N-CBRF subscales. On the Clinical Global Impressions scale, 62% of the patients were rated as having mild or absent symptoms at endpoint compared with 2% at baseline. The three most common adverse events were somnolence, headache, and rhinitis.

Conclusions: Risperidone had a good overall risk-benefit profile and was effective for the long-term treatment of children with significant conduct problems and subaverage intellectual functioning.

NR738 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Comorbid Psychiatric Illness and Response to Treatment in Pediatric OCD

Daniel A. Geller, M.D., *Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02478*; Joseph Biederman, M.D., David J. Carpenter, M.S., Diane Gallagher, M.S.C., Karen D. Wagner, M.D., Graham J. Emslie, M.D.

Summary:

Objective: To examine the influence of psychiatric comorbidity on response and relapse rates in children and adolescents treated with paroxetine for obsessive-compulsive disorder (OCD).

Method: Patients responding following 16 weeks of treatment (Phase I) were assigned to continued paroxetine or to placebo for 16 additional weeks (Phase II). OCD response (Phase I) and

relapse (Phase II) criteria were based on the CGI (Improvement) scale and the CY-BOCS. The presence of OCD and other psychiatric disorders was ascertained using the K-SADS-PL interview.

Results: At entry, 193/335 (57.6%) patients had at least one psychiatric disorder in addition to OCD and 102/335 (30.4%) had multiple other disorders (≥2). The most common comorbidities were GAD (20.0%), ADHD (19%), specific phobia (16%), tic disorder (15%), separation anxiety disorder (10%), dysthymia (8%), oppositional defiant disorder (8%), and MDD (6%). The response rates in patients with comorbid ADHD, tic disorder, or oppositional defiant disorder (55.6%, 52.9%, and 39.3%, respectively) were significantly less than in patients with OCD only (74.6%, ITT LOCF; $p < 0.05$). Psychiatric comorbidity was associated with a greater overall relapse rate (45.6% for ≥1 comorbid disorder vs. 32.2% for no comorbidity, $p = 0.04$). When multiple (≥2) comorbid psychiatric disorders were present the overall relapse rate increased to 56.2%.

Conclusion: The results of these post hoc analyses have important clinical and research implications for the treatment of children and adolescents with OCD comorbid with other psychiatric illness.

NR739 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Fluoxetine Treatment 20mg Versus 40–60mg for Pediatric Fluoxetine 20mg Nonresponders

Sharon L. Hoog, M.D., *Department of Neuroscience, Eli Lilly and Company, Lilly Corporate Center, DC 2543, Indianapolis, IN 46285*; John H. Heiligenstein, M.D., Karen D. Wagner, M.D., Robert L. Findling, M.D., Daniel E. Ernest, B.A., Mary Nilsson, M.S., Jennie G. Jacobson, Ph.D.

Summary:

Objective: To determine efficacy and safety of fluoxetine 40–60mg/day vs. fluoxetine 20mg/day in pediatric outpatients with major depressive disorder who did not meet protocol-defined response criteria after double-blind fluoxetine 20mg/day.

Method: In an earlier report, pediatric outpatients randomized to fluoxetine 20mg/day experienced statistically significantly greater improvement in CDRS-R score than placebo-treated patients. Patients from this study who did not meet response criteria (> = 30% decrease in CDRS-R score) after nine weeks of fluoxetine 20mg/day were re-randomized to 20mg/day or 40mg/day fluoxetine. After four weeks, patients not responding to 40mg/day could increase to 60mg/day.

Results: Twenty-nine patients, aged 9–17 years, were re-randomized to continue on fluoxetine 20mg/day or to dose escalation to fluoxetine 40–60mg/day. Clinical response to 40–60mg/day was robust, but due to small sample size, findings were not statistically significant. Ten patients (71%) receiving 40–60 mg/day met response criteria, compared with five patients (36%) receiving 20mg/day ($p = 0.128$). Adverse events were similar in both groups.

Conclusion: Although acute fluoxetine treatment (20mg/day) demonstrated statistically significantly greater improvement than placebo in depressed pediatric outpatients, re-randomization of patients who did not respond to 20mg/day demonstrated benefits of dose escalation to 40–60mg/day. Fluoxetine 20–60mg/day appeared safe and well-tolerated.

NR740 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Measuring the Quality of Mental Health Care for Children and Adolescents

Terri L. Miller, Ph.D., *Department of Psychiatry, University of AR Medical School, 5800 West 10th Street, Suite 605, Little Rock, AR 72204*; Teresa L. Kramer, Ph.D., James Robbins, M.D., J. Lynn Taylor, M.D., Barbara J. Burns, Ph.D.

Summary:

Objective: To develop and apply a comprehensive set of evidence and consensus-based quality indicators to address the need for improved measurement of processes of routine care in child and adolescent mental health services.

Method: Indicators were derived from a systematic review of current literature on practice guidelines, randomized clinical trials of interventions, and other relevant work. Twenty-three measures assessing global aspects of treatment were developed, as well as 26 measures assessing aspects of treatment specific to selected disorders. Measures were applied to review of treatment records of 36 adolescents 11 to 17 years old who received care in one inpatient and three outpatient settings. Participants were recruited from a validation study of the Adolescent Treatment Outcomes Module (ATOM).

Results: Concordance of chart documentation with specified criteria for quality care was generally low to moderate. Only 33% of charts documented appropriate psychotherapeutic interventions, while only 24% documented appropriate pharmacological interventions.

Conclusions: Results suggest there may be significant gaps in global and disorder-specific aspects of routine mental health care for youths. Further investigation utilizing alternative sources of quality-of-care data is necessary to determine whether findings indicate deficiencies in quality of services provided or in record-keeping practices.

Funding: This work was supported by NIMH grants 5-R01-MH57887-02 and 1-T32-MH20024-01.

NR741 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Neural Mechanism Mediating Emotional Stress in Childhood Asthma

Bruce D. Miller, M.D., *Department of Psychiatry, University of New York at Buffalo, 219 Bryant Street, Buffalo, NY 14222*; Beatrice L. Wood, Ph.D.

Summary:

The Autonomic Nervous System Dysregulation Model of the Influence of Emotions on Asthma (Miller, 1987) proposes that depressed, despairing, or hopeless states are associated with autonomic instability and/or a cholinergic (vagal) bias that potentiates cholinergically (vagally) mediated airway constriction in asthma. Findings from previous studies conducted in our laboratory demonstrate the link between depressed/hopeless emotions, vagal activation, and pulmonary function in asthma. The current study addresses the question of whether asthmatic children are different from non-asthmatic children in overall vagal tone and/or in vagal reactivity. Twenty-three healthy children and 24 severe asthmatic children watched an emotionally challenging movie while having their heart beat measured. Respiratory sinus arrhythymia (RSA), computed from heart rate variability, was used as an index of vagal activation. Results showed that asthmatic children had lower vagal tone than non-asthmatic children (mean = 6.6 versus 7.3, $p < 0.001$) but that they had greater vagal reactivity as indexed by within-subject RSA SD across the movie (Mean = 0.62 versus 0.43, $p < 0.03$) reflecting more dramatic shifts in vagal activation in response to the varying emotional scenes. These findings demonstrate psychophysiologic linkages between emotional stress and physical illness, thus furthering knowledge of how mind and brain influence physical well being.

NR742 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Effects of Negative Attachment on Asthma: A Direct Psychophysiological Link?

Beatrice L. Wood, Ph.D., *Department of Psychiatry, SUNY at Buffalo, 219 Bryant Street, Buffalo, NY 14222;* Bruce D. Miller, M.D., Kendra B. Klebba, M.P.H.

Summary:

Psychoanalytic theory has posited that negative family relations and parent-child attachment issues are implicated in asthma. However, no studies have identified specific family relational patterns nor demonstrated a direct psychophysiological link by which such patterns may influence asthma. Wood's Biobehavioral Family Model (Wood, 1993) poses a heuristic model of how negative family relations evoke hopelessness and increased vagal (cholinergic) activation, thus potentiating cholinergically mediated airway constriction in asthma. In a preliminary of test this model, 20 patients with asthma watched an emotionally challenging family movie, then participated with their families in emotional discussions while having respiratory sinus arrythymia (an index of vagal activation) continuously measured. Reliable family observation interaction ratings (interater $r > 0.60$) indicated that negative/conflictual family interaction and mother-child rejection were associated with *increased* vagal activation ($r = 0.44$, $p < 0.05$; $r = 0.39$, $p < 0.08$). Mother-child support was associated with *decreased* vagal activation ($r = -0.42$, $p < 0.06$). Father-child rejection showed a similar trend ($r = -0.36$, $p < 0.13$). There were indications that negative family interaction and mother-child rejection were correlated with child hopelessness ($r = 0.36$, $r = 0.35$, $p < 0.10$). Findings suggest that negative family relations and parent-child attachment may directly influence asthma by evoking hopelessness accompanied by vagally mediated airway constriction.

NR743 Thursday, May 10, 12:00 p.m.-2:00 p.m.

EPS and Tardive Dyskinesia in Children and Adolescents Treated with Risperidone

Sanjay S. Chandragiri, M.D., *Tri-County Human Services Center, P O Box 514, 185 Fallbrook Street, Carbondale, PA 18407;* Edwin A. Feliciano, M.D.

Summary:

Objective: To assess the occurrence of tardive dyskinesia and extrapyramidal side effects associated with risperidone in children and adolescents.

Method: A group of 28 children and adolescents, treated with risperidone for various psychiatric disorders, were examined using a cross-section study design. Subjects were evaluated for extrapyramidal side effects and tardive dyskinesia using the Simpson Angus (SA) scale and the Abnormal Involuntary Movement (AIM) scale. Demographic data, individual subject diagnosis, risperidone dose, length of treatment, and liver function tests results were obtained after a chart review.

Results: The mean score in the SA scale was 2.57 (standard deviation 3.09) (range 0 to 12). The mean score in the AIM scale was 12.36 (standard deviation 1.14) (range 12 to 18). The average daily dose of risperidone was 1.63 mg (range 0.25 mg to 6 mg). The average length of treatment was 11.27 months (range 1.5 months to 25 months). The average age of the subjects was 11.04 (range four years old to 18 years old).

Conclusion: The occurrence of tardive dyskinesia and extrapyramidal side effects has not been well established in children and adolescents. This cross-sectional study demonstrated a low prevalence of these symptoms.

NR744 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Prepubertal Bipolar Disorder and ADHD: Diagnostic Considerations

Edith M. Jolin, M.D., *P O Box 1518, Duxbury, MA 02331*; Laura E. Sanchez, M.D., Owen R. Hagino, M.D., Carrie E. Bearden, Ph.D., Kathleen Hoffman, B.A., Ronald A. Weller, M.D., Elizabeth B. Weller, M.D.

Summary:

Objective: Prepubertal bipolar disorder may be confused with ADHD. To clarify the relationship between these disorders, the natural history and phenomenology of bipolar disorder and ADHD were assessed in 301 prepubertal children.

Methods: Subjects were obtained from a sample of 301 consecutively hospitalized prepubertal children who received comprehensive psychiatric evaluations including structured diagnostic interviews. Three board-certified child and adolescent psychiatrists reviewed all diagnostic information available and then assigned DSM-III-R Axis I consensus diagnoses. This study included 61 subjects in three diagnostic categories: seven subjects had bipolar disorder only (BP Only), 17 subjects had bipolar disorder with comorbid ADHD (BP+ADHD), and 37 subjects had ADHD (ADHD only). These three groups were compared as to clinical symptomatology, comorbidity, previous medication history, cognitive profile, neuroendocrine findings, family history of psychiatric disorders, and environmental stressors.

Results: The BP only group was more likely than the ADHD only group to have comorbid depression ($p = .005$), hallucinations ($p = .03$), severe aggression ($p = .05$), and lower GAF score at intake ($p = .024$). The BP+ADHD subjects compared with ADHD only subjects had a significantly greater number of comorbid diagnoses ($p = .0007$) including history of delusions ($p = .03$), previous hospitalizations ($p = .002$), neuroleptic exposure ($p = .04$), and thyroid abnormalities ($p = .04$). Both bipolar groups had increased familial incidence of bipolar disorder ($p = .005$).

Conclusion: Psychiatric comorbidity, psychotic thought processes, and history of bipolar disorder in the family appeared to distinguish bipolar disorder from ADHD in this sample.

NR745 Thursday, May 10, 12:00 p.m.-2:00 p.m.

A Comparison Between Children with ADHD and Children with Oppositional Defiant Disorder

Turkay Demir, M.D., *Bakirkoy Akil Hastanesi, Umatem, Istanbul, Turkey;* Kultegin Ogel, M.D., Demet E. Demir, M.D., Leyla Alkas, M.D., Levent Kayaalp, Kengiz Albayrak

Summary:

Objective: Disruptive behavior disorders display frequent comorbidity with each other. Due to the high comorbidity and symptom similarity, characteristics specific to each disorder cannot be adequately discerned. This study aims to investigate the differences between ODD and ADHD.

Method: Subjects consisted of patients presenting to the outpatient clinic who were diagnosed with ADHD or ODD according to DSM-IV. ADHD subjects with comorbid ODD or conduct disorder were excluded. Twenty four ADHD and 15 ODD subjects participated in the study. The two groups were compared using data obtained from a detailed interview form and psychiatric scales.

Results: Children in the ODD group were older; ADHD had its onset earlier than ODD. Groups differed in that the ODD group had a higher percentage of girls. Less ODD subjects attended nursery school. According to the mothers' opinions, ODD parents were less consistent toward their children with regard to discipline matters, and ODD parents tended to spend less time with their children. According to clinicians' evaluations, ODD children were less willing to cooperate with the clinicians. In the ODD group, comorbidity with other psychiatric disorders was higher.

Conclusion: The differences between the two groups lends support the idea that ODD is a separate clinical entity. Differences suggest that ADHD represents "developmental" and ODD represent "environmental" aspects of the disruptive behavior disorders.

NR746 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Compliance with Newer Antipsychotics in Adolescent Patients

David L. Pogge, Ph.D., *Department of Psychology, Four Winds Hospital, 800 Cross River Road, Katonah, NY 10536;* Melissa Singer, M.A., Victoria Deluca, M.A., Lale Bilginer, M.A., Hilary Bertisch, M.A., Martin Buccolo, Ph.D., Philip D. Harvey, Ph.D.

Summary:

Compliance with antipsychotic treatment has increased since the introduction of newer medications. Few data are available regarding antipsychotic medication compliance in adolescent patients, particularly comparative compliance across different medications. In an ongoing study, adolescent psychiatric patients discharged from an inpatient psychiatric admission taking either olanzapine (N = 32) or risperidone (N = 35) were followed up an average of 6 months post-discharge and evaluated for compliance with treatment, side effects, and related factors. Fifty-seven percent of the risperidone patients and fifty-six percent of the olanzapine patients were still taking their medications as prescribed. There were no statistically significant differences in the rate of spontaneous discontinuation on the part of the patients (5% risperidone and 3% olanzapine) or in the rate of discontinuations of medication initiated by physicians after discharge (28% risperidone and 25% olanzapine). Survival analysis indicated that there were no differences in the time course of discontinuations, regardless of reason. Although patients treated with olanzapine gained significantly ($p < 0.05$) more weight over the follow-up period (32 lb versus 20), the extent of weight gain for both samples was higher than previously reported for adult patients. Interestingly, physician-initiated discontinuations were not associated with increases in weight gain in either medication group. These data indicate that medication compliance with newer antipsychotic medications is quite high, particularly from the perspective of patient-initiated discontinuation. At the same time, weight gain in this population appears to be a significant factor, the long-term consequences of which merit further attention.

NR747 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Adolescent Depression, Anxiety, and PTSD Symptoms

Lee Matthews, Ph.D., *Department of Psychiatry, Tulane University, 2280 Desmond Drive, Decatur, GA 30033*; Siham Muntasser, M.D., James W. Lowe, M.D.

Summary:

Background: Although there has been an active interest in understanding and assessing childhood and adolescent depression, only in the past decade has as much interest been focused on anxiety disorders.

Objective: The purpose of this study was to examine the comorbid relationship between depression, anxiety, PTSD, and substance abuse in a population of adolescents hospitalized in an acute psychiatric unit.

Materials and Methods: The study included 350 patients, between the ages of 13–17, diagnosed with severe emotional, conduct, and/or substance abuse problems. Upon admission to the hospital, each patient was subjected to a full psychiatric, psychosocial, and psychological evaluation. Specific psychopathology measures utilized in this study included the Revised Children's Manifest Anxiety Scale (RCMAS), the Beck Depression Inventory (BDI), the Beck Anxiety Inventory (BAI), the Trauma Symptom Checklist for Children (TSCC), and the Substance Abuse Subtle Screening Inventory (SASSI).

Results: The data were analyzed using Statistics Assessment Software (SAS). Analysis of variance statistics (ANOVA) and chi-square were used to examine between-group differences. Results indicated a significant relationship between the presence of anxiety/depression symptoms and PTSD symptoms in both male ($p < 0.05$) and female ($p < 0.05$) subjects. Significant relationships were also noted between anxiety/depression, PTSD, and alcohol use ($p < 0.05$) as well as substance abuse ($p < 0.05$) in female subjects. No such findings were present for male subjects.

Conclusion: Our data suggest that in adolescents, comorbidity between anxiety and depression is an indicator of severe pathology often involving PTSD, alcohol and/or substance abuse, and conduct problems. These findings indicate the need of a more aggressive follow-up of adolescents who exhibit signs and symptoms of anxiety as well as depression that should focus on family dynamics, aggressive treatment of substance abuse, providing role models in the form of mentors, and as professional and academic counseling.

NR748 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Effect of Methylphenidate on Attention Shifts in Children with ADHD

Martin H. Teicher, M.D., *Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02478*; Steven B. Lowen, Ph.D., Cynthia E. McGreenery, Ann M. Polcari, R.N., Mary Foley, R.N.

Summary:

Inattention is a hallmark of ADHD. Computerized vigilance tasks have been used to assess attention by providing aggregate measures of response latency and error rates (omission, commission). However, attention is not a static parameter but a dynamic and fluctuant process. Better insight into the nature of ADHD may arise from the assessment of attention shifts. Attention was measured using a 15-minute GO/NO-GO vigilance task (Teicher et al. 1996) with randomly positioned 8- and 5- pointed stars as stimuli. For each successive 30 second segment response was divided into On-task, Impulsive, Distracted, or Random Responding, based on predefined criteria. Sixty children with ADHD (hyperactive-impulsive or combined subtype DSM-IV by K-SADS-E; 9–12 years) and eight controls were studied off all medication. ADHD children were retested 120 minutes after methylphenidate (MPH 0.4 mg/kg PO). ADHD children shifted attention state 2.4 times more often than controls ($p < 0.0001$). MPH reduced attention shifts by 45% ($p < 00001$), to a rate not significantly different than normal. Children with ADHD were on-task during 42.6% of the segments vs. 82.4% for controls ($p < 0.001$). MPH increased the ADHD on-task rate to 75.4% ($p < .00001$). Attention shifts and on-task rates provided superior discrimination of ADHD and medication effects than traditional static measures.

NR749 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Quetiapine and Donepezil in Dementia

Mahmoud A. Parsa, M.D., *Department of Psychiatry, University Hospital, 11100 Euclid Avenue, Cleveland, OH 44106*; Elis Poggi, L.C.S.W., Lorna M. Barte, M.D., Fatemeh Nematzadeh, M.D., Jeffrey M. Goldstein, Ph.D.

Summary:

Introduction: Psychotic and behavioral symptoms are not uncommon in patients with dementia. It is rational to assume that many dementia patients would benefit from an antipsychotic agent as well as a cognitive enhancer to manage their symptoms. Quetiapine is an atypical antipsychotic agent with proven efficacy in the treatment of psychosis and behavioral disturbances associated with dementia. Donepezil is a cholinesterase inhibitor currently used to improve memory and cognitive performance in patients with Alzheimer's disease (AD) and other types of dementia.

Objective: This study was intended to assess the efficacy and tolerability of a combination regimen of quetiapine and donepezil to treat psychosis and behavioral disturbances in dementia patients.

Methods: A retrospective chart review was conducted at our hospital on 30 patients with dementia, including AD, vascular, mixed, or Lewy body disease (LBD). All patients were treated with a combination of quetiapine and donepezil for psychosis and behavioral disturbances. The "Positive" and "Excited" components of the Positive and Negative Syndrome Scale (PANSS), adapted Cohen-Mansfield Scale, and Clinical Global Impression (CGI) scale were used as efficacy measures. The Simpson-Angus Scale, vital signs, laboratory tests, and adverse event questionnaire were used as tolerability measures. The Mini-Mental State Examination (MMSE) assessed cognitive function.

Results: All patients showed significant improvement in their symptoms during treatment with quetiapine and donepezil, as measured by the above scales. Furthermore, the combination regimen of quetiapine and donepezil was well tolerated by all patients.

Conclusion: Co-administration of quetiapine and donepezil is safe and effective in the treatment of dementia patients with psychotic and behavioral symptoms. Further double-blind comparative studies are warranted to confirm these preliminary findings. This study was supported by an unrestricted educational grant from AstraZeneca, the manufacturer of quetiapine ("Seroquel").

NR750 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Effect of Aging on the CCK System

Alastair J. Flint, M.B., *Department of Psychiatry, Toronto General Hospital, 200 Elizabeth Street, 8 EN-238, Toronto, ON M5G 2C4, Canada*; Jacques Bradwejn, M.D., Franco J. Vaccarino, Ph.D., Diana Koszycki, Ph.D.

Summary:

Objective: Older age is associated with diminished behavioral and cardiovascular response to the panicogenic agent cholecystokinin tetrapeptide (CCK-4). This study examined whether there are age-related changes in the CCK system that could account for this finding.

Method: Under single (subject)-blind conditions, 20 healthy subjects aged 18–30 years and 20 healthy subjects aged 65–85 years received an intravenous injection of placebo and, 50 minutes later, an intravenous injection of 50 μg of CCK-4. Plasma concentrations of total CCK were measured at baseline and at 2, 5, 10, and 15 minutes after each injection. Lymphocyte CCK-B receptor binding (which was used as a proxy for CCK-B receptor binding in the brain) was also measured at baseline.

Results: Compared with younger subjects, older subjects had significantly decreased CCK-B receptor binding ($p = 0.001$). There was a nonsignificant trend toward a higher basal concentration of CCK in the elderly ($p = 0.08$). Following injection of placebo, plasma CCK concentrations did not significantly change from baseline in either age group, but the elderly had significantly higher concentrations than the young at 2, 5, and 10 minutes ($p < 0.03$). Following injection of CCK-4, the plasma concentration of CCK peaked at 2 minutes and declined after that. The elderly had significantly higher concentrations (i.e., a slower decline) at 5, 10, and 15 minutes ($p < 0.01$).

Conclusions: These findings are consistent with the hypothesis that extracellular concentrations of CCK are increased in later life (possibly due to decreased enzymatic degradation), resulting in desensitisation of CCK-B receptors. Decreased receptor sensitivity could explain the diminished panicogenic response to CCK-4 in the elderly.

NR751 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Relationship Between Clinical Variables and Anxiety in Geriatric Depression

Alastair J. Flint, M.B., *Department of Psychiatry, Toronto General Hospital, 200 Elizabeth Street, 8 EN-238, Toronto, ON M5G 2C4, Canada*; Sandra L. Rifat, Ph.D.

Summary:

Objective: To determine whether anxiety that is symptomatic of late-life depression is associated with other clinical variables and, if so, how much of the variance in anxiety is explained by this association.

Method: 101 men and women, 60 years or older, with an episode of DSM-III-R nonpsychotic unipolar major depression and a HAM-D score ≥16 participated in the study. None of these subjects had a concurrent axis I diagnosis or acute medical illness. The anxiety subscale of the Hospital Anxiety and Depression Scale was used to quantify anxiety that was symptomatic of depression at index assessment and following completion of acute treatment. The following clinical variables were selected to determine whether they were associated with severity of anxiety: depression severity, burden of chronic physical illness, cognitive function, life events and life difficulties preceding onset of the depression, and intensity of psychosocial support. Pearson correlation coefficients were computed to examine the linear association between anxiety and the independent variables. Stepwise multiple regression analyses were then used to determine which variables accounted for a statistically significant part of the variance in anxiety scores.

Results: There was a significant association between severity of anxiety and severity of depression at index assessment ($r = 0.422$, $p < 0.001$) and following the completion of treatment ($r = 0.721$, $p < 0.001$). There was a weak association between severity of negative life events and severity of anxiety at index assessment ($r = 0.214$, $p = 0.03$) and between physical illness burden and severity of anxiety following completion of treatment ($r = 0.214$, $p = 0.03$). At index assessment, depression was the only factor to significantly contribute to the variance in anxiety scores. Following completion of treatment, depression scores accounted for 52% of the variance in anxiety scores; physical illness burden contributed to only an additional 2% of the variance.

Conclusion: Chronic physical illness burden, impaired cognitive function, and negative psychosocial circumstances did not contribute, in a clinically significant way, to variability in anxiety scores in late-life depression. The implications of these findings for the conceptualization and treatment of symptomatic anxiety will be discussed.

NR752 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Use of Neuroleptics in Demented and Nondemented Nursing Home Residents

Olayinka M. Johnson, M.D., *Department of Mental Health, Baltimore Veterans Affairs, 10 North Greene Street, Baltimore, MD 21201*; Bruce A. Kaup, M.D., David J. Loreck, M.D., Allen Raskin, Ph.D., Srikumar Menon, M.D., Paul E. Ruskin, M.D., Ann L. Gruber-Baldini, Ph.D.

Summary:

Objective: Neuroleptic medication is used in nursing home residents for reasons such as agitation, psychosis, delirium, and behavioral problems. One aim of this study was to compare and contrast the frequency of use of neuroleptics in demented and nondemented nursing home residents. An additional aim was to identify other factors associated with the use of neuroleptics in these residents.

Method: The sample consisted of a subset of 336 nursing home residents selected from a larger group of 2,285 residents in 54 Maryland nursing homes. Psychotropic medication use was docu-

mented at baseline (within two weeks of admission). The diagnosis of dementia was based on the determination by an expert panel of neurologists, psychiatrists, and a geriatrician. Predictor variables included gender, race, and two subscales of the PsychoGeriatric Dependency Rating Scale (PGDRS), orientation and behavior, and the Cornell Depression Scale for persons with dementia. These instruments were completed at baseline.

Results: Patients with diagnosis of dementia were significantly more likely to be prescribed neuroleptics (10%) than their nondemented counterparts (0.82%). Variables that significantly predicted neuroleptic use included the orientation and behavioral subscale scores of the PGDRS and the Cornell Depression Scale.

Conclusion: Demented nursing home residents were prescribed neuroleptics more frequently than nondemented residents. The high rate of use was probably due to the high rate of behavioral and psychiatric symptoms in demented residents.

NR753 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Atypical Antipsychotics for Severe Geriatric Anxiety: A Novel Indication

Luis Aguera-Ortiz, M.D., *Department of Psychiatry, 12 de Octubre Hospital, Av. Andalucia KM 5400, Madrid 28041, Spain*; Ana Pascual, M.D., Ainkoa Garibi, M.D., Rita Henriquez, M.D., Tomas Palomo, M.D.

Summary:

Objective: To examine the efficacy and safety of atypical antipsychotics (AA) in elderly patients with severe anxiety.

Method: Case series description. Twenty outpatients aged ≥60 with severe anxiety (HAM-A >25) alone or associated with conditions other than psychosis, bipolar illness, or dementia (MMSE> 24), received low doses of an AA. Follow-up time ≥6 months at a university clinic setting. Main changes measured independently by CGI for global results, anxiety, depression, and sleep.

Results: Female sex: 85%; mean age: 75.6; primary diagnosis: GAD: 40%; adjustment disorder: 35%; major depression: 15%; disthymia: 10%.

Antipsychotic used: olanzapine 70%, mean dose: 5 mg/day (2.5–7.5); risperidone 30% mean dose: 0.79 mg/day (0.25–1.5).

After six weeks: Global CGI >5 (much or very much improved): 78%, anxiety CGI>5: 79%; sleep CGI>5: 13%. mood CGI>5: 78%. Improvement was independent of sex, diagnosis, type of drug, or physical illness and was maintained long term.

Absence or generally mild side effects were found except for four patients whose treatment was discontinued.

Conclusions: Low-dose atypical antipsychotics seem to be a safe and highly effective treatment for severe geriatric anxiety. This condition is not infrequent in the elderly population. Its treatment with benzodiazepines is often ineffective and potentially dangerous. Atypical antipsychotics may well be an acceptable alternative.

NR754 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Risperidone Versus Olanzapine in Elderly Patients with Schizophrenia

Dilip V. Jeste, M.D., *Department of Psychiatry, VA San Diego Health Care System, 3350 La Jolla Village Drive, San Diego, CA 92161*; Subramoniam Madhusoodanan, M.D., Foram Barak, M.D., Rick A. Martinez, M.D.

Summary:

Background and Method: An international, double-blind, eight-week study was conducted in 176 patients, age >60 years, with DSM-IV schizophrenia or schizoaffective disorder. Patients were randomly assigned to receive flexible doses of risperidone (1–3mg/day) or olanzapine (5–20mg/day).

Results: At median doses of 2 mg/day risperidone and 10 mg/day olanzapine, Positive and Negative Syndrome Scale (PANSS) total score (primary endpoint) decreased significantly in both groups at endpoint ($p < 0.001$). Risperidone treatment resulted in significantly greater improvement on PANSS than olanzapine at four weeks ($p = 0.05$), but there was no significant between-group difference at endpoint. Scores at baseline and endpoint on the Clinical Global Impressions (CGI) scale, Hamilton Depression Scale, and MMSE were similar in the two groups. About two-thirds of all patients had minimal or greater improvement on CGI. Although baseline Extrapyramidal Symptom Rating Scale (ESRS) scores were equivalent, risperidone-treated patients improved significantly at each assessment relative to baseline, while there was no significant difference on ESRS scores versus baseline with olanzapine. Risperidone and olanzapine groups did not differ in incidence of common adverse events.

Conclusions: At doses appropriate in elderly patients with schizophrenia, significant reductions in psychopathology occurred in both treatment groups with a suggestion for earlier improvement with risperidone. Overall side-effect profiles were similar but there was a trend favoring risperidone in total ESRS scores.

NR755 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Longitudinal Changes in Subclinical Structural Brain Disease in Normal Aging

Andrew F. Leuchter, M.D., *Department of Psychiatry, Neuropsychiatric Institute-UCLA, 760 Westwood Plaza, Room 37-426, Los Angeles, CA 90024-8300*; Ian A. Cook, M.D., Melinda L. Morgan, Ph.D., Steven David, B.A., Jennifer Dunkin, Ph.D., Robert Lufkin, M.D.

Summary:

Objective: To examine the natural history of subclinical structural brain disease (SSBD) in the elderly.

Content: Twenty-five normal control subjects, ages 60–89.

Methods: Subjects were enrolled in a longitudinal examination of SSBD with volumetric analysis of MRI to measure the volumes in milliliters of sulcal and ventricular fluid, PVH, and DWMH in right and left hemispheres, anterior and posterior regions. Assessments were performed on two occasions at least two years apart (mean interval 3.7 ± 0.8 years). Subjects underwent neuropsychological testing to evaluate processing speed, executive functions, language, and other cognitive functions. The associations between changes in SSBD volumes and cognitive performance were evaluated with regression and correlation models.

Results: Volumes of all types of SSBD increased between assessments, although increases were small for many subjects. Change over time in volume of PVH, but not other types of disease, was associated with cerebrovascular risk factors at enrollment. Increases in PVH were significantly associated with poorer performance on word generation and abstract reasoning tests; increases in volume of other types of SSBD were not significantly associated with changes in cognition.

Importance: There are detectable increases in the volume of SSBD over two to six year follow-up, although the mean increase is small for most types of disease, and many subjects have minimal increases. Only PVH is significantly associated with vascular risk factors on short-term follow up, and results in changes in cognition. Because change in PVH, a cerebrovascular form of SSBD, showed association with vascular risk factors at time of enrollment, these risk factors may merit attention even in asymptomatic elderly patients.

NR756 Thursday, May 10, 12:00 p.m.-2:00 p.m.

White and Gray Matter Volumes on MRI in Geriatric Depression

Helen Lavretsky, M.D., *Department of Psychiatry, UCLA-NPI, 760 Westwood Plaza, Room 37–425, Los Angeles, CA 90095*; Anand Kumar, M.D., Daniel Pham, B.S., Ivo Dinov, Ph.D., Michael S. Mega, M.D., Arthur Toga, Ph.D., Laverne Estanol, M.S.

Summary:

Objectives: The objectives of our study were to compare elderly depressed patients with normal controls on global measures of gray and white matter volumes and to examine the relationship of gray: white matter volumes to relevant clinical measures such as severity of depression (HAM-D), apathy, cognition, medical burden, and stroke risk factors in depressed patients.

Methods: Thirteen controls (10 women) and 14 patients (10 women) diagnosed with unipolar major depressive disorder and matched by age and gender (sample mean age = 71.6) received comprehensive neuropsychiatric evaluation and 1.5T structural MRI. 1.5 mm coronal SPGR images were used in our analysis. Estimates of the gray (GM) and white matter (WM), and CSF were obtained and normalized to the intracranial volumes (ICV). The groups were compared on the variables of interest with the ANCOVA. The relationships between neuroimaging and clinical measures were examined using the Spearman Correlation Coefficient.

Results: The groups did not differ on global measures of gray:white matter volumes. In the depressed patients, the white matter volume correlated negatively with age ($r = .58$, $p = 0.03$), stroke risk factors ($r = 0.7$, $p = 0.006$), and medical burden ($r = -0.7$, $p = 0.009$). It did not correlate significantly with the HAM-D or apathy. The gray matter volume did not correlate with any of the variables.

Conclusion: Our results suggest that there are no differences in whole brain gray and white matter volumes between our patient and control groups. However, our results indicate that normalized whole brain white matter volumes are closely related to global medical burden and stroke risk factors in elderly depressed patients and underscore the importance of neuronal white matter in the pathophysiology of depression.

Supported in part by the NARSAD Young Investigator award to Dr. Lavretsky.

NR757 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Mortality in Elderly Veterans with Comorbid Medical and Psychiatric Symptoms Enrolled in the "UPBEAT" Program

Helen Lavretsky, M.D., *Department of Psychiatry, UCLA-NPI, 760 Westwood Plaza, Room 37-425, Los Angeles, CA 90095*; Roshan Bastani, Ph.D., Robert Gould, Ph.D., David L. Huang, Ph.D., Annett Maxwell, Ph.D., Lissy F. Jarvik, M.D.

Summary:

Objectives: Predictors of mortality were investigated in elderly veterans with comorbid medical and psychiatric symptoms.

Methods: Patients admitted to inpatient services of nine VA Medical Centers were screened for symptoms of depression and anxiety, and re-examined at six, 12, and 24 months. Using ANOVA, we compared survivors and deceased at 24 months with regard to severity of symptoms of anxiety and depression, and composite scores (MCS and PCS) of the SF-36 scale, as well as medical burden (CIRS). To assess predictors of mortality, we used Cox proportional hazard model survival analysis.

Results: Mortality at 24 months for the 958 "UPBEAT" patients was 14.3%. In the survival analysis, mortality was predicted by the PCS score, the total CIRS score, the CIRS indexes. Depression, anxiety, and MCS at baseline did not predict mortality. Patients who demonstrated improvement in depression or anxiety by at least three points at six months had significantly lower mortality than those who had worsening of these symptoms.

Conclusions: Medical burden and self-rated physical health predicted mortality in the survival analysis model. Although depression and anxiety at baseline did not predict mortality, worsening of these symptoms over time may contribute to the overall mortality.

Supported in part by the NARSAD Young Investigator Award to Dr. Lavretsky.

NR758 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Subclinical Structural Brain Disease in Normal Aging: Cognitive and Physiological Correlates

Ian A. Cook, M.D., *Department of Psychiatry, UCLA, 760 Westwood Plaza, Rm 37-426, Los Angeles, CA 90024-1759*; Andrew F. Leuchter, M.D., Melinda L. Morgan, Ph.D., Steven David, B.A., Jennifer Dunkin, Ph.D., Robert Lufkin, M.D.

Summary:

Purpose: Four types of brain structural change are described in "normal aging": cortical atrophy, central atrophy, deep white-matter hyperintensities (DWMH), and periventricular hyperintensities (PVH). We examined the volumes of these types of "subclinical structural brain disease" (SSBD) and the associations of SSBD, physiology, and cognitive function.

Methodology: 43 normal subjects, ages 60–93, were assessed with volumetric MRI (sulcal and ventricular fluid, PVH, DWMH), neuropsychological testing, and quantitative EEG coherence (i.e., functional connectivity between brain regions).

Results: Regression models demonstrated significant associations between SSBD and age. Cortical and central atrophy and PVH; but not DWMH, were associated with age. Posterior atrophy showed stronger associations with age than anterior atrophy. Only a subset showed large volumes at higher ages; primarily the variance increased with aging. Although all cognitive scores were normal, SSBD volume was inversely associated with performance. Coherence had significant associations with SSBD; for several measures, cognitive performance was better explained by coherence than by SSBD.

Importance: Modest volumes of SSBD were associated with decrements in cognition within the normal range in normal subjects. Lower coherence was associated with greater volumes and increasing age. Shared variance models suggest SSBD may exert effects on cognition through impairment of functional connectivity.

NR759 Thursday, May 10, 12:00 p.m.-2:00 p.m.

The Prevalence of Depressive Symptoms and Their Impact on General Health Status in an Elderly Korean Population

Sang-Yeol Lee, M.D., *Department of Psychiatry, Wonk Wang University, 144-23 Dongsan-Dong, Iksan, Chonbuk, ON 570-060, Korea*; Min-Cheol Park, M.D., Kyung-Jin Kim, M.D.

Summary:

Objectives: The number of elderly people in Republic of Korea is ever increasing. It is estimated that elderly population 65 years old and over will increase 13.1% by year 2021. It is important to recognize depressive symptoms and it's impact on general health condition in elderly people. This study assesses the prevalence of depressive symptoms in a Korean elderly population, comparing sociodemographic factors, general health status between elderly people with depressive symptoms (depressive group) and without depressive symptoms (nondepressive group), and the impact of depressive symptoms on the general health status in the depressive group.

Methods: In the survey of elderly Koreans, aged 65 years and older, living in Iksan selected by random sampling from 20 Dongs (village), which are located in rural (10) and urban (10) areas. The prevalence of depression was determined using the Beck Depression Inventory (BDI) using cut-off point 21 (H-M Han, 1986). The subjects with 19 point and over of Mini Mental Status Examination were excluded. The general health status was assessed using the Short-Form-20-Health Survey (SF-20).

Results: From the total of 488 people (301 male and 187 female) the adjusted overall prevalence of depressive symptoms was 25%. The depressive elderly group showed significantly in more female with, lower educational level, longer duration after bereavement, lack of communication with family members, lower economic level with less spending money and presence of physical illness than non-depressive elderly group. The depressive elderly group showed significantly lower score in each dimension (physical, social, and role functioning as well as mental health, pain, and health perception) of SF-20. There were significant negative correlations between BDI and physical functioning, BDI and mental health, BDI and health perception, BDI and social functioning, BDI and pain.

Conclusion: The results of this study suggest that the prevalence of depressive symptoms in an Korean elderly population is 25% and that depressive elderly people have lower general health than nondepressive elderly people do, and depressive symptoms has negative impact on general health status. This study also suggest that we must realize that depression is likely to be a prevalent source of poor general health among elderly people and that when depression strikes the elderly people, it often goes unrecognized and untreated.

NR760 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Executive Function and Treatment Outcome in Geriatric Mania

Robert C. Young, M.D., *Department of Psychiatry, Weill Cornell, 21 Bloomingdale Road, White Plains, NY 10605*; Christopher Murphy, Ph.D., Jose M. De Asis, M.D., William J. Apfeldorf, M.D., George S. Alexopoulos, M.D.

Summary:

Background: Striato-frontal (SF) circuit abnormalities have been implicated in the pathophysiology of geriatric mania as well as of geriatric depression. In geriatric depression, evidence of SF impairment, such as executive dysfunction, is associated with slower/poorer acute antidepressant response, and with more fragile remission. We therefore hypothesized that executive dysfunction is associated with less reduction in symptoms during acute pharmacotherapy of geriatric mania.

Methods: Inpatients aged ≥60 years with diagnosis of manic disorder (RDC) were studied. Mania Rating Scale (MRS; Young et al.) scores were documented before and after at least three weeks of pharmacotherapy. Executive function was assessed using the Mattis DRS Initiation-Perseveration subscale (IP).

Results: Thirty-three (n = 33) patients were studied. Their mean age was 71.5 years (SD = 7.8 years); 29 were female. Lower (poorer) IP scores were associated with less reduction in MRS scores ($r_s = 0.56$; $p < .001$).

Discussion: These preliminary findings suggest that executive dysfunction may be associated with limitation of acute therapeutic outcome in geriatric mania. If validated, such an association is important in part because executive dysfunction is clinically accessible. Such an association also presents a heuristically useful model for neuropharmacologic investigation.

Supported by NIMH grants MH52763, MH49762, and MH01192.

This presentation is intended for health care providers and investigators. Background in mood disorders, geriatrics, and neuropsychology is helpful but not necessary.

NR761 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Association of Cerebral Blood Volume Changes with Depression in Dementia Patients

Helen H. Kyomen, M.D., *Department of Psychiatry, McLean Hospital, 115 Mill Street, Belmont, MA 02478-9106*; John Hennen, Ph.D., Gary L. Gotlieb, M.D., Jeanne Y. Wei, M.D., Perry F. Renshaw, M.D.

Summary:

Objective: To assess the relationship in dementia patients between cerebral blood volume (CBV) values and scores on the Geriatric Depression Scale (GDS), Mini-Mental State Examination (MMSE), Behavioral Pathology in Alzheimer's Disease scale (BEHAVE-AD), and Activities of Dally Living (ADL) scale.

Method: Left and right temporoparietal:cerebellar CBV ratios, scores on the GDS, MMSE, BEHAVE-AD, and ADL scales, and demographic information was obtained through retrospective chart review of 139 records of dementia patients evaluated from 1993 to 2000 in an outpatient memory evaluation clinic. A multivariate regression analysis was carried out with GDS total score as the outcome variable.

Results: Depression, as measured by the GDS, was found to be significantly predicted by lower left versus right temporoparietal:cerebellar CBV ratio ($t = -2.534$, $p < 0.019$). This finding remained statistically significant after controlling for age, sex, years of education, and years of memory loss ($t = -3.008$, $p < 0.011$). There was no significant association of MMSE, BEHAVE-AD, or ADL scale score or demographic characteristics with the left versus right temporoparietal:cerebellar CBV ratio.

Conclusions: In this study, lower left versus right temporoparietal:cerebellar CBV ratio was correlated with greater depression, as measured by the GDS.

Funding: This research was supported in part by HHS grants AG08812 and AG00294.

NR762 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Efficacy and Safety of Sertraline Treatment of Late-Life Depression

Sanford I. Finkel, M.D., *C1 Jewish Elderly Geriatric Institute, 3003 West Touhy Avenue, Chicago, IL 60645*; Tal Burt, M.D., Cathryn M. Clary, M.D., Jack Mardekian

Summary:

Background: The field of geriatric psychiatry still suffers from a death of large controlled, psychopharmacological studies. In an analysis of a large database of geriatric depressed patients participating in controlled clinical trials, the efficacy and safety of sertraline treatment were examined.

Methodology: Three large, multicenter, parallel-group, double-blind, randomized studies were pooled and analyzed. Two studies were active-controlled and one placebo-controlled (sertraline N = 591, placebo N = 376; active comparator N = 222). The studies were 8–12 weeks in duration.

Results: Baseline Hamilton Rating Scale for Depression (HRSD, 17-item version) score was 22.8 (SD = 3.92) for the sertraline group and 21.4 (SD = 2.65) for the placebo group (results from the comparator analyses were reported elsewhere [1,2]. Change from baseline to endpoint was 9.2 (SD = 7.4) in the sertraline group and 6.6 (SD = 6.4) in the placebo group ($p < 0.001$). The most common adverse events (defined as occurring in greater than 10% of patients) did not differ in severity or frequency from

those seen in younger adults and included insomnia, somnolence, diarrhea, nausea, dry mouth, and headache.

Conclusions: Sertraline is effective and safe in the treatment of geriatric depression. No overall differences in the pattern of efficacy and safety were observed in the geriatric population relative to those reported in younger subjects.

NR763 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Efficacy of Risperidone in Behavioral and Psychological Symptoms of Dementia

Daniel Matusevich, M.D., *Department of Psychiatry, Italian Hospital, Lavalleja 1260, Buenos Aires 1414, Argentina*; Judith Szulik, M.D.

Summary:

Objective: The purpose of this trial was to assess the efficacy and safety of risperidone in the treatment of behavioral and psychological symptoms of dementia and the effects on caregiver's burden in institutionalized patients with dementia.

Methods: An open-label trial was designed for before-after comparison in patients with diagnosis of Alzheimer's disease, vascular dementia, or mixed dementia (according to DSM-IV) and significant behavioral and psychological symptoms. Treatment with risperidone, in doses ranging from 0.25 to 1.50 mg/day, lasted 16 weeks. Primary endpoints were Behavioral Pathology in Alzheimer's Disease rating scale (BEHAVE-AD) and a caregiver's burden questionnaire. Tolerability assessments were Mini-Mental State Examination (MMSE) and Webster Scale. These parameters were analyzed using Nonparametric Multicomparison Tests.

Results: Forty patients were enrolled, and 35 patients completed the study. On the BEHAVE-AD scale: mean scores for the symptomatic and global assessment showed a reduction from 19.9 and 3.6 at baseline to 2.3 and 0.4 at week 16, respectively ($p < 0.01$ for both tests). The caregiver's burden mean score was 51.8 at baseline and 26.0 and week 16 ($p < 0.01$). MMSE mean score was 11 at baseline and 12.1 and week 16 ($p < 0.05$). Adverse events included hypotension (17.5%), excessive sedation (2.5%), and drowsiness (2.5%).

Conclusions: It can be concluded that risperidone is effective and well tolerated in the studied population, improving caregiver's burden.

NR764 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Direct and Indirect Costs of Alzheimer's Disease: A Longitudinal Study

Micheline Dugue, M.D., *Department of Psychiatry, Mount Sinai, 1 Gustave Levy Place, Box 1230, New York, NY 10029*; Deborah B. Marin, M.D., James Schmeidler, Ph.D., Judith A. Neugroschl, M.D., Elizabeth Fine, C.S.W., Kenneth L. Davis, M.D.

Summary:

Introduction: This study investigated the longitudinal course of direct and indirect costs in a sample of community-dwelling Alzheimer's patients.

Methods: 44 patients who resided with caregivers were evaluated over a 1 1/2-year period. The direct costs that were assessed include physician visits, medication use, hospitalizations, institutionalization, and paid homecare. Indirect costs were assessed with the Caregiver Activity Survey, a five-item instrument that measures the amount of time a caregiver spends in daily tasks with the patient. Cognition and function were measured with the Mini Mental State Exam (MMSE) and Physical Self Maintenance Scale (PSMS).

Results: The average monthly direct and indirect costs totaled $638 and $3,065, respectively. Paid homecare and indirect costs were significantly correlated with MMSE and PSMS scores at baseline and subsequent study visits. In contrast, hospitalizations, physician visits, medication use, and institutionalization were not correlated with cognition or function at most study visits. These cross-sectional relationships between costs and illness severity were maintained in longitudinal analyses.

Conclusion: For outpatients with Alzheimer's disease, unpaid caregiving accounts for the majority of costs associated with the illness. Both unpaid and paid caregiving costs are significantly correlated with cognitive and functional impairment. Overall, paid homecare is the only direct cost that accounts for a substantial percentage of costs and correlates with illness severity.

Supported in part by National Institute of Aging grant #AG-O2219, and a grant from Novartis.

NR765 Thursday, May 10, 12:00 p.m.-2:00 p.m.

A Comparison of Urban and Suburban Geropsychiatric Patients

Indu C. Mirchandani, M.D., *Department of Psychiatry, UBHC C Level C66, 215 South Orange Avenue, Newark, NJ 07103*; Peter M. Aupperle, M.D., Kevin Chen, Ph.D., Saila B. Donepudi, M.D.

Summary:

Objective: We assessed presenting symptoms in ambulatory urban and suburban geriatric psychiatric patients to elicit any subcohort effect.

Method: We compared baseline self-reports of behavior and symptom questionnaire (Basis 32) of two groups of gero-psychiatric patients on admission to a suburban university-based clinic ($N = 257$) and urban university-based clinic. ($N = 209$).

Results: Females outnumbered males (3:1), 61% of the patients were under 75 years and 39% were 75 years and older. Suburban patients reported more difficulties in depression ($p < .10$) and anxiety ($p < .05$) than urban patients. The urban patients reported greater difficulty in confusion ($p < .05$) hearing voices ($p < .01$) and mood swings ($p < .05$). Further breakdown of the data by age groups showed that the urban-suburban difference in depression occurs mainly among the older group age 75+ ($p < .01$), but not as much among those aged 65–74; the difference in mood swings occurs mainly among those 65–74 ($p < .05$) but not among the older group. Among urban patients, those age 65–74 reported more problem in depression and anxiety than those aged 75+ ($p > .05$), while this age difference is not true among suburban patients.

Conclusion: There were significant differences between self-reports of suburban and urban patients, as well as differences between the younger and older age groups. These findings need to be further replicated in other clinical care systems serving geriatric patients.

NR766 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Reading Ability of Ideographic Irregular Words in Alzheimer's Patients

Yoshiharu Kim, M.D., *Adult Mental, NIMH-Japan, 1-7-3 Kohnodai, Ichikawa 2720-827, Japan*; Keiko Matsouka, M.A., Noriyoshi Takei, M.D., Hisanori Hiro, M.D., Yuki Yamamoto, M.D., Kumiko Fujita, M.D., Kuniaki Tanaka, M.D.

Summary:

Reading ability of irregular words has been confirmed to be well preserved in an English speaking sample of patients with mild phases of Alzheimer and other dementing diseases, upon which the National Adult Reading Test was invented to estimate the premorbid IQ level. Our aim is to validate this finding in the language with ideographic writing system that use Chinese "Kanji"

characters, which is adopted in Japan, China, and Korea, as well as by their immigrant cohorts in America and Europe. The Kanji is equivalent to English irregular words, as we have to memorize patterns of the ideographic figure and the way of pronunciation. We performed a reading test of 50 Kanji-compound words, selected according to the frequency of usage published by the National Institute of Language of Japan, with 55 Japanese DAT patients with mild or moderate severity and 41 normal elderly. Among DAT patient group, reading of Kanji-compound words in mild-DAT group were equivalent to that of normal controls, whereas IQ and six subtests of Wechsler Adult Intelligence Scale-Revised significantly declined. Moderate-DAT group showed lower reading and WAIS-R IQ. In conclusion, reading ability of Kanji-compound words was comparable with WAIS-R subtests in mild DAT patients.

NR767 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Delusional Thought and Frontal Cortex Metabolism in Alzheimer's Disease

David L. Sultzer, M.D., *Department of Psychiatry, University of California at Los Angeles, 3 South, 116AF, 11401 Wilshire Boulevard, Los Angeles, CA 90073*; Charles Brown, M.D., Mark Mandelkern, M.D., Stephen T. Chen, M.D., Michael E. Mahler, M.D., Jeffrey L. Cummings, M.D.

Summary:

Delusional thoughts are common in patients with Alzheimer's disease (AD) and contribute prominently to patient morbidity. The neurobiological factors involved in the expression of delusions in AD are not well understood, although functional activity in the frontal or temporal cortex has been implicated. We used fluorodeoxyglucose PET imaging to examine the relationship between regional cortical metabolism and severity of delusional thought.

Twenty-five patients with probable AD were studied (mean MMSE = 16.5). Severity of delusions was assessed using a semi-structured interview and the Neurobehavioral Rating Scale. Metabolic rates in frontal and temporal cortical regions of interest were derived from PET images.

The relationship between severity of delusions and regional cortical metabolism was examined using a stepwise multiple linear regression model that controlled for effects of cognitive impairment. The model demonstrated significant relationships with three frontal regions: the right lateral prefrontal cortex ($b = -3.68$; $p < 0.001$), the right inferior frontal pole ($b = -11.51$; $p = 0.001$, and the right lateral orbitofrontal cortex ($b = 8.45$; $p = 0.01$). The model r^2 was 0.81. Relationships were also examined using bivariate Spearman partial correlation coefficients, controlling for cognition. Relationships with metabolic activity in the right lateral prefrontal cortex ($r = -0.61$; $p = 0.002$) and right superior prefrontal cortex ($r = -0.59$; $p = 0.002$) were most robust. There were also significant relationships with other right prefrontal regions, some homologous left prefrontal regions, and the left anterior cingulate gyrus. Substantial relationships with temporal cortex metabolism were not apparent.

These results indicate that the severity of delusional thought in AD is associated with functional activity in specific prefrontal cortical regions, predominantly in the right hemisphere. Activity in the cingulate gyrus may also be relevant. Delusions are at least partly a reflection of the regional brain dysfunction of AD. (Supported by MH56031)

NR768 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Psychosis of Alzheimer's Disease: Validity and Response to Risperidone

Lon S. Schneider, M.D., *Department of Psychiatry, Univ. of Southern CA/ Keck School of Medicine, 1975 Zonal Avenue, KAM-400, Los Angeles, CA 90033*; Ira R. Katz, M.D., Sohel Park, M.S., Stanley Azen, Ph.D., Rick A. Martinez, M.D.

Summary:

Objective: The concept of "behavioral and psychological symptoms in dementia" has been criticized as a heterogeneous grouping of poorly defined, miscellaneous symptoms, and of unclear severity, clinical significance, duration, or natural history. The concept of psychosis of AD (Jeste and Finkel, 2000) has been advanced as a relatively homogeneous syndrome with potentially specific diagnostic criteria, and a potential target for a therapeutic drug claim (FDA, March 9, 2000). We sought evidence for its validity by examining a database of AD patients enrolled in a placebo-controlled, randomized trial of risperidone (Katz et al, 1999).

Method and Results: Of 625 patients enrolled, 463 were identified as most probably fulfilling criteria for psychosis of AD. Compared with the other patients who had psychotic symptoms ($n = 69$), and to those who did not ($n = 93$) during the screening period, patients with psychosis of AD were significantly more likely to be female, have much higher MMSE scores, and have much better ambulatory ability. Two-thirds of patients (treated with placebo) maintained psychosis criteria over the 12-week observation period. There was a clear and robust overall response to risperidone, 1 or 2 mg/d, especially with respect to aggressiveness.

Conclusion: These analyses provide evidence of the validity of psychosis of AD, its course, and the response of patients with psychosis of AD to antipsychotic treatment.

NR769 Thursday, May 10, 12:00 p.m.-2:00 p.m.

A Placebo-Controlled Study of Memantine in Advanced Alzheimer's Disease

Barry Reisberg, M.D., *Department of Psychiatry, New York University Medical School, 550 First Avenue, (THN 316), New York, NY 10016*; A. Stoeffler, M.D., Steven H. Ferris, Ph.D., Fred Schmitt, M.D., Rachelle S. Doody, M.D.

Summary:

Preclinical studies have shown that agents that block the pathological stimulation of the NMDA receptor can protect against glutamate-mediated neurotoxicity. Based upon these data, it has been hypothesized that memantine, an uncompetitive NMDA receptor antagonist, may be efficacious in the treatment of Alzheimer's disease (AD). Patients with advanced AD (Global Deterioration Scale stage 5 or 6, Functional Assessment Stage (FAST) ≥6a, and MMSE scores 3–14), were randomized to receive 28 weeks of either memantine 20mg/day ($n = 126$) or placebo ($n = 126$). Efficacy measures included the ADCS-Activities of Daily Living scale (ADCS-ADL), the NYU CIBIC-Plus, the Severe Impairment Battery (SIB), and the FAST. The mean MMSE score at Baseline was 7.9. At Week 28, the ADCS-ADL showed significantly less deterioration in memantine-treated patients compared with placebo (–2.49 compared with –5.86; $p = 0.003$). For the CIBIC-plus, a significant benefit was also observed in favor of memantine ($p = 0.025$). Evaluation of cognition using the SIB and the FAST also demonstrated significant benefits in favor of memantine ($p < 0.01$). Memantine treatment was safe and well tolerated. These results indicate that memantine is a safe and efficacious treatment for the functional, global, and cognitive deficits of advanced AD.

NR770 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Response to Rivastigmine Treatment in Key Domains of Alzheimer's Disease

Martin K. Farlow, M.D., *Department of Neurology, Indiana University, 550 University Boulevard, Room 3124, Indianapolis, IN 46202*; Ravi Anand, M.D., Richard Hartman, Ph.D.

Summary:

Objective: In Alzheimer's disease, response to drug therapy may not be the same across different symptom domains. Using a multi-domain responder analysis, we determined the proportion of AD patients who responded to rivastigmine treatment in cognition, activities of daily living (ADL), or global functioning.

Method: Patients participated in one of three double-blind trials comparing rivastigmine with placebo. Analyses were performed on the U.S. trial and pooled trials. Cognition, ADL, and global functioning were measured with ADAS-Cog, PDS, and CIBIC-Plus, respectively. For this analysis, significant clinical improvement from baseline was defined as either ADAS-Cog≥4-points, PDS≥10% improvement, or CIBIC-Plus <4. Stabilization of disease was defined as ADAS-Cog≥0-points, PDS≥0% improvement, or CIBIC-Plus<5.

Results: For the U.S. study (6–12 mg/d), clinically significant differences were observed in 25% for ADAS-Cog, 24% for CIBIC-Plus, and 26% for PDS. Overall, 54% demonstrated a clinically significant improvement in ≥1 domain. At Week 26, stabilization was observed in 52% on ADAS-Cog, 60% on CIBIC-Plus, 45% on PDS, and 90% showed stabilization in ≥1 domain. Results from the pooled analysis were similar.

Conclusions: Patients respond to rivastigmine in different symptom domains. Since benefits in different domains appear substantially independent of each other, an overall rating of efficacy should take into account all domains.

This study was sponsored by Novartis Pharmaceuticals Corporation.

NR771 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Memantine Enhances Ischemic Tolerance

Chris Parsons, Ph.D., *Department of Research and Development, Merz and Company, Eckenheimer Landstrasse 101-104, Frankfurt/Main, Germany*; Tadeusz Frankiewicz, Jerzy Lazarewicz, Roman Gadamski

Summary:

Memantine, an NMDA antagonist used in Germany for treating dementia, has been shown in clinical trials to have efficacy for both Alzheimer's disease and vascular dementia, both of which share a vascular component and involve excitotoxic pathology. Ischemic tolerance (decreased susceptibility to a subsequent ischemic/hypoxic insult following a short ischemic/hypoxic episode) might be an endogenous neuroprotective mechanism in both dementia types. Rat hippocampal slices were perfused with glucose free, deoxygenated media for 7 min to evoke hypoxia/hypoglycemia. Averaged responses (CA1 fEPSP peak) 31–60 min following the reintroduction of oxygen and glucose were normalized with respect to the 30-min control period. Ischemic tolerance in anesthetized Mongolian gerbils *in vivo* was induced by 2 min common carotid artery occlusion 48 hours prior to 3 min of forebrain ischemia. 3-NP (20 mg/kg i.p.) 24 h prior to the *in vitro* experiment significantly protected against hypoxia/hypoglycemia-induced suppression of fEPSPs (67.2% [SD = 12.2] versus 16.8% [SD = 9.4] in control subjects). Additional 3 days pretreatment with memantine (20 mg/kg/day i.p.) significantly improved recovery still further (89.7% [SD = 7.2]). *In vivo* results will be presented at the conference. Thus, memantine at therapeutically relevant brain concentrations increases the neuroprotective effect of ischemic tolerance.

NR772 Thursday, May 10, 12:00 p.m.-2:00 p.m.

The Effects of Ziprasidone on Cholesterol, Triglycerides, and Glucose

Steven J. Kingsbury, M.D., *Department of Psychiatry, University of Southern California, 2020 Zonal Avenue, Los Angeles, CA 90033*; Mohamed H. Fayek, M.D., Dorina Trufasiu, M.D., Jafaar Zada, M.D., George M. Simpson, M.D.

Summary:

Objective: Increasing concern about the effects of the atypical antipsychotics on various health indices necessitates the examination of other new atypical antipsychotics. We examined the effects of ziprasidone on body mass index (BMI), glucose, cholesterol, and triglycerides.

Method: As part of a multicenter study examining different strategies for switching to ziprasidone from other antipsychotics, we evaluated weight, glucose, cholesterol, and triglyceride measurements at baseline and following 6 weeks of ziprasidone treatment in 37 patients at our site.

Results: Short-term treatment with ziprasidone led to significant reduction in cholesterol and triglyceride levels independent of changes in BMI. Ziprasidone treatment had no significant effect on BMI or glucose, perhaps due to the small number of subjects.

Conclusions: Ziprasidone appears to independently lead to a lowering of serum lipid levels. Limitations of this study are discussed.

NR773 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Comparison of Depressive Symptoms Among Depressed Caucasian, Hispanic, and Asian-American Patients in the Primary Care Setting

Albert Yeung, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WACC 812, Boston, MA 02114*; Megan M. Smith, B.A., Andrea H. Sickinger, B.A., Dan V. Iosifescu, M.D., Shamsah B. Sonawalla, M.D., Jonathan E. Alpert, M.D., Maurizio Fava, M.D., David Mischoulon, M.D.

Summary:

Objective: To investigate whether depressed Caucasian, Hispanic, and Asian-American patients in the primary care setting differ in regard to depressive symptoms.

Method: Patients with major depressive disorder (MDD) were recruited from the primary care clinics of two community healthy centers in Boston serving predominantly minority populations. Patients in the waiting areas of the primary care clinics were screened for MDD using the Beck Depression Inventory (BDI). Patients who screened positive (BDI ≥ 16) were interviewed by a psychiatrist using the Structured Clinical Interview for DSM-IV-patient version (SCID-I/P). The scores on each of the 21 BDI items for the depressed Caucasian, Hispanic, and Asian-American patients were compared using ANPVA and linear regression analyses.

Results: A total of 1,378 patients in the primary care clinics of the two community centers were screened for depression and 80 patients with MDD were recruited. There were nine (11%) Caucasians, 27 (34%) Hispanics, 41 (51%) Asian-Americans, and three (4%) classified as "other ethnicity." The average scores of most BDI items were comparable among the Caucasian, Hispanic, and Asian-American patients. We found that, after controlling for possible confounding effects of age, BDI score, and gender, Caucasian patients scored higher than Hispanic patients on guilt feelings (item 7) and Hispanic patients scored higher than Asian-American patients on appetite loss (item 18).

Conclusion: Caucasian, Hispanic, and Asian-American patients with MDD in the primary care setting have similar depressive symptoms and a few differences among the three groups.

NR774 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Nightmare of Refugees from Kurdistan

Zachias Cernovsky, Ph.D., *Department of Psychiatry, University of Western Ontario, 98 Greembrier Crescent, London, ON N6J*

3X9, Canada; Mariwan Husni, M.D., Narmen Koye, M.D., John M. Haggarty, M.D.

Summary:

Objective: Recurrent nightmares are an important diagnostic marker in the assessment of PTSD. We assessed the frequency of escape-related nightmares in refugees from Kurdistan.

Method: Fifty-four Kurd refugees (36 men and 18 women) were interviewed about their nightmares about escaping from Kurdistan or oppression in Kurdistan.

Results: Only six (11.1%) reported recalling no nightmares on these topics. When questioned about the frequency of these nightmares in the last six months, the majority of the Kurd refugees (30, i.e., 55.6%) reported dreaming almost daily. The frequency of these nightmares was inversely correlated to the number of years since the escape from Kurdistan ($r = .49$, $p < .001$) and to the overall satisfaction with life in the host country ($r = .44$, $p = .002$): those who arrived more recently and those less satisfied with the host country reported more frequent nightmares.

Conclusions: Almost all participants had the refugee nightmares, the majority on a daily basis, and their frequency appears to decrease with the number of years since escape.

NR775 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Relationship of Irritable Bowel Syndrome and Major Depression in Mumbai, India

Sumit Sharma, M.D., *Department of Psychiatry, SUNY-UMU, 750 East Adams Street, c/o P. Masand, Syracuse, NY 13210*; Charles Pinto, M.D., Subhdeep Virk, M.D., Sanjay Gupta, M.D., Nikhil Nihalani, M.D., David E. Kaplan, M.D., Prakash S. Masand, M.D.

Summary:

Irritable bowel syndrome (IBS) has been reported in 10–20% of adults. Among patients seeking medical attention for IBS, 70-90% may have psychiatric comorbidity, most commonly major depression. In contrast, few studies have looked at the prevalence of IBS in psychiatric patients. Using a semistructured clinical interview, we studied the prevalence of IBS among panic disorder patients in Mumbai, India. We compared 50 patients seeking treatment for major depression in a psychiatric outpatient setting to a control group of 86 patients who were seeking treatment for medical illnesses in a medicine inpatient unit of Nair Hospital (a university hospital affiliated to T.N. Medical College) in Mumbai, India. Patients in the control group did not have any axis I disorder. IBS was diagnosed according to the criteria of Drossman et al. Nine patients (18.0%) with major depression met the criteria for IBS, in contrast to three patients (3.5%) in the control group ($p = 0.0104$). In a similar study in U.S. patients with major depression, the prevalence of IBS was 27% versus 2.5% patients in the control group ($p < 0.00005$). Prospective studies should address the question whether treatment of depression leads to an improvement or resolution of the symptoms of IBS.

NR776 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Seafood Consumption and Bipolar and Anxiety Disorder Prevalence Rates

Simona F. Noaghiul, M.D., *CGEU, Columbia University, 1051 Riverside Drive, Unit 24, New York, NY 10032*; Joseph R. Hibbeln, M.D., Myrna M. Weissman, Ph.D.

Summary:

Background: Omega-3 and omega-6 essential fatty acids are crucial components of synaptic cell membranes, yet are available only from dietary sources, such as seafood. Prior cross-national studies have described a robust relationship between higher seafood consumption and lower prevalence rates of major depression and postpartum depression. An effective treatment response to omega-3s has been reported in bipolar patients. We predicted that greater seafood consumption would predict lower prevalence rates of bipolar disorder.

Methods: In 10 countries, epidemiological data were identified that quantified prevalence rates of bipolar disorder using structured interviews for diagnosis, population sampling methods, and standardization for demographic variables. Similar prevalence data were identified for anxiety disorders among 12 countries. These prevalence data were compared to measures of seafood consumption (disappearance of seafood from economy, calculated as total catch plus imports minus exports), using simple nonlinear regression models.

Results: Greater seafood consumption rates predicted lower rates of bipolar I ($r = -0.55$, $p = 0.06$), bipolar II ($r = -0.75$, $p = 0.02$), and bipolar spectrum disorders ($r = -0.67$, $p = 0.02$), with an apparent threshold for increased vulnerability below 50–75 lbs of (seafood per person per year). There was no relationship between prevalence rates of anxiety disorders and seafood consumption ($r = -0.6$, $p =$ n.s.), suggesting a specific relationship to affective disorders.

Conclusion: We conclude that the epidemiological data are consistent with the hypothesis of an inverse relationship between greater seafood consumption and lower prevalence rates of bipolar disorder.

NR777 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Childhood Socioeconomic Status and the Lifetime Risk of Major Depression

Stephen E. Gilman, S.M., *Department of Health & Social Behavior, Harvard University, 677 Huntington Avenue, Boston, MA 02115*; Ichiro Kawachi, M.D., Garrett Fitzmaurice, Ph.D., Stephen L. Buka, Sc.D.

Summary:

Background: Major depression is persistently associated with lower socioeconomic status (SES). This association may be due to the adverse consequences of low SES or to the downward socioeconomic drift of depressed individuals or both. Longitudinal studies are needed to evaluate these hypotheses.

Design: We interviewed 1,150 of the 4,140 births enrolled in the Providence (Rhode Island) site of the National Collaborative Perinatal Project between ages 17 to 39. We used multivariate discrete-time survival analysis to estimate the risk that childhood SES, indexed by parental occupation at birth and age 7, conferred on the incidence of DSM-III and DSM-IV major depression.

Results: Analyses revealed a significantly higher risk of depression among participants from lower SES backgrounds. The adjusted odds ratio indicating the increased risk of depression among participants from lower SES categories relative to the highest SES category was 1.91 (95% CI = 1.33-2.75). The risk of depression associated with low childhood SES was more pronounced among females than males. Moreover, stratified analyses revealed that adult gender differences in depression existed only among individuals from low SES backgrounds.

Conclusions: Childhood socioeconomic conditions contribute to socioeconomic and gender differences in depression.

NR778 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Determinants of Perceived Need for Mental Health Care in the Australian Community

Graham N. Meadows, M.D., *Department of Psychiatry, University of Melbourne, Royal Park Campus, Private Bag 3, Post Office, Parkville, VC 3052, Australia*; Philip Burgess, Carol Harvey, M.D., Irene Bobevski, Siaw-Teng Liaw, Ellie Fossey

Summary:

Objective: To ascertain the influences of diagnosis, demographic variables, and disability on perceived need for mental health care, including perceived need for specific interventions.

Method: We report findings from a Federal Government-funded, national community survey of mental health problems in Australia, employing clustered probability sampling, with a response rate of 78.2% and a final sample size of 10,641 individuals. Diagnosis was assessed with sections of the Composite International Diagnostic Interview. Perceived need for mental health care, including specific items regarding information, medication, counseling, social interventions, and skills training, was assessed with the Perceived Need for Care Questionnaire (1).

Results: The overall rate of perceived need, previously reported (2), was 13.8%. In this report we present data showing that this rate was greater in female (16.5%) than in male (10.4%) subjects.

Among all subjects with disorders, the rate of perceived need was 61.1% (affective disorders = 83.3%, anxiety disorders = 66.8%, and substance misuse disorders = 47.4%). Disability increased all perceived needs. Age effects included relatively reduced perceived need for medication and counseling in young adults and reduced perceived need for all interventions except medication in the elderly.

Conclusions: Perceptions of need for mental health care are substantially influenced by diagnosis and disability and also by demographic variables.

NR779 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Epidemiology of Adverse Childhood Experiences and Depressive Disorders

Daniel P. Chapman, Ph.D., *Health and Aging Branch, CDC, 4770 Buford Highway NE, MS K45, Atlanta, GA 30341*; Robert F. Anda, M.D.

Summary:

Childhood physical abuse, sexual abuse, and emotional abuse have been associated with increases in both the prevalence of psychiatric disorders and the length of stay among patients hospitalized with depression. Although the different types of childhood abuse commonly cooccur, previous research has been largely restricted to assessment of individual types of abuse. Moreover, the relevance of childhood observation of maternal battery to the etiology of depressive disorders has also not been examined in previous research, despite prior investigations indicating between 30% to 59% of mothers of abused children are also battered. To better examine the association between childhood abuse and depressive disorders, we analyzed data from the Adverse Childhood Experiences (ACE) Study, a retrospective cohort investigation of San Diego Kaiser Permanente patients receiving standardized medical evaluations (n = 9,346). Using standardized interviews, respondents reported their lifetime and recent histories of depression, as well as their childhood exposure to seven ACEs—including observation of maternal battery—assessing abuse and household dysfunction. A total of 23.1% and 10.9% of respondents reported a history of lifetime and recent depression, respectively; of these, 60% reported at least one ACE and 39% reported >2 ACEs. Each type of ACE was associated with increased odds of depression and, when cooccurent, assumed a dose-response relationship ($p < .0001$). These findings suggest that individuals reporting childhood abuse are at increased odds for depression and that experiencing multiple forms of child abuse appears to be particularly predictive of depressive disorders.

NR780 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Disability, Health Status, and Depressive Disorders in Women

Daniel P. Chapman, Ph.D., *Health and Aging Branch, CDC, 4770 Buford Highway NE, MS K45, Atlanta, GA 30341*; Vincent A. Campbell, Ph.D.

Summary:

Prior assessments of the relationship between disability and depression among women have not examined the potentially mediating role of health status to the increased prevalence of depressive disorders in this population. In this investigation, data were analyzed from the National Health Interview Survey on Disability, Phase I, a probability sample household survey of health status in the U.S. civilian noninstitutionalized population (n = 41,012 women). Respondents were categorized as either unable to perform the major activity for their age group (i.e., attend school, work, keep house), limited in their major activity, limited in other activities (i.e., recreation, visiting friends, attending worship services), or as having no limitation. Respondents were asked if they frequently felt depressed or anxious; those who reported they had experienced depressed mood and loss of interest in almost all activities for at least two weeks in the preceding year were categorized as having experienced major depression. Respondents whose reported activity limitations were caused by a mental disorder were removed from the analysis. A significant positive association was observed between degree of disability and major depression. When health status variables were entered into the model, the relationship between disability and major depression was reduced, but remained statistically significant. These findings suggest that as depression cannot solely be attributed to health status among disabled women, the presence and severity of activity limitation remains a potentially important indicator of depressive disorders in women.

NR781 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Determinants of Depression in Adult Women: Data from National Health Interview Survey, Disability Supplement, Phase I (NHIS-D1)

Vincent A. Campbell, Ph.D., *Environmental Health Department, CDC, 4770 Buford Highway, NE, F-35, Atlanta, GA 30341*; Daniel P. Chapman, Ph.D.

Summary:

Data from the 1994 National Health Interview Survey, Disability Supplement, Phase I (NHIS-D1), were subjected to logistic regression analysis to determine the relative contribution of selected independent variables to reports of frequent depression/anxiety or severe depression among adult women. The sample for this analysis included 33,876 respondents. The seven independent variables were age group (18–44, 45–64, 65–80, 80+ years), race, marital status, family income, employment status, degree of activity limitation (i.e., disability), and health status. Because of the complex, multistage cluster sampling design of the NHIS-DI, SUDAAN was employed to analyze the data. Results indicated that the seven-variable model accounted for 7.4% of the variance in the occurrence of frequent depression/anxiety and 2.3% of the variance in the occurrence of severe depression. All of the explanatory variables reached significance in both models; however, their relative importance differed for the two categories of depression with health status, disability, marital status, and employment status contributing most to the occurrence of frequent depression/anxiety and age group, health status, disability status, and race contributing most to the occurrence of severe depression.

This presentation is designed for mental health epidemiologists and researchers.

NR782 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Seafood, DHA in Breast Milk, and Prevalence Rates of Postpartum Depression

Joseph R. Hibbeln, M.D., *LMBB, NIAAA/NIH, 12420 Parklawn Drive, MSC 8115, Rockville, MD 20852*

Summary:

Mothers selectively transfer the omega-3 fatty aciddocosahexaenoic acid to their fetuses to support optimal neurological development during pregnancy. Without sufficient dietary intake, mothers become depleted of DHA and may increase their risk of suffering a postpartum depression. We predicted that the DHA content of mothers' milk and seafood intake would both predict rates of postpartum depression accross countries.

Results: Higher concentrations of DHA in mothers' milk ($r = -0.84$, $p = 0.0001$ n = 16 countries) and greater seafood consumption ($r = -0.81$, $p = 0.0004$, n = 22 countries) both predicted lower prevalence rates of postpartum depression. AA content of mothers' milk was not predictive. These findings were not significantly altered by the exclusion of Asian countries or after examination of potentially confounding factors including study time postpartum, low socioeconomic status, presence of a partner, young maternal age, or educational status.

Conclusions: Both lower DHA content of mothers' milk and lower seafood comsumption appear to be associated with higher rates of postpartum depression. These results do not appear to be an artifact of cross-national differences in well-established risk factors for postpartum depression. These data do not demonstrate a causal relationship.

NR783 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Mental Disorders and Homicidal Behavior in Adolescents

Kari Toivonen, M.D., *Vanha Vaasa Hospital, P B 13, Vaasa 65381, Finland*; Markku E.J. Eronen, M.D.

Summary:

Objective: Homicide is of interest not only because of its severity but also because it is a fairly reliable barometer of all violent crimes. Although schizophrenia, antisocial personality disorder, and alcohol abuse/dependence appear to have a statistically significant relationship with homicidal behavior in adult population, there are very few quantitative epidemiological studies concerning adolescent homicidal behavior. This study examines the association between some specific DSM III-R/DSM-IV disorders and adolescent homicidal behavior.

Methods: In Finland, where the homicide solving rate during recent decades has been almost 95%, most homicide offenders are subjected to an intensive forensic psychiatric examination. The author reviewed forensic psychiatric examination reports of 200 adolescent (under 23 yrs) homicide offenders over a 13-year period (January 1987-December 1999).

Results: Adolescent homicide offenders had about 10-fold higher odds ratio than the control group for having schizophrenia. The disorders with the most substantially higher odds ratios were alcohol abuse/dependence and antisocial personality disorder.

Conclusions: These preliminary findings suggest that mental disorders appear to have a statistically significant relationship with adolescent homicidal behavior.

NR784 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Epidemiological Study of Mental Illness of Urban Homeless People in Korea

Oh-Su Han, M.D., *Department of Psychiatry, Asan Medical Center, Seoul, Korea*; Jong I. Park, M.D., Jun-Ho Ahn, M.D., Jin Pyo Hong, M.D., Maeng-Jae Cho, M.D., Chang-Yoon Kim, M.D.

Summary:

Objective: The purpose of the study was to capture the overall picture of mental disorders in homeless people after the economic crisis in Korea.

Method: Four hundred thirty-three homeless people who stayed at three shelters were interviewed using Structured Clinical Interview for DSM-IV Axis I Disorders (SCID) after completing questionnaires on sociodemographic data. The lifetime and current prevalence of major mental disorders in this study were compared to those from other studies in the Korean general population and in foreign homeless people.

Results: Nearly 69% reported having been homeless for 1 year or less. The mean length of time of homelessness for all respondents was 11 months. The lifetime prevalences of major depressive disorder and bipolar disorder were 26.8% and 0.5%. And those of schizophrenia, psychotic disorder NOS, schizoaffective disorder, and substance-induced psychotic disorder were 2.1%, 0.7%, 0.2%, and 0.7%, respectively. Fifty-three percent of our respondents were diagnosed with alcohol dependence or abuse. The lifetime and current prevalences of major mental disorders were 67.0% and 47.6%, respectively.

Conclusions: Alcoholism was the most prevalent mental disorder in homeless people. The proportion of psychotic disorder in our respondents seems to be low compared to that of a foreign study. The main cause of sudden increasing homelessness was closely linked to economic difficulties, especially the financial crisis in Korea.

NR785 Thursday, May 10, 12:00 p.m.-2:00 p.m.

High-Resolution Brain SPECT Imaging in ADHD Using Statistical Parametric Mapping (SPM)

Isaac Hwang, M.D., *Department of Psychiatry, A Jou University School of Medicine, 5 Wonchon-dong, Paladal-gu, Suwon, Kyunggi-do 442721, South Korea*; Eun Young Oh, M.D., Young-Ki Chung, M.D., Suk Nam Yoon, M.D., Chan-Hee Park, M.D., Ji-Sun Jang

Summary:

Objectives: We examined the abnormalities of regional cerebral blood flow(rCBF) in children with attention deficit hyperactivity disorder(ADHD) without comorbidity and ADHD with chronic tic disorder using statistical parametric mapping(SPM)method.

Method: Tc- 99mECD brain SPECT was performed on 85 patients (M:F = 72:13, 10.03+2.5y) with the DSM-IV diagnosis of ADHD and seven normal control group (M:F = 6:1, 10.29+4.1y). ADHD group are divided into two groups: one is ADHD patients without comorbidity (M:F = 50:10, 10.35+2.6y), another is ADHD patients with chronic tic disorder(M:F = 22:3, 9.89+2.29y). Using SPM methods, we compared individual and patient group's SPECTs with those of the seven control subjects and measured extent of the area with significant hypoperfusion($p < 0.01$) in predefined 34 cerebral regions.

Results: (1) Left temporal area and left orbitofrontal area showed significantly hypoperfusion in total ADHD patients(n = 85) as compared with control subjects(n = 7)($p < 0.01$). (2) Only the left temporal area showed significantly hypoperfusion in ADHD patients without comorbidity (n = 60) as compared with control subjects(n = 7) (3) Left temporal area, left parietal area, left orbitofrontal area, and both basal ganglia showed significantly decreased rCBF in ADHD patients with chronic tic disorder (n = 35) as compared with control subjects(n = 7)

Conclusion: Left temporal area rCBF was decreased in ADHD group whether subjects have comorbidity or not, as compared

with control groups. According to this result, the left temporal dysfunction may mediate ADHD symptoms in children.

NR786 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Prevalence of Cardiovascular Disease Comorbidities and Risk Factors in Severe and Persistently Mentally Ill Patients

Terrance J. Bellnier, M.P.A., *Pharmacy Department, University of New York at Buffalo, 36 Forest Meadow Trail, Rochester, NY 14624*; Anthony H. Labrum, M.D., Kashinath B. Patil, M.D., Tulio R. Ortega, M.D., Shyam D. Karki, Ph.D., Adam Decatur, Ph.D.

Summary:

Objective: The severe and persistently mentally ill population has not been extensively studied concerning comorbidities and physical and behavioral risk factors of cardiovascular disease. We propose to determine the prevalence of these comorbidities and risk factors in this population.

Method: We conducted a chart review of all adult inpatients (N = 179) of a state psychiatric hospital during July and August 2000. All subjects had a medical history, physical exam, screening blood tests, and an ECG. The prevalence of cardiovascular disease in our population was compared to a control group matched for age and sex.

Results:

Subject Characteristics: Meanage-47 years, SD-16; 113 were male; 29% African were American, and 10% were Hispanic.

Cardiovascular Disease Comorbidities: ECG abnormalities: 40%; hypertension: 15%; Diabetes: 10%; thyroid dysfunction: 7%; and CAD: 6%.

Physical and Behavioral Risk Factors: 69% were overweight (BMI ≥ 25), 38% were obese (BMI ≥ 30), 18% had hyperlipidemia, 67% had nicotine abuse, 49% had alcohol abuse, and 35% were chemically addicted.

Conclusion: 49% had cardiovascular disease comorbidities. 62% had multiple behavioral and physical risk factors for developing cardiovascular disease in their life time. The sample size limits our ability to make population inferences, yet an association between severe and persistently mentally ill patients and a increased risk for cardiovascular disease exists in our group ($t = -8.101$, $df = 356$, $p < 0.00001$).

NR787 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Use of MDMA by Young Males in Spain

Maria P. Gonzalez, Ph.D., *Department of Psychiatry, Oviedo University, Julian Claveria 6, # 3, Oviedo 33006, Spain*; Pilar A. Saiz, Ph.D., Begona Paredes, M.D., Sara Martinez, M.D., Aranzazu Sanchez, M.D., Teresa Bascaran, M.D., Julio B. Bobes, Ph.D.

Summary:

Objectives: To measure the prevalence of MDMA use and determine the psychological profile of MDMA users.

Subjects / Method: WHO Drug Consumption Questionnaire, EPQ-A, Zuckerman Sensation Seeking Scale were administered to 3,634 conscripts [mean age (SD) = 20.19 (2.52)] who entered military service between 1995–99.

Results: Prevalence of MDMA use—lifetime: 10.9%, previous year: 7.8%, previous month: 4.5%. When individuals used MDMA for the first time, they were likely to use it again (71% of individuals who had ever used MDMA had used it in the past year, 41% the last month). The mean rate of illegal drug consumption is higher in MDMA users [5.15 (2.54) vs 1.74 (1.31), p = .000]. Recruits who had used MDMA during the previous year had significantly higher scores on the EPQ-Neuroticism [12.88 (5.71) vs 12.03 (5.80), p = .000] and EPQ-Psychoticism [7.15 (4.44) vs 5.21 (3.61), p = .000], and reported higher levels of sensation seeking [TAS: 7.04 (2.46) vs 6.95 (2.51); ES: 6.54 (1.70) vs 5.79 (1.77); DIS: 8.03 (1.72) vs 7.55 (1.77); BS: 5.71 (2.03) vs (5.24); Overall score: 27.29 (5.40) vs 25.50 (5.56); All cases: p = .000].

Conclusions: Differences in personality and sensation seeking between MDMA users and non-MDMA users could potentially reflect MDMA-induced brain serotonin injury.

NR788 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Improving Informed Consent for Psychiatric Inpatients to Participate in Research

Russell Omens, Psy.D., *Department of Psychiatry, University of IL at Chicago, 1601 West Taylor Street, M/C 912, Chicago, IL 60612*; Philip G. Janicak, M.D., Boris M. Astrachan, M.D., Cherise Rosen, M.A., Rajiv P. Sharma, M.D., Martin Harrow, Ph.D., Sheila Donovan, C.S.W.

Summary:

Objective: The ability for acutely ill psychiatric patients to give meaningful informed consent is an ethical issue underpinning all psychiatric research. Recently, there has been increased attention to protecting the rights of psychiatric patients in terms of ensuring they understand protocols for which they volunteer. This study seeks to determine how well patients understand their role in research and whether intensive education will improve the informed consent process.

Method: 20 psychiatric research inpatient patients with a diagnosis of either a major affective or psychotic disorder were assessed using the MacArthur Competence Assessment Tool for Clinical Research (at baseline, during medication washout, and when clinically stable) in addition to standardized instruments (i.e., PANSS and GAS). Subjects were selected if they were clinically assessed as able to give informed consent and agreeing to participate in an independent research study (study A). Consent was obtained after a detailed review of that study's procedures. Subjects were then randomly assigned to two different weekly groups: a general education group and a specific education that focused on details of study A procedures only. At every administration of the MacArthur CAT-CR, study A procedures were reviewed with both groups.

Results: Data indicate clinical improvement in both groups from baseline to final ratings (i.e., PANSS and GAS). There was a significant correlation between clinical status (GAS) and reasoning ($r = 0.84$). Analyses also revealed a trend for increased understanding and appreciation of study A in the specific as compared to the general education group. There were no differences in the understanding of 'general research procedures' between groups.

Conclusions: These early results should be verified with a larger sample size but suggest that repeated review of a specific study improves patients' consent-giving ability.

NR789 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Comparing Patient, Family, and Staff Views Regarding Forced Admission and Treatment

Wilson M. Lit, M.D., *Community Division, Homewood Health Center, 150 Delhi Street, Guelph, ON N1E 6K9, Canada*; Steve S. Abdool, M.A., Diane K. Whitney, M.D., Noreen Stuckless, Ph.D.

Summary:

Objective: To compare patients' attitudes with those of their family and staff members concerning involuntary admission, restraint, forced treatment, insight, trust, dignity, and treatment compliance.

Methods: Questionnaire surveys, which included 34 Likert-scored items and four open-ended qualitative items, were adminis-

tered to lucid, adult certified patients within 72 hours of admission as well as to significant others and staff members. Data synthesis included description of demographical information, analysis of the reliability of the scale being used, statistical inferential assessment, and qualitative scrutiny of open-ended questions. To date, the study has included 50 patients, 35 significant others, and 19 staff at two large psychiatric facilities in Canada.

Results: Preliminary results show that, as compared with family and staff responses, patients were significantly more likely to believe that they had control over their thoughts and actions, were able to care for themselves, and were much less likely to believe their wishes should be overridden. Staff viewed themselves as more empathetic and helpful than patients did. Family were substantially more likely to believe that mental illness caused the patient's condition, that the illness affected their decision-making ability, and that patients needed treatments other than medication to help them feel better.

Conclusions: The results from this study will provide stakeholders with the necessary information to collaboratively develop a decision-making process that would enhance the continuity of care for patients, thus ensuring respect for patients' rights, dignity, optimal care, and fiscal responsibility. The researchers gratefully acknowledge the generous grant from the Homewood Health Centre Foundation for the pilot phase of this study.

NR790 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Rearrest: Does HIV Serostatus Make a Difference?

Victoria L. Harris, M.D., *University of Washington, 901 Boren, Suite 1100, Seattle, WA 98104*; Karina K. Uldall, M.D.

Summary:

It is clear that correctional facilities have become collection and containment centers for HIV seropositive individuals. This is likely due to factors that affect incarceration in general: past criminal behavior, age, and crime type. In addition, the sex-trade industry, intravenous drug use, and community instability are likely factors affecting this particular population. The objective of this study was to determine whether HIV seropositive offenders had higher rates of rearrest than HIV seronegative offenders.

Methods: A sample of HIV seropositive offenders (N = 57) was seen for mental health evaluation at the King County Correctional Facility (KCCF) in Seattle, Washington. They were compared to a historical sample (N = 254) of HIV seronegative individuals also from the KCCF.

Results: The 57 HIV seropositive individuals were predominately male and between the ages of 30–39 years. Unemployment was common (63%), as was a previous history of incarceration at KCCF (89%). After 3 months, 50% of both the seropositive and seronegative samples had been rearrested. Using the log rank test in Kaplan-Meier survival analysis, statistical difference in the relative risk of rearrest occurred for the HIV seropositive group (log rank = 0.03). Statistical adjustment for mental illness, age, race, ethnicity, substance abuse history, and past criminal history did not affect rearrest significantly.

Conclusions: HIV seropositive individuals who presented with mental health needs appeared to be significantly more vulnerable to rearrest after the first 3 months of release into the community. This work is of particular interest to community and correctional psychiatrists.

Acknowledgements: This work was generously supported by the HIV/AIDS Bureau, Health Resources and Services Administration, Special Projects of National Significance, Grant # 6H97 00052-03 1R1.

NR791 Thursday, May 10, 12:00 p.m.-2:00 p.m.

First-Episode Homicide: A Diagnostic Challenge

Dominique Bourget, M.D., *Department of Psychiatry, Royal Ottawa Hospital, 1145 Carling, Ottawa, ON K1Z 7K4, Canada*; Alain Labelle, M.D., Pierre W. Gagne, M.D., Pierre Tessier

Summary:

Objective: In recent years, the concept of first-episode psychosis has emerged in an attempt to improve the prognosis of patients diagnosed with psychotic illnesses. This concept promotes the early detection of psychosis and early interventions in order to reduce the harm associated with untreated psychosis. Although the concept of first-episode psychosis has become popular, its association with violence, and specifically homicidal violence, is not well understood.

Method: This descriptive study reviews a series of 15 cases of murderers who have been diagnosed after the act with a first psychotic episode. A variety of demographic, clinical, and event-related variables were collected for descriptive analysis. DSM-IV criteria were used.

Results: The majority were charged with the killing of a close relative. All cases presented with an insidious onset of their psychotic illness, and most had gone unrecognized until their murderous acting out. A schizophrenic process was present.

Conclusions: The homicidal behavior may represent a distinct expression of the illness. In several instances, the homicidal behavior was found to be a useful indicator to determine more accurately the nature of the psychotic illness. The authors will discuss the relevant clinical indicators and the complexity of diagnostic issues in a forensic context.

NR792 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Performance of Professionals in Court as a Predictor of Outcome: Preliminary Data

Jagannathan Srinivasaraghavan, M.D., *Department of Psychiatry, Southern Illinois University, Choate Mental Health Center, Anna, IL 62906*; Alan R. Felthous, M.D., Wenona Whitfield, J.D., Sarah Andrew, Ph.D., Nancy Watkins, B.S.

Summary:

Objective: To test the hypothesis that ratings of 1) the quality of testimony of the psychiatrist and 2) performance of both the state's attorney and public defender can differentiate between cases where the petition for administration of psychotropic medications over objection was granted or denied.

Subjects: From 1991 to 1999, in Southern Illinois, there were 17 denials and 109 granting of petitions for administration of psychotropic medications. This preliminary study involved transcripts of randomly selected six denials and eight granted petitions.

Method: From the court transcripts, any reference to final decision was deleted. An academic forensic psychiatrist and a law professor rated the content and process of psychiatric testimony and performance of legal professionals, respectively, on a scale of one to four (poor, fair, good, and excellent).

Results: Mean rating of the performance of the psychiatrist, state's attorney, and defense attorney for granted and denied petitions were noted. There were six psychiatrists, four state's attorneys, two defense attorneys, and one judge involved.

Analysis: While the Hotelling T square did not reach significance, 13 of the 14 cases were correctly classified. Ratings of all psychiatrist variables were significantly inversely correlated correlated with ratings of all defense attorney variables.

Conclusion: Co-efficient of the linear discriminant function suggests that the most important variable for discriminating between the two groups was the rating of overall performance of the psychiatrist.

NR793 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Malingering and Dissimulation in Forensic Evaluations

Keith A. Caruso, M.D., *Department of Forensics, Treadway Clinic, 113 Seaboard Lane, Suite C-150, Franklin, TN 37067*; David Benedek, M.D., Pamela Auble, William Bernet, M.D.

Summary:

Dissimulation is the concealment of genuine psychiatric symptoms in an attempt to present a picture of psychiatric health. In this pilot study, we set out to demonstrate that defendants may conceal psychiatric illness even in forensic settings, contrary to their apparent self-interest.

Methods: We reviewed our records for forensic assessments of dissimulators and malingerers. We classified dissimulators as "intentional" or "defensive" depending on whether their concealment of symptoms appeared to be a volitional act or an unconscious defense driven by a lack of insight.

Results: Although there were obvious diagnostic differences, the only other significant difference between malingerers and dissimulators was that malingerers were more likely to be facing charges involving financial crimes ($x^2 = 4.22$, df = 1). Defensive dissimulators were significantly older (41.2 ± 1.3 vs. 33.8 ± 3.3 yr., $t = 4.93$ $p < 0.01$ df = 13), and more likely to be psychotic (100% vs. 60%, $x^2 = 4.61$ $p < 0.05$ df = 1), particularly delusional (100% vs. 20%, $x^2 = 10.91$ $p < 0.01$ df = 1), and schizophrenic (80% vs. 0%, $x^2 = 8.57$ $p < 0.01$ df = 1) than were intentional dissimulators.

Discussion: Although forensic psychiatrists are vigilant in attempts to detect malingering, these data suggest that we should be equally vigilant to the possibility of dissimulation.

Conclusion: Although further study is indicated, it appears that dissimulators are a heterogeneous diagnostic grouping.

NR794 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Screening for Neuropsychiatric Disorders in a Juvenile Home

Henrik Soderstrom, M.D., *Department of Forensic Psychiatry, Goteborg University, Box 4024, Hisings Backa 42204, Sweden*; Ats Ustafson, M.D., Anita Amberntsson, B.A., Eva Da Silva, M.S.C., Birgitta Arvidsson, R.N., Jean-Michel Saury, M.S.C., Maria Rastam, M.D., Anders Forsman, M.D., Christopher Gillberg, M.D.

Summary:

Objective: To explore the role of neuropsychiatric disorders in social maladjustment, we have screened, diagnosed, and treated these disorders in all boys (15–19 years old) placed at Fagared, a large correctional school in Sweden, due to criminality or a hazardous lifestyle.

Methods: During a 10-month period, neuropsychiatric and neuropsychological examinations were made of all consenting subjects (n = 63 out of 67 possible inclusions). Medical files from earlier child psychiatric contacts were scrutinized. Clinical psychiatric diagnostics, corroborated by structured instruments and collateral interviews, were accommodated to strict operational DSM-IV criteria. Neuropsychological examinations included the WISC-III or WAIS-R.

Results: Five subjects (7.9%) had severe attention deficit/hyperactivity disorder. Another five (7.9%) had a pervasive developmental disorder (1 Asperger's disorder, 4 PDD NOS), a significantly higher prevalence ($p = 0.0053$) than that of 1.21% in Swedish seven-year-olds (Kadesjo et al. 1999). In addition, 24 (38.1%) had a pharmacologically treated anxiety or mood disorder. Test profiles reflecting cognitive impairment were common.

Conclusion: Almost half of the boys had a DSM-IV Axis I disorder (other than substance-related disorders) requiring specialized psychiatric treatment. In attempts to change antisocial behavior, the identification and treatment neuropsychiatric disorders must not be overlooked.

NR795 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Alcohol Misuse Among College Athletes: Self-Medication for Psychiatric Symptoms

Andres J. Pumariega, M.D., *Department of Psychiatry, James H. Quillen College of Medicine, ETSU, Box 70567, Johnson City, TN 37614-0567*; Barney E. Miller, Ph.D., Merry N. Miller, M.D., Ruth Verhegge, R.N., Holly H. Linville, M.D.

Summary:

A collegiate athlete population was surveyed for alcohol abuse as well as self-reported depression, anxiety, and other psychiatric symptoms. This study revealed that in a group of 262 athletes, there were 21% who reported high alcohol use and problems associated with its use. Significant correlations were found between reported alcohol abuse and self-reported symptoms of depression and general psychiatric symptoms. Subjects with positive depression and psychiatric symptom ratings in the "severe" range had a significantly higher rate of alcohol abuse than subjects who had low depression and low or mild symptom ratings. Conversely subjects reporting higher rates of alcohol misuse had more psychiatric symptoms. These findings suggest a possible causal link between psychopathology and serious alcohol abuse among college athletes. They also point to the need for routine depression and anxiety screening in college students who are typically beginning a significant exposure to alcohol.

NR796 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Child Sexual Abuse in Sweden: A Five-Year Population-Based Survey

Anita Carlstedt, M.S.C., *Department of Forensic Psychiatry, Box 4024, Hisings Backa 42204, Sweden*; Anders Forsman, M.D., Henrik Soderstrom, M.D.

Summary:

Objective: To characterize perpetrators, victims, and offenses in a total cohort of sexual child abuse cases tried and convicted in court.

Methods: The 14 courts in the Västra Götaland region (population 1.5 million) in Sweden provided extensive documentation on all sexual crimes against minors (0–15 years of age) resulting in conviction between 1993 and 1997. Data on crimes, perpetrators, victims, and sanctions were registered in standardized protocols for computerized analysis.

Results: The total number of 203 cases of sexual child abuse involved 283 victims and 196 perpetrators, all men. Girls were victims in 85% of cases, and the estimated risk of being the victim of sentenced sexual child abuse before the age of 15 was 5 in 1,000 girls and 8 in 10,000 boys. The victim knew most perpetrators, 83%, concerned hands-on crimes, and 72% of the perpetrators. Most often, the severe offences, such as penetrating sexual intercourse, took place within the family ($p < 0.001$) and were committed by biological relatives ($p = 0.004$). Sanctions were generally milder than expected had the victims been adults.

Conclusions: A wide range of acts was classified as sexual child abuse, but most common was sexual penetration of a female child perpetrated by a household member.

NR797 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Examination of Postconcusion-Like Symptoms in a Healthy Sample

Rael T. Lange, Ph.D., *Department of Psychiatry, University of British Columbia, 2255 Wesbrook Mall, Vancouver, BC V6T 2A1, Canada*; Grant L. Iverson, Ph.D., Amir Sepehry

Summary:

Objective: Clinicians frequently rely on self-reported symptoms to diagnose postconcussion syndrome. The purpose of this study was to examine the prevalence of postconcussion-like symptoms in a sample of non-head-injured healthy control subjects.

Method: Participants (N = 122) completed the British Columbia Postconcussion Symptom Inventory-Short Form (BC-PSI-SF), a test designed to measure both the frequency and intensity of ICD-10 criteria for postconcussion syndrome, and the Beck Depression Inventory-II.

Results: Specific endorsement rates of postconcussion-like symptoms ranged from 38.8% to 73.3% for any experience of the symptoms in the past 2 weeks, and from 1.7% to 12.4% for the experience of more severe, "clinically significant" symptoms. Clinically significant experiences of fatigue, poor concentration, and irritability were reported most frequently (9.2% to 12.4%), while feelings of nausea and sickness, sensitivity to noises, and the presence of headaches were less frequently endorsed (1.7% to 3.3%). The majority of participants (88.2%) endorsed three or more symptoms on the scale, although only 20% endorsed three or more "clinically significant" symptoms. Symptoms reported on the BC-PSI-SF showed a moderately high correlation with self-reported depressive symptomatology (r = 0.76).

Conclusion: This study illustrates that postconcussion symptoms are not unique to mild head injury and are commonly found in individuals free from neurologic and/or psychiatric disorder.

NR798 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Tests of a New Interviewing Technique for Children

Stuart Thomas, Ph.D., *Department of Psychology, Marshall University, 400 Hal Greer Boulevard, Hungtington, WV 25755-2672*; Marc A. Lindberg, Ph.D., Mary Tantalo-Chapman, M.A., Anders Lindberg, J.D.

Summary:

Objective: Three forensic interviewing techniques for children were compared: Yuille et. al's (1993) stepwise technique that is now standard in Canada; the one advocated by child protection that utilizes dolls (Action for Child Protection Inc.; 1994), and a modified structured interview developed out of the cognitive interview, (Geiselman et. al., 1993; Saywitz, 1995).

Method: First, 64 college students were trained on one of the three interview techniques. All college students used the same rapport building and beginning general question, but differed on the follow-up questions. The CPS group, for example, was instructed in the use of dolls, the Yuille training condition was given the steps and video tape of Yuille (Personal Communication, 1995), and those in the modified structured interview condition developed here were instructed on how to use the "differential diagnosis sheets." Sixty four children from grades one (6.62 yrs) and two (7.82 yrs) viewed a film depicting two boys coming home from school and one of them getting severely hit by the mother. The experimenter then gave the children a subtle suggestion about blood, and coached the children to tell the college student interviewer that the older boy was hit with a wooden spoon for wetting his pants. The college students, who did not know what was in the film, were randomly assigned to one of the children for interviewing and then ranked and evaluated the "evidence."

Results: Preliminary data analyses found that the interviewers followed their training protocols. Multivariate analyses of variance found that the structured interview revealed significantly more correct to incorrect "where" information than the other techniques and was significantly better at finding out if "coaching" had occurred. However, the college student data demonstrated that the interviewers could not differentiate between witnessed, suggested, or coached information.

Conclusions: Although the technique developed here was superior in several ways, several cautions will be offered.

Funding Source: Marshall University.

NR799 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Malingering Versus Level of Psychopathology as an Explanation for Cognitive Impairment in Mild Head-Injured Litigants

Jim Andrikopoulos, Ph.D., *Department of Neuropsychology, Mercy Hospital, 1111 6th Avenue, West Building, Suite 400, Des Moines, IA 50314*

Summary:

Objective: The present study hypothesized that cognitive impairment in litigants with mild head injuries is not influenced by the degree of psychopathology but likely feigned in the context of litigation.

Method: A MMPI-2 psychopathology index (PI) was developed for consecutively testing litigants with mild head injuries (MHI, N = 115) and a nonpsychotic psychiatric outpatient control group (PC, N = 95). Their T scores were added and divided by the number of T scores that were 65 or over to obtain a PI for each patient. Within the MHI and PC groups, patients were divided into a low and high psychopathology group based on whether their PI fell below or above the group mean.

Results: There was no difference in the PC group on neuropsychological testing between those with a high PI versus those with a low one. Within the MHI group, those with a high PI had lower neuropsychological test scores than those with a low PI.

Conclusions: In the MHI group, a high level of psychopathology is seemingly associated with greater cognitive impairment, but the absence of this relationship in an equally emotionally disturbed PC group suggests that the effects of psychopathology on cognitive function in the MHI group should be absent.

NR800 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Do Single Mothers Use More Mental Health Services Than Married Mothers?

John Cairney, M.A., *Department of Community Health Sciences, Brock University, 500 Glenridge Avenue, St. Catherine's, ON L2S 3A1, Canada*; Terrance J. Wade, Ph.D., Julio E. Arboleda-Florez, M.D.

Summary:

Objectives: This paper examines the use of mental health care services among single parent and married mothers in Canada. While there seems little doubt that single parent mothers are more likely to suffer depression than married mothers, it is not as clear whether they are more or less likely to receive professional services for their mental health care needs.

Methods: We employ a secondary data analysis of the 1994–95 National Population Health Survey.

Results: Single parent mothers are significantly more likely than married mothers to have seen a health professional for mental health care in the previous 12 months and have a higher frequency of utilization of services. Among single and married mothers who fit the criteria for major depression, there is no difference in rates of utilization. Among those who do not fit this criteria, single mothers are more likely to seek professional care.

Discussion: Single mothers are more likely to seek professional help for mental health issues, yet major depression does not account for this difference despite the fact that the prevalence of this disorder is much higher among single mothers. These findings are discussed in terms of other factors that may account for differences in utilization.

NR801 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Psychiatric Disorders and Comorbidity Among Married and Single Mothers

Terrance J. Wade, Ph.D., *Department of Psychiatry, University of Cincinnati, PO Box 670840, Cincinnati, OH 45267-0840, England*; John Cairney, M.A., David J. Pevalin, M.A., Julio E. Arboleda-Florez, M.D.

Summary:

Objectives: This analysis provides 12-month national prevalence rates of a broad range of affective, anxiety, and substance use psychiatric disorders as well as psychiatric comorbidities among single and married mothers. Given the rise in single parent families in the U.S. over the previous decades and the significantly higher levels of stress and strain associated with being a sole caregiver and provider, interest in the mental health consequences among mothers in this prevalent family structure is increasing.

Methods: The analysis uses the National Comorbidity Survey collected in 1992/93 and focuses on women between 15 and 55 years of age with children (N = 1,346). Psychiatric diagnoses are based on DSM-III-R criteria and measured by the UM-CIDI.

Results: Compared with married mothers, separated/divorced/widowed mothers have elevated rates of disorders. These differences vary across racial groups and age categories. Single mothers who were never married manifest rates of disorders similar to that of married mothers but generally lower than mothers who experience a marital disruption.

Discussion: These results indicate that marital separation is a marker in predicting higher rates of psychiatric disorder and comorbidity among women. These findings are discussed with respect to issues surrounding mental health service utilization.

NR802 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Leucine Enkephalin Metabolism and Psychiatric Disorders

Marion E. Wolf, M.D., *Department of Mental Health, VA Medical Center, 3001 Green Bay Road, North Chicago, IL 60064*; Tao D. Nguyen, M.D., Aron D. Mosnaim, Ph.D.

Summary:

Leucine^5-enkephalin (LEU) appears to modulate the effects of various neurotransmitters at selected central and peripheral synaptic sites. Since N-terminal exopeptidase-catalyzed hydrolysis of LEU's tyrosine-glycine amide bond is responsible for over 95% of its vitro tissue and plasma degradation, it has been suggested that alterations in LEU metabolism, resulting in significant changes in its bioavailability, may influence the course and severity of some conditions characterized by abnormal synaptic transmission. We now report that a number of drugs containing the phenothiazine molecule in their chemical structure significantly decrease the in vitro plasma rate of LEU degradation in a dose-dependent manner (10^{-6} through 10^{-3} M). The following drugs (conc. 10^{-4} M) produced a statistically significant increase in the half-life (in min.) of elimination (thioridazine: 21.2 ± 1.1; fluphenazine: 19.6 ± 1.0; 10-alpha-diethylaminopropionyl phenothiazine: 17.2 ± 0.9; promethazine: 17.1 ± 1.0; chlorpromazine: 17.0 ± 1.1; control: 11.8 ± 1.0) as well as a significant decrease in the initial velocity of LEU degradation (0.77 ± 0.2, 0.82 ± 0.2, 0.92 ± 0.3, 0.93 ± 0.2, and 0.94 ± 0.3 pg LEU/min, respectively; control = 1.10 ± 0.3). This effect, however was lacking in about half of the phenothiazine-like drugs tested (ethopropazine, methotrimeprazine, prochlorperazine, and trifluoperazine), in all of the non-phenothiazine antipsychotic agents studied (clozapine, haloperidol, loxapine, molindone, sulpiride, and thiothixene), as well as in various miscellaneous medications including some triptan-type antimigraine agents (sumatriptan and naratriptan). Our results emphasize the discriminatory nature of chemical structures required to substantially modify plasmatic aminopeptidase activity.

NR803 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Efficacy and Safety of Venlafaxine for PMDD

Ellen W. Freeman, Ph.D., *Department of OBGYN/Psychiatry, University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104*; Nadia R. Kunz, Pharm.D., Karl Rickels, M.D., Mary K. McPherson

Summary:

Objective: To evaluate efficacy of venlafaxine in treating premenstrual dysphoric disorder (PMDD).

Method: After three screening cycles, 157 women with PMDD who met the selection criteria were randomly assigned to double-blind treatment. Venlafaxine (50 to 200 mg/day) or placebo was administered b.i.d. for four menstrual cycles. Primary outcome measure was the total premenstrual symptom score as assessed by the Daily Symptom Report (DSR).

Results: Improvement in PMDD was significantly greater with venlafaxine than placebo (DSR total change from baseline: 12.3 versus 4.4 for placebo, $p < 0.001$), and this was maintained throughout the study ($p < 0.001$ for venlafaxine-placebo difference). Only seven subjects (9%) receiving venlafaxine and five subjects (6%) given placebo discontinued because of adverse events (AEs) ($p = 0.56$). AEs reported most frequently with venlafaxine versus placebo were nausea (45% versus 13%), insomnia (35% versus 16%), and dizziness (32% versus 5%).

Conclusions: Venlafaxine was significantly better than placebo for treating PMDD. Efficacy occurred early, at a relatively low dosage, and treatment was well tolerated.

NR804 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Maternal Depression and Child Psychiatric Illness

Holly A. Swartz, M.D., *Department of Psychiatry, Western Psychiatric Institute and Clinic, 3811 O'Hara Street, Pittsburgh, PA 15213*; M. Katherine Shear, M.D., Esther G. Sales, Ph.D., Carol A. Anderson, Ph.D., Tracey Wang, M.Ed., Wynne S. Korr, Ph.D.

Summary:

Objective: This study (NIMH, MH-56848) examines the relationship between child psychiatric illness and maternal depression in mothers bringing their nonpsychotic children to a community mental health clinic for treatment.

Methods: We conducted structured diagnostic interviews with mothers and their children, comparing mothers meeting criteria for depressive disorders (n = 59) with mothers who did not meet any diagnostic criteria (n = 82) at baseline and six months later.

Results: Compared with children of nondiagnosed mothers, children of depressed mothers met criteria for significantly more diagnoses on the KSADS ($p = 0.01$) with higher baseline scores on the anxious/depressed, delinquent behavior, and somatic complaints subscales of the Child Behavior Check List (CBCL; for all, $p < 0.05$). Fifty-two percent (25/48) of depressed mothers with six-month follow ups continued to meet full criteria for a depressive disorder. Although they were referred for treatment at the time of assessment, only 28% (13/45) attended a single treatment session. At six months, the children of mothers who were depressed

at baseline still met criteria for more diagnoses on the KSADS ($p = 0.01$) and had higher scores on the withdrawn, thought problems, and anxious/depressed subscales of the CBCL (for all, $p < 0.01$).

Conclusion: Despite suffering from clinically significant symptoms, depressed mothers who bring ill children for mental health treatment do not follow through with referrals for their own treatment. Untreated depression in mothers was associated with persistent symptomatology in their children.

NR805 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Levels of Distress Shortly After Genetic Testing for BRCA1 Mutations

Jon G. Reichelt, M.D., *Department of Psychiatry, Aker Hospital, Sognsvannsveien 21, Oslo N-0320, Norway*; Alv A. Dahl, Ph.D.

Summary:

Objective: To find out how family members of families with an autosomal dominant disease, hereditary breast and ovarian cancer (HBOC), cope with being tested.

Method: Out of a clinical sample of 207 members of Norwegian families with founder mutations in the Brcal gene contributing to baseline data, 182 chose to be tested. They were sent a short-term, follow-up questionnaire six weeks following testing, measuring psychological distress.

Results: We found that females with a personal history of cancer were significantly more distressed than females without such a history both before and following testing. Females who had not experienced cancer personally had levels of distress comparable with the normal population both before and following testing. There were no differences in levels of distress between females receiving a positive test result ("bad news") and females receiving a negative test result ("good news") six weeks following testing. In a model of multiple regression 44% of the variance in post-test distress was explained by pre-test levels of distress measured by the same instrument.

Conclusions: Independent of the test result, no short-term adverse psychological consequences seem to arise from genetic testing of members of families with known founder mutations.

NR806 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Cross-Sectional Study Comparing Weight Gain and Androgen Levels in Women with Epilepsy Taking Lamotrigine (LTG) or Valproate (VPA) Monotherapy

Ann E. Taylor, M.D., *Rep Endo Unit, Massachusetts General Hospital, Bartlett Hall, Ext 5, Boston, MA 02114*; Adam Crisp, Ph.D., Pat Tennis, Ph.D., John A. Messenheimer, M.D., Marcus E. Risner, Ph.D.

Summary:

Women with epilepsy may develop hormonal and metabolic disorders associated with polycystic ovary syndrome (PCOS) when taking certain anti-epileptic drugs. There is now growing concern that the use of these drugs for psychiatric conditions may also lead to PCOS. This study compared the incidence of PCOS symptoms in women with epilepsy taking either lamotrigine (LTG) or valproate (VPA) monotherapy. In a cross-sectional observational study, women on a regimen of LTG or VPA monotherapy for 8 to 60 months completed a study visit on day 1–3 of their menstrual cycle. During the follow-up phase, they completed menstrual diaries and urine ovulation tests. 119 LTG and 103 VPA patients completed the study visit. Women in the VPA group had significantly higher total serum testosterone (0.96 nmol/l versus 0.72 nmol/l, $p = 0.001$) and androstenedione (12.6 nmol/l versus 10.1 nmol/l, $p = 0.015$) levels than the LTG group. The mean weight of the VPA group increased between start of VPA treatment and study visit (from 63.0 kg to 67.7 kg), while that of the LTG group did not change (from 71.5 kg to 71.5 kg). Patients taking VPA reported longer and more variable cycle lengths (29.5 days, SD = 5.9) than LTG patients (28.3 days, SD = 3.0). Preliminary results suggest LTG monotherapy is a desirable option for women taking anti-epileptic drugs because it is not associated with weight gain, does not disrupt menstrual cycle length or variability, and has a favorable endocrine profile.

NR807 Thursday, May 10, 12:00 p.m.-2:00 p.m.

The Prevalence of Depressive Symptoms in Women with Polycystic Ovarian Syndrome

Joffee Hadine, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WANG-ACC 815, Boston, MA 02114*; Caragh J. Reilly, B.A., Lee S. Cohen, M.D., Marion C. Eakin, M.D.

Summary:

Objective: Polycystic ovarian syndrome (PCOS) is a common gynecological-endocrine disorder in premenopausal women that manifests with irregular menstrual cycles, hirsutism, and acne. We examined whether the prevalence of depressive symptoms is increased in premenopausal women with PCOS.

Methods: All women seen in a primary care clinic during a 6-month period were asked to complete a questionnaire about their gynecological history, psychiatric history, and current mood state. The questionnaire included self-report of past depression diagnosis and gynecological disorders, including PCOS, and data to determine menopausal status. The Community Epidemiology Scale for Depression (CES-D) was used to screen for current symptoms of depression, with a CES-D score ≥ 25 suggesting a depression diagnosis. Among all women aged 17–45 years who completed the questionnaire, the prevalence of a CES-D score ≥ 25 in women with PCOS was compared with the prevalence of a CES-D score ≥ 25 in all other premenopausal women.

Results: Forty-three of the 866 premenopausal women aged 17–45 years had PCOS. Eleven (25.6%) women with PCOS had a CES-D score ≥ 25, compared with 93 (11.3%) premenopausal women ($\chi^2 = 7.9$, $p = 0.005$). One-quarter of all subjects reported a past depression diagnosis. After controlling for a history of depression, women with PCOS were 2.23 times more likely to have a CES-D score ≥ 25 than other premenopausal women (95% CI = 1.04–4.82, $p = 0.04$).

Conclusions: In this preliminary study, women with PCOS were at increased risk for clinically significant depressive symptoms. The association between PCOS and an increased risk of depressive symptoms warrants further investigation.

NR808 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Gender, Suicide Attempts, and Low Serum Cholesterol Levels

Jose de Leon, M.D., *Department of Psychiatry, University of Kentucky, 627 West 4th Street, MHRC 627, Lexington, KY 40508-1207*; Eloy Garcia-Res, M.D., Enrique Baca-Garcia, M.D., Hilario Blasco, M.D., Dolores Braquehais, M.D., Jeronimo Saiz-Ruiz, M.D.

Summary:

Objective: Low serum cholesterol has been related to suicidality in epidemiological, animal, and psychiatric studies. Low levels of cholesterol may be associated with decreased serotonergic neurotransmission and increased impulsivity. This clinical study explores the relationship between serum cholesterol levels and impulsivity in suicide attempts.

Methods: During 1999-00, 241 patients were studied after being admitted to a general hospital in Madrid (Spain) for a suicide

attempt. Patients were assessed with Beck's Suicidal Intent Scale,' impulsivity was calculated by the sum of scores of two items (degree of planning and degree of premeditation). Serum cholesterol levels were assessed within 24 hours following the suicide attempt. ANOVA was used to compare cholesterol levels in these two groups of suicidal behavior (impulsive/nonimpulsive) by gender.

Results: One-fifth of the attempts were not impulsive (20%). There was an interaction between gender and impulsivity on the cholesterol levels of suicide attempters ($F = 5.28$; $df = 1$; $p = 0.022$). Male with impulsive attempts have the lowest cholesterol levels. The opposite happened in females.

Conclusion: The relationship between impulsivity and cholesterol levels in suicide attempts may be modulated by gender.

This study was supported by a Spanish grant (Comunidad Autonoma de Madrid).

NR809 Thursday, May 10, 12:00 p.m.-2:00 p.m.

A Comparative Study of Body Image and Death Anxiety in Breast Cancer Patients: Mastectomy Versus Those Treated Nonsurgically

Jitendra K. Trivedi, M.D., *Department of Psychiatry, K G Medical College, Shah Mina Road Chowk, Lucknow, UP 226003, India*; Bandna Gupta, M.B., P. K. Dalal, M.D., Arun Chaturvedi, M.S., P. K. Sinha, M.S.C., Rajul Tandon, M.D.

Summary:

Breast cancer has been studied widely with respect to its psychological impact as it threatens an organ intimately associated with self image, sexuality, and femininity.

This study was conducted to compare the body image problem and death anxiety in the mastectomized and breast conserved females suffering from breast carcinoma.

Twenty-seven patients of the mastectomy group (MG) and 18 patients of the nonsurgical group (NSG) were assessed and compared by instruments measuring alteration in the body image and fear of death (instruments used were Death Anxiety Scale—DAS and Body Image Index—BII).

Finding suggested no significant difference in two subgroups on comparing BII (mean BII in MG & NSG were 13.71 ± 2.03 & 13.39 ± 2.40, respectively). Reason for this unexpected finding could be advanced stage of breast multilating tumor in the NSG. Nonsignificant difference was observed between the two groups as a whole on DAS (mean score in the MG and NSG 15.56 ± 7.62 & 16.16 ± 8.26, respectively). The death anxiety was significantly higher in the urban (NSG mean 22.57 ± 8.68 versus 12.09 ± 4.87), comparatively richer (MG mean 19.0 ± 8.96 versus 11.56 ± 3.61), and in nuclear family (NSG mean 20.01 ± 9.24 versus 10.87 ± 1.95 in joint family). The results and reasons will be discussed during presentation.

NR810 Thursday, May 10, 12:00 p.m.-2:00 p.m.

A Comparative Study of Coping Skills and Psychological Distress in Breast Cancer Patients: Mastectomy Versus Those Treated Nonsurgically

Jitendra K. Trivedi, M.D., *Department of Psychiatry, K G Medical College, Shah Mina Road Chowk, Lucknow, UP 226003, India*; Bandna Gupta, M.B., P. K. Dalal, M.D., Arun Chaturvedi, M.S., P. K. Sinha, M.S.C., Rajul Tandon, M.D.

Summary:

Illness like breast cancer can cause psychological distress, when diagnosed late as well as at an early stage. Late diagnosis is frequently associated with poor prognosis and an early diagnosis may result in mastectomy.

This study was conducted to compare the coping skills and psychological distress in the two groups of patients. Twenty-seven patients of the mastectomy group (MG) and 18 patients of the nonsurgical group (NSG) were assessed and compared on instruments measuring coping skills (coping strategy checklist) and distress (comprehensive psychopathological rating scale—CPRS, Rotterdam symptom checklist—RSCL). The result showed nonsignificant difference between the two groups on the total coping scores (mean 20.41 ± 2.95 & 19.9 ± 3.36). Denial was used more by the mastectomized patients (mean 8.74 ± 2.01 & 7.72 ± 2.42). Late-stage cancer patients used more coping skills. Coping skills of internalization and emotional outlet were used more by rural background patients. Late-stage cancer patients of MG were more depressed (mean depression score on CPRS 15.82 ± 2.35 versus 13.83 ± 2.20) and patients on NSG were more anxious (mean anxiety score on CPRS 5.22 ± 3.85 versus 3.85 ± 1.41). Total distress score was higher in the NSG (mean score on RSCL 31.72 ± 8.22 versus 27.29 ± 5.12).

NR811 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Mental Status Changes After Deep Brain Stimulation (DBS) in Severe, Refractory OCD

Loes Gabriels, M.D., *Department of Psychiatry, U. Z. Antwerpen, Wilrijkstraat 10, Edegem B-2650, Belgium*; Paul Cosyns, M.D., Bart Nuttin, M.D.

Summary:

Alleviation of obsessive-compulsive symptoms has been observed after chronic DBS in anterior limbs of the internal capsules in patients with treatment-refractory OCD.

Objective: Evaluation of changes in appearance, attitude, speech, and affect prompted by electrical stimulation in three OCD patients.

Method: Reviewers analyzed video-recordings of a standardized semi-structured interview obtained during four consecutive randomized 1-hour sessions: two stimulation-on (DBSON) and two stimulation-off (DBSOFF) settings. Reviewers, interviewer, and patients were blinded with regard to the stimulation condition. Changes in eye contact, facial expression, cooperation, assertiveness, spontaneity, speech (voice-intonation and speed), attention/concentration, motor-activity level, tension, anxiety, and discomfort were evaluated using Likert-type interval scores (0–8), and reviewers rated whether DBS was on or off.

Results: All scores evolved toward normalization for all three patients during the DBSON session. Significant changes ($p < 0.05$) during the DBSON session were found for spontaneity in all three patients; for facial expression, assertiveness, voice-intonation, and discomfort in two of three patients; and for eye contact, speed of speech, attention/concentration, and tension in one of the patients.

In 11/12 video-recordings at least 10/12 reviewers assessed the stimulation condition correctly (5 video-recordings: 12/12 correct; 5 video-recordings: 11/12 correct; 1 video-recording: 10/12 correct; 1 video-recording: 7/12 correct).

Conclusion: DBS elicits immediate, prominent, and positive changes in several mental status aspects in treatment-refractory OCD patients.

NR812 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Evaluation of HPA Function in Chronic Fatigue Syndrome

Magda Fahmy, *Suez Canal University, 105 Nozha Street, Heliopolis, Cairo 11361, Egypt*; Nouran Elghandour, H. Mohab Halim

Summary:

Recently, it has been reported that patients with CFS might have impaired hypothalamic-pituitary-adrenal (HPA) axis function, and it has been suggested that a part of the pathogenesis of the disease might be associated with abnormalities of the endocrine system and that the illness is not simply a manifestation of an underlying psychiatric disorder. To clarify this impairment the present study included 20 patients with CFS but without concurrent psychiatric disorder and 20 normal volunteers matching in weight, age, and sex as control subjects. All subjects were evaluated by semistructured psychiatric interview, guided by the ICD-10 symptom checklist for mental disorders. The Beck Depressive Inventory scale (BDI), and the Multidimensional Fatigue Inventory scale (MFI-20). Basal activity of the HPA axis was estimated by measuring baseline morning and evening serum cortisol and adrenocorticotrophic hormone (ACTH) concentrations, and the diurnal changes in hormonal levels were assessed. Results of clinical psychiatric interview excluded any psychiatric disorders while the BDI scale excluded depression and showed that minor depressive symptoms were significantly increased ($p < 0.05$) in CFS patients than in normal controls. The MFI-20 scale showed that general fatigue, mental fatigue, physical fatigue, reduced activity, and reduced motivation were all significantly increased ($p < 0.05$ for each) in CFS patients compared to normal controls. Meanwhile, total fatigue showed significant increase ($p < 0.01$) in CFS patients. Morning cortisol levels were significantly lower ($p < 0.01$) in CFS patients while evening levels were significantly higher ($p < 0.01$). The diurnal change in cortisol level was significantly impaired in CFS patients compared to the controls ($p < 0.01$). ACTH concentrations were significantly higher in both morning ($p < 0.01$) and evening ($p < 0.01$) compared to the control subjects. A significant negative correlation between cortisol and ACTH levels was encountered in CFS patients only in the morning, while control subjects showed this significant negative correlation in both morning and evening samples. A reduced diurnal variation in cortisol level was observed in CFS, and this showed negative significance with the five subscales of the MFI-20 scale ($p < 0.01$ in each), which suggests that the diurnal cortisol variation was related to fatigue in its five subscales.

Conclusion: The pattern of adrenocortical function in CFS patients is different from that in healthy subjects, which suggests a hormonal basis for this syndrome in addition to its psychological element.

NR813 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Role of Impaired Glucose Tolerance and Iron Status in Tardive Dyskinesia

Siow A. Chong, M.B., *Department of Research, Woodbridge Hospital, 10 Buangkok Green, Singapore 539747, Singapore*; Mythily Subramaniam, M.D., Rathi Mahendran, M.D., Kang Sim, M.D., Alvin Lam, M.D.

Summary:

Objectives: The pathophysiology of tardive dyskinesia (TD) is likely to involve the complex interactions of various factors. We examined the association of iron status and impaired glucose tolerance in schizophrenic patients with the vulnerability for TD.

Methods: One hundred and ninety-four patients with DSM-IV schizophrenia participated in the study after giving written informed consent. Dyskinesia was assessed with the Abnormal Involuntary Movement Scale (AIMS), and parkinsonism was assessed with the Simpson-Angus Rating Scale by raters "blind" to the laboratory results. Schooler and Kane's criteria were used in the diagnosis of TD.

Patients were given an oral glucose tolerance test. Fasting glucose and insulin levels were determined along with iron indices (i.e., serum iron, ferritin, and total iron binding capacity [TIBC]).

Results: The 86 (44.3%) patients with persistent TD did not differ in their mean age, sex distribution, and Simpson-Angus scores from those without TD (N = 108). Those with TD had a lower daily dose of neuroleptic and a lower fasting glucose level ($p < 0.001$ and $p = 0.004$, respectively, Mann-Whitney U tests). There were no correlations between TD and 1- and 2-hour glucose levels.

Conclusions: Contrary to prior studies, our findings do not suggest that hyperglycemia or abnormal iron indices are risk factors for TD.

NR814 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Interleukin-2 Levels in Chronic Schizophrenic Patients

Rathi Mahendran, M.D., *Woodbridge Hospital, 10 Buangkok View, Singapore 539747, Singapore*; Ratha Mahendran, Ph.D., Yiong Huak Chan, Ph.D.

Summary:

Objective: To determine IL-2 levels in chronic schizophrenic Asian patients (Chinese, Malays, and Indians) in relation to duration of illness, psychopathology, and treatment effects.

Methods: Thirty chronic schizophrenic patients fulfilling DSM-IV criteria for schizophrenia were entered. They had no comorbid conditions. Demographic data and medication dosage were noted; symptom severity was scored on the PANSS, and blood sampling was done. Ten healthy Chinese males were recruited as control subjects. Phytohemagglutinin-stimulated production of serum levels of IL-2 were measured by enzyme-linked immunosorbent assay.

Findings: Significantly lower IL-2 levels were seen in all 30 patients (1327.0, SD = 596.2) than in the Chinese control subjects (2420.0, SD = 342.5) ($p < 0.001$, Mann-Whitney U test). No ethnic differences in IL-2 levels were detected. IL-2 levels of all patients were significantly lower than control subjects regardless of illness duration. Using multiple regression to take into account age, total PANSS score, and CPZ equivalent doses as covariates, the IL-2 levels of the patients were significantly lower than the control subjects regardless of illness duration.

Conclusion: Our findings reveal a decrease in IL-2 levels among Asian schizophrenic patients. Duration of illness and CPZ equivalent doses of neuroleptic medication had significant effect on IL-2 levels, indicating that cytokine dysregulation may be ongoing and that neuroleptic medication has little effect in reversing it.

NR815 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Significant Menstrual Cycle-Related Changes in Cortical Excitability

Mark J. Smith, M.D., *LCS 10, Room 3D41, NIMH, 10 Center Drive, Bethesda, MD 20892*; Linda F. Adams, B.A., Jersino Jean-Mary, B.A., John C. Keel, B.A., Peter J. Schmidt, M.D., David R. Rubinow, M.D.

Summary:

Objective: In vitro cortical excitability increases with estradiol (E2) and decreases with progesterone (P4) metabolites, which may act through the GABA-A receptor. Human cortical excitability may be measured by paired-pulse transcranial magnetic stimulation (pTMS), which appears sensitive to changes in the cortical glutamate/GABA balance.

Method: pTMS measured the effect of a subthreshold conditioning pulse on the response to a second suprathreshold test pulse; results were expressed as the ratio of the amplitudes of the conditioned to the test pulses. Menstrual cycle variation in pTMS ratio means were studied in 14 normal women by ANOVA-R on measures done in the early follicular (days 2–5: low E2, low P4), late

follicular (days 9–12: high E2, low P4), and luteal phases (6–12 days after the LH surge: high E2, high P4). E2 and P4 levels at each time point were consistent with ovulatory cycles.

Results: pTMS ratios showed a significant effect of phase ($F = 3.81$; $p = 0.035$), increasing from early follicular (mean = 0.871) to late follicular phase (mean = 1.001), then decreasing in the luteal phase (mean = 0.880). Post-hoc Bonferroni tests showed significant differences between early follicular and late follicular phases ($t = 2.5$, $p < 0.05$) and between late follicular and luteal phases ($t = 2.32$, $p < 0.05$).

Conclusions: These results suggest that the follicular rise in cortical excitability may be related to the rise in estradiol levels and that there may be P4-enhanced GABA activity related to the decrease in cortical excitability during the luteal phase.

NR816 Thursday, May 10, 12:00 p.m.-2:00 p.m.

A Retrospective Analysis of Guanfacine Treatment of Austism

David J. Posey, M.D., *Department of Psychiatry, Indiana University-Riley Hospital, 702 Barnhill Drive, Room 3701, Indianapolis, IN 46202-5200*; Jessica Decker, B.A., Teresa M. Sasher, B.A., Arlene Kohburn, B.A., Naomi B. Swiezy, Ph.D., Christopher J. McDougle, M.D.

Summary:

Objective: To retrospectively review the effectiveness of guanfacine in an outpatient clinic sample of autistic subjects.

Method: Seventy-four subjects (10 female, 64 male), ranging in age from 3 to 18 years (mean = 7.6 years, SD = 3.4) with pervasive developmental disorders (PDDs) (autistic disorder, N = 42; Asperger's disorder, N = 6; and PDD not otherwise specified (NOS), N = 26) were treated with guanfacine (0.25 to 9 mg daily in divided doses, mean = 2.6 mg, SD = 1.8, for 298 days [SD = 362]). Charts were reviewed by the patient's primary psychiatrist to determine severity of symptoms and improvement after guanfacine treatment using the Clinical Global Impressions Scale (CGI). In addition, severity and improvement ratings for the following symptoms were determined: inattention, hyperactivity, impulsivity, aggression/self-injury, anxiety/worry, irritability/noncompliance, insomnia, repetitive behavior, tics, social impairment, and communication impairment.

Results: 16 of 74 subjects (21.6%) were rated as "responders" ("much improved" or "very much improved" on the CGI). The greatest response rates were seen in the symptoms of tics (50%, N = 3 of 6), insomnia (26%, N = 13 of 50), and hyperactivity (21.7%, N = 15 of 69). Greatest response was seen in those subjects with Asperger's disorder (50%, N = 3 of 6) and PDD NOS (38.5%, N = 10 of 26) compared to those with autistic disorder (9.5%, N = 4 of 42). Guanfacine was well tolerated with the most common adverse effect being transient sedation.

Conclusions: In this open-label, retrospective review, guanfacine was well tolerated and modestly effective in treating some symptoms associated with PDDs, including tics, insomnia, and hyperactivity. Symptom improvement was much greater in patients with PDD NOS and Aspérger's disorder than in autistic disorder.

NR817 Thursday, May 10, 12:00 p.m.-2:00 p.m.

The Effects of Vagus Nerve Stimulation (VNS) on Sleep in Depression

Roseanne Armitage, *Department of Psychiatry, University of Texas at Southwestern, 5323 Harry Hines Boulevard, Dallas, TX 75390-9070*; Mustafa M. Husain, M.D., Robert Hoffman, Ph.D., A. John Rush, M.D.

Summary:

Objective: A preliminary study evaluated the effects of vagus nerve stimulation (VNS) on sleep and biological rhythms in EEG in four treatment-resistant depressed patients.

Method: Sleep studies were performed at baseline and after 10 weeks of VNS therapy. Changes in sleep macroarchitecture (i.e., total sleep time, % sleep stages, REM characteristics, etc.) and microarchitecture (i.e., temporal coherence, periodicity and amplitude of EEG rhythms) were evaluated.

Results: Pre-treatment, baseline sleep studies revealed severe sleep disruption and particularly dampened EEG rhythms. After VNS, self-reported sleep quality improved in all patients. Sleep macroarchitectural changes included less non-restorative Stage 1 sleep and intermittent wakefulness accompanied by increased Stage 2 sleep. Most notably, VNS treatment was associated with a substantial increase in the strength of EEG rhythms to near normal levels.

Conclusions: Unlike most antidepressant medications, VNS treatment improved both subjective and objective sleep characteristics and reversed the dampening of EEG rhythms. These effects may be of clinical benefit, since persistent sleep disturbance increases the risk of relapse and recurrence.

Research supported by Cyberonics, Inc.

NR818 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Device for Quantifying Elbow Cogwheel Rigidity

Arnaldo E. Negron, M.D., *Department of Psychiatry, UMDNJ-RWJMS, 667 Hoes Lane, Piscataway, NJ 08855*; Robert Edelberg, Ph.D.

Summary:

Objective: Since the current clinical examination of drug-induced extrapyramidal symptoms (DIEPS) is both subjective and imprecise, we intended to develop a digital instrument for the objective measure of DIEPS. Briefly, this experimental device standardizes the rate of movement and the pattern of force application, and measures the actual force of any counter-torque exercised by the patient. The purpose of this study was to evaluate the sensitivity and specificity of this device in quantifying elbow cogwheel rigidity, an index of EPS.

Method: Twenty-five outpatients, from university-based clinic, treated with antipsychotics, and with at least mild EPS were included in the study. They were compared with an age-matched control group that consisted of nonpsychiatric patients. Both groups underwent subjective and objective measurements of EPS.

Results: The two study groups were comparable in age, gender, and total body mass (TBM). The outpatient group had an average of 10 $\pm$ 10 years history of antipsychotic drug treatment. There was a significant difference in the Simpson-Angus scores between populations ($DF = 48$, $F = 157$, $p < 0.00001$). There were significant differences in torque measures on flexion ($DF = 48$, $F = 14.4$, $p < 0.001$) and extension ($DF = 48$, $F = 17.7$, $p < 0.001$) on testing with the digital device.

Conclusions: This electromechanical instrument provided a sensitive and specific measure of DIEPS.

NR819 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Cognitive Effects of Pharmacologic Ovarian Suppression

Julia K. Warnock, M.D., *Department of Psychiatry, University of Oklahoma at Tulsa, 4502 East 41st Street, Tulsa, OK 74135*; David W. Morris, M.A., Julia K. Warnock, M.D., J. Clarke Bundren, M.D.

Summary:

Objective: Many researchers have examined the relationship between sex steroids and cognitive functioning in women. Recently, several studies have documented memory impairment in young women undergoing acute ovarian suppression induced and maintained by GnRH agonist therapy. The purpose of this study was twofold: 1) to assess memory impairment associated with GnRH agonist-induced hypoestrogenic states and 2) to assess the effects of sertraline in treating any GnRH agonist-induced memory impairment.

Design: Twenty-one women undergoing a GnRH agonist-induced hypoestrogenic state were given either sertraline or a placebo during GnRH agonist therapy. A comparison group was recruited. Participants were excluded if they met criteria for any psychiatric disorder including premenstrual dysphoric disorder. All participants were given the Wechsler Memory Scale—Third Edition (WMS-III), as well as the HAM-D and the HAM-A, at baseline and 3 months later.

Results: The results suggest that patients undergoing pharmacologically induced ovarian suppression experience an increase in subjective memory dysfunction. The frequency of subjective memory complaints may be significantly reduced by the administration of an SSRI. An analysis of the WMS-III data did not indicate any significant between-group differences.

Conclusions: Traditional objective measures of memory may not be sensitive enough to measure the subtle changes in cognitive functioning associated with brief pharmacologic ovarian suppression. However, other methods of assessment, such as measurements of physiologic brain functioning, may be more effective.

NR820 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Effects of Antipsychotics on the Heat Shock Protein 70 and 90 in Patients with Schizophrenia

Jae-Hyun Kim, M.D., *Department of Psychiatry, WonKwang University Hospital, 144-23 Dongsan Dong, Ikan Chonbuk 570-060, South Korea*; Jung-Jin Kim, M.D., Oh-Joo Kwon, Ph.D., Young-Chul Chung, M.D., Soo-Jung Lee, M.D., Chul Lee, M.D., In-Ho Patk, M.D.

Summary:

Objectives: Antibodies to stress proteins, which play a protective role against environmental stresses in a cell, might be related to the pathogenesis of schizophrenia. In this study, we examined antibodies to HSP70 and HSP90 in patients with schizophrenia before and after medication. Association between clinical variables and immunoreactivity to HSP70 and HSP90 were also investigated.

Methods: IgG antibodies to HSP70 and HSP90 in 70 patients with schizophrenia and 83 normal control subjects were measured by enzyme-linked immunosorbent assay (ELISA).

Results: The levels of HSP70 and HSP90 antibodies were higher in patients with schizophrenia than in normal control subjects. The level of HSP70 antibody and frequency of positive HSP70 antibody decreased in the patients after medication. However, the level of HSP90 antibody and frequency of positive HSP90 antibody were not significantly changed after medication. The scores of symptom severity (per the Brief Psychiatric Rating Scale, BPRS) were significantly higher in patients who showed positive HSP70 antibody. After medication, BPRS scores were not different between the positive and negative HSP70 antibody groups. By contrast, the levels of HSP90 antibody were not related with BPRS scores and did not change after medication.

Conclusion: Our results suggest that the antipsychotics might affect the immunoreactivity to HSP70 but not to HSP90 in patients with schizophrenia.

NR821 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Euthyroid Psychosis: A New Clinical Syndrome?

Carol A. Beresford, M.D., *Department of Psychiatry, Children's Hospital, 1056 East 19th Avenue, Denver, CO 80218*; Thomas P. Beresford, M.D.

Summary:

Objective: Thyroid disorders may present primary symptoms not easily distinguished from classically described psychiatric syndromes. Poor response to psychoactive medications may suggest the presence of thyroid disorder, but usually when thyroid function tests are abnormal. Recent clinical experience suggests that normal hormonal parameters may not always reflect euthyroid status behaviorally.

Method: We report a familial disorder in an adolescent female whose first symptoms of psychosis responded to thyroid replacement despite euthyroid laboratory parameters. The presentation included (1) visual and auditory hallucinations and wide mood fluctuations; (2) low to low normal TSH, mid-range free T4 and total T4, and normal T3 levels; (3) absent anti-thyroid antibodies; and (4) a history of similar symptoms in the child's mother, the mother's twin sister, and the maternal grandmother.

Results: Thyroid replacement raising T4 levels to high normal range reversed the symptoms of psychosis, returning the patient to normal functioning. Similar reversal of psychiatric symptoms was found in the child's mother and aunt.

Conclusion: This case suggests the existence of a hitherto unreported syndrome of thyroid insufficiency presenting as psychosis in the absence of gross laboratory indications of failure. A possible mechanism may be a deficiency in hormone signaling in the hypothalamus-pituitary-thyroid axis and appears to be genetic in nature, perhaps expressed as an X-linked abnormality.

NR822 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Negative Syndrome as a Dimension: Factor Analysis of Positive and Negative Syndrome Scale in MDD and CVA or Dementia

Matthew S. Milak, M.D., *Department of Psychiatry, Beth Israel Medical Center, First Avenue at 16th Street, 9 Fierman, New York, NY 10003*; Alexander Prikhojian, M.D., Alice John, M.D., Lisa J. Cohen, Ph.D., Igor I. Galynker, M.D.

Summary:

Factor analysis of the Positive and Negative Syndrome Scale (PANSS) item scores was performed in 82 patients with major depressive disorder (MDD), and 75 patients with dementia or stroke (CVA) and no (other) Axis I diagnoses. Factor analysis (extraction method: principal component analysis) PANSS item scores of MDD patients yielded eight factors with Eigen values greater than one, accounting for more than 65% of the cumulative variance. The factor accounting for almost 14% of the variance was the negative syndrome factor. Similar analysis of PANSS in subjects with CVA or Dementia yielded seven factors, accounting for 100% of the cumulative variance, with factor number one also being the negative syndrome factor. In this case the negative factor accounted for more than 28% of the variance. The negative syndrome factor emerging in depression and CVA or dementia had almost identical composition to the factor number one described repeatedly in the schizophrenia literature. Thus, it appears that negative syndrome is a clinical dimension that may occur as a result of several disorders, rather than being unique to schizophrenia. We further suggest that research is needed regarding the mechanism and potential treatment of negative syndrome across nosologic entities.

NR823 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Disordered Metal Metabolism in a Large Autism Population

William J. Walsh, Ph.D., *HR1, 1804 Centre Point Circle, Naperville, IL 60563*; Anjum Usman, M.D., Jeffrey Tarpey

Summary:

Objective: To investigate the incidence of metal metabolism disorders in an autistic-spectrum patient population.

Method: Chemical analyses of blood and urine samples from 503 patients diagnosed with autistic disorder (n = 318), Asperger's disorder (n = 23), or atypical autism (n = 162) were evaluated.

Results: Of patients tested, 428 (85%) exhibited severely elevated Cu/Zn ratios in blood (average 1.78) compared with a population of healthy controls (average 1.15). Another 30 patients (6%) exhibited a pyrrole disorder associated with seven Zn deficiency. Of the remaining subjects (n = 49), 45 reported undergoing aggressive Zn therapy at the time of sampling. A total of 499 of the 503 autism-spectrum patients exhibited evidence of a metal metabolism disorder.

Conclusion: The absence of Cu and Zn homeostasis and severe Zn deficiency are suggestive of a metallothionein (MT) disorder. MT functions include neuronal development, detoxification of heavy metals, and immune response. Many classic symptoms of autism may be explained by a MT defect in infancy including GI tract problems, heightened sensitivity to toxic metals, and abnormal behaviors. These data suggest that an inborn error of MT functioning may be a fundamental cause of autism.

NR824 Thursday, May 10, 12:00 p.m.-2:00 p.m.

The Visuospatial Performance in Chronic PTSD

Tamara V. Gurvits, M.D., *Department of Research Services, VA Medical Center, 228 Maple Street, 2nd Floor, Manchester, NH 03103*; Natasha B. Lasko, Ph.D., Linda J. Metzger, Ph.D., Michael L. Macklin, B.A., Mark W. Gilbertson, Ph.D., Roger K. Pitman, M.D., Scott P. Orr, Ph.D.

Summary:

The ability to copy simple line drawings is acquired as part of normal cognitive development. By age 9 it is expected that a normal child will be able to copy a cube. A copy figure test (CFT) consisting of two-and three-dimensional line drawings was designed and administered to 60 subjects. The sample included 32 Vietnam combat veterans males and four adult females sexually abused as children with chronic posttraumatic stress disorder (PTSD), and 16 veterans and eight females non-PTSD exposed to trauma but who never developed PTSD (controls) to investigate differences in performance on the CFT. Subjects with PTSD demonstrated considerably more impaired performance on six of the seven figures, compared with subjects without PTSD. After separately adjusting for age, years of education, estimated IQ score, and compromised developmental history, the group differences remained significant. Significant correlations were observed between CFT performance and severity of PTSD, WAIS IQ score, total number of neurological soft signs, and education. The authors discuss the possibility that poorer CFT performance reflects pretrauma impairment.

NR825 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Opiate Sensitivity Test in OCD Spectrum Disorders

Ede Frecska, M.D., *Department of Psychiatry, VA Medical Center, 10000 Bay Pines Boulevard, Bay Pines, FL 33744*; Mihaly Arato, M.D., Beverly Adams, Dominique Thuriere, M.D., Donald E. Addington, M.D.

Summary:

Background: Patients with repetitive self-hurting behavior may have different pain perception, since they feel gratification or even euphoria when they perform normally painful self-hurting. Some preliminary data about the therapeutic use of opiate antagonists (naltrexone), agonists (tramadol), and opiate receptor desensitization by morphine (Warneke 1997) also suggest the possible role of opiate mechanisms in the pathophysiology of these disorders. The aim of this study was to investigate the possible involvement of the opioid mechanism in repetitive self-injurious behavior in patients with obsessive-compulsive spectrum disorder (OCSD) manifesting skin picking or hair pulling. Subanasthetic doses of the mu opiate receptor agonist fentanyl induce robust, transient prolactin release. The quantitative indicators of this hormone response to fentanyl may reflect the sensitivity of the mu opiate receptors and related mechanisms (Frecska et al., 1989).

Method: Ten comparison subjects received a 0.1 mg/70kg dose of fentanyl in a slow 5-minute IV infusion in the AM and PM hours. Placebo control was also performed in five of them. A dose of 0.05 mg/70kg fentanyl was given in the AM hours to eight comparison subjects and 22 OCSD patients. Blood samples were obtained for prolactin measurements at 0, 15, 30, 45, and 60 minutes.

Results: Fentanyl elevated plasma prolactin concentrations in a dose-dependent manner ($F = 2.94$; $df = 8.80$; $p = 0.006$). There was increased opiate sensitivity in the evening compared with the morning ($F = 8.16$; $df = 4.36$; $p = 0.0001$). Patients with skin picking, but not hair pulling, showed significantly increased opiate sensitivity ($F = 4.98$; $df = 8,108$; $p < 0.0001$).

Conclusion: This finding supports the implication of endogenous opiates in the pathomechanism of repetitive, self-hurting behavior.

NR826 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Monoamine Metabolites in the Chronic Fatigue Syndrome as Predictors of Early Death in Psychiatric Inpatients

Anders Manhem, M.D., *Department of Psychiatry, Forensics, Box 4024, Hisings Backa 42204, Sweden*; Henrik Soderstrom, M.D., Anders Forsman, M.D.

Summary:

Objective: To assess the relationship between monoamine metabolite patterns in the CSF of psychiatric inpatients and risk of early death.

Methods: 826 inpatients, voluntarily admitted to a psychiatric ward, were offered an extended neuropsychiatric investigation as part of a naturalistic study. Morning lumbar punctures were performed between L4 and L5 following at least 8 hours of rest in bed. 5-HIAA, HVA, and HMPG were assessed and their concentrations in CSF were compared with survival during a follow-up of 13–24 years in a logistic regression model. Data on the patients were collected from the Cause of Death Register.

Results: Forty-two of the total number of 205 deaths during the follow-up were suicides, indicating a 16-fold risk increase compared to the general population. A low CSF concentration of 5-HIAA indicated an increased risk of suicide and was, in contrast to earlier observations, more closely related to death due to intoxication than to violent suicides.

Conclusion: CSF monoamine assessments can be used in the prediction of future suicide. There are some confounding factors that should be taken into account in clinical applications.

NR827 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Rapidly Changing Psychiatric Symptoms and Epilepsy

Arne E. Vaaler, M.D., *Department of Psychiatry, NTNU Medical Facility, Box 3008 Lade, Trondheim 7441, Norway*; Karl H.

Melle, M.D., Gunnar Morken, M.D., Olav M. Linaker, Ph.D., Trond Sand, Ph.D.

Summary:

Objectives: To compare the frequency of epilepsy among acutely admitted patients with rapid changing psychiatric symptoms and acutely admitted depressed patients.

Methods: Acutely admitted patients with rapid changing psychiatric symptoms were compared with age- and sex-matched patients acutely admitted with major depression. All patients were assessed with quantitative EEG evaluation three times during the first 10 days of the stay, with psychometrical tests, clinical chemistry including prolactin peaks and cerebral MRI.

Results: Until December 2000, six patients are included in the study group and five in the group of depressed controls. Of the six patients in the study group, two had pathological EEG before inclusion, three had pathological EEG during the first 10 days of their stay, and one had peak of prolactin levels shortly after change of symptoms. In the group of depressed controls one patient had pathological EEG. Results from more included patients will be reported at the meeting.

Conclusions: Preliminary results indicate that patients admitted to hospital with rapid changing psychiatric symptoms have more pathological EEG and peaks of prolactin than depressed patients. It is important to be aware of epilepsy among patient with rapid changing psychiatric symptoms.

NR828 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Patient Self-Report Versus Staf Ratings of the BASIS-32

Catherine A. Leslie, M.D., *Western State Hospital-CSU, 1301 Richmond Road, Staunton, VA 24402*; Michael S. Shutty, Ph.D., Ludmila Kryzhanovskaya, Ph.D., Jack W. Barber, M.D.

Summary:

Objective: The aim of this study was to evaluate the descriptive and construct validity of the BASIS-32 as a self-report methodology for assessing psychiatric symptom severity and level of psychosocial functioning.

Method: Patient self-report data from the BASIS-32 and their respective treatment team ratings of psychiatric functioning were compared in a state psychiatric hospital. The discrepancies between patient versus staff ratings were evaluated following independent clinician symptom ratings with the BPRS and PANSS.

Results: Twenty-five psychiatric inpatients (76% males) preparing for discharge with an average age of 39 years (SD = 9.7) reported an average total BASIS-32 scale score of 15.7 (SD = 13.2), which was significantly lower ($p < 0.001$) than their treatment team ratings (mean = 38.6, SD = 18.0). This difference was evidenced across all BASIS-32 subscales. PANSS and BPRS ratings were significantly ($p < 0.05$) and positively correlated with staff ratings ($r = 0.65$ and $r = 0.62$, respectively) but not patient ratings ($r = 0.24$ and $r = 0.32$, respectively). Analysis of the staff versus patient discrepancy scores across subscales indicated that PANSS and BPRS ratings of symptom severity and insight about mental illness, but not patient demographics of age, gender, or number of previous hospitalizations, were associated with the patients' lower ratings on the BASIS-32.

Conclusions: These findings suggest that patients underreport problems as measured by the BASIS-32. This response bias appears to be associated with patients who have higher symptom ratings, particularly limited insight regarding the nature and severity of their mental illness. These findings raise concerns regarding the validity of using the BASIS-32 as a self-report methodology for chronic patients who are preparing for discharge but have residual symptoms.

NR829 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Response to Reinitiation of Fluoxetine Treatment by Patients Relapsing Upon Switching to Placebo During Long-Term Treatment of Depression

Maurizio Fava, M.D., *Department of Psychiatry, Massachusetts General Hospital, 15 Parkman Street, WAC 812, Boston, MA 02114*; Mark E. Schmidt, M.D., Shuyu Zhang, M.S., Jill Gonzales, B.S., Nancy Raute, B.A.

Summary:

Objective: Anecdotal reports suggest restarting drug treatment in depressed patients who have prematurely discontinued the drug may be associated with diminished response. We evaluated the likelihood of response to fluoxetine re-initiation in patients who relapsed after switching to placebo during long-term treatment.

Methods: Depressed outpatients who relapsed during double-blind continuation treatment with placebo, fluoxetine 20 mg daily, or enteric-coated fluoxetine 90 mg once weekly were offered double-blind rescue treatment. Patients relapsing following random assignment to placebo resumed treatment with fluoxetine 20 mg daily. Treatment and response of patients relapsing during active drug treatment are described elsewhere. Analyses included percentage of responders (50% reduction of $HAMD17^4$ and CGI-Severity ≤ 2) and baseline-to-endpoint changes (HAMD, CGI-Severity).

Results: Of 57 (47%) patients relapsing, 55 (95%) elected double-blind rescue treatment, and 62% responded to fluoxetine re-initiation. Mean $HAMD17^4$ decreased from 20 to <9 and was maintained for up to 6 months.

Conclusion: Initial fluoxetine responders, who relapsed upon switching to placebo, have a high probability of responding to fluoxetine re-initiation. These results challenge the view that efficacy of prematurely discontinued agents is diminished when restarted and support re-initiation of the same antidepressant as a 'first-line' treatment strategy for patients who relapsed after stopping a previously effective antidepressant.

Research funded by Eli Lilly and Company, Indianapolis, Indiana 46285.

NR830 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Response to an Increased Dose of Fluoxetine by Patients Relapsing During Long-Term Treatment of Depression

Mark E. Schmidt, M.D., *Neuroscience, Eli Lilly and Company, Lilly Corporate Center DC 1730, Indianapolis, IN 46285*; Richard Bergstrom, Ph.D., Maurizio Fava, M.D., Shuyu Zhang, M.S., Jill Gonzales, B.S., Nancy Raute, B.A.

Summary:

Objective: To evaluate the likelihood of response to an increased fluoxetine dose in patients who relapsed during a study of the long-term efficacy of two different dosing regimens of fluoxetine. Possible mechanisms of apparent loss of antidepressant activity were explored through analyses of drug plasma concentrations.

Methods: Depressed outpatients who relapsed during double-blind continuation treatment with placebo, fluoxetine 20 mg daily, or enteric-coated fluoxetine 90 mg once weekly were offered double-blind rescue treatment during which they received fluoxetine 20 mg daily, fluoxetine 40 mg daily, or enteric-coated fluoxetine 90 mg twice weekly, respectively. Analyses included percentage of responders and baseline-to-endpoint changes (HAMD and CGI-Severity). Blood serum samples were collected to assess fluoxetine and norfluoxetine concentrations.

Results: The results of the 40 mg daily and 90 mg twice weekly group are reported here. Patients responded well to an increase in dose (57%, 40 mg/day; 72%, 90 mg twice weekly). $HAMD_{17}^4$

scores decreased from a mean of 20 to ≤ 10 and were maintained up to 6 months. Mean plasma concentrations were higher during the rescue treatment corresponding to the larger prescribed dosage.

Conclusion: Patients relapsing after initially responding to fluoxetine can benefit from an increase in fluoxetine dose. The robust response to an increase in concentration appears to rule out an inverted concentration response in which higher concentrations of drug or metabolites lead to disease relapse or a worsening of the condition.

Research funded by Eli Lilly and Company, Indianapolis, Indiana 46285.

NR831 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Two Antidepressant Mechanisms Are Better Than One Melancholia

Laura Ferrando, M.D., *Instituto IAP, C/Velazquez 156 1 IZQ, Madrid 28002, Spain*; Jose M. Montes, M.D., Jeronimo Saiz-Ruiz, M.D.

Summary:

Objective: Selective serotonin reuptake inhibitors (SSRIs) have shown low remission rates in the treatment of major depression (Ferrier 1999) and their efficacy in melancholia has been questioned (Roose et al 1994). The aim of this study was to evaluate the rate of remission obtained with SSRIs in a clinical setting and the efficacy of treatments with combined mechanisms of action.

Method: The study involved a prospective, naturalistic, six-month, follow-up of 44 consecutive unipolar depressed (DSM-IV) outpatients (CGI ≥ 4). A SSRI was chosen as first treatment. After six weeks, patients were classified as remitted (HAM-D_{17} score ≤ 7), responders (≥50% improvement in HAM-D_{17} but still higher than 7) and nonresponders. Nonresponders were switched to a SSRI-heterocyclic antidepressant (HCA) combination or, when contraindication, to venlafaxine in monotherapy.

Results: Eight patients (18%) remitted at six weeks and remission was maintained at six months. Sixty-six percent (6/9) of responders achieved remission at six months. Nonresponse to SSRIs (61%) was associated to melancholic features. Ninety-six percent (26/27) of nonresponders achieved remission with the therapy proposed.

Conclusions: These results show low remission rate with SSRIs, especially in melancholia, and a greater benefit by using treatment with a combined serotonin-norepinephrine activity.

NR832 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Donepezil Treatment of Cognitive Deficits in Residual Schizophrenia: A Six-Month Follow-Up

Elisabetta Coli, M.D., *Department of Psychiatry, University of Pisa, Via Roma 67, Pisa 56100, Italy*; Elisabetta Maltinti, Alessandro Nassinbeni, M.D., Letizia Tiano, M.D., Annalisa Bassi, M.D., Enzo Poggi, M.D., Alessandro Lenzi

Summary:

Background: Some authors have hypothesized that cognitive impairment in schizophrenia may be a direct expression of the underlying neurochemical-structural dysfunction and sometimes preceed the onset of psychotic symptoms, and persist during the residual phase. Donepezil, a medication for the treatment of Alzheimer's dementia, has proven effective in schizophrenia as it improves cognition and has antidepressant effects. The aim of this study was to test donepezil efficacy in the treatment of neurocognitive deficits in residual schizophrenic patients, in a six month follow-up.

Methods: Twenty-one subjects (18–45 years) affected by schizophrenia, residual type, according to DSM-IV criteria, with an illness lasting at least 2 years, were administered 60 mg/day donepezil; concomitant pharmacological treatment was continued.

Results: Nearly half of the patients (n = 11) showed a cognitive improvement as regards executive and social functioning, with favorable implications for treatment compliance. The remaining 10 patients dropped out, mainly because of the development of psychomotor agitation (n = 6).

Conclusion: Results from this pivotal study suggest that donepezil may have a dishinibiting effect, leading to an overall improvement in half of the patients, and in a relapse in the remainder. Further studies are needed to clarify this issue and detect predictor of treatment outcome.

NR833 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Treatment Received for Depression in Psychiatric Care

Heikki K. Rytsala, M.D., *Department of MHAR, NPHI, Mannerheimintie 166, Helsinki 00300, Finland*; Tarja K. Melartin, M.D., Ulla S. Leskela, M.A., Paula S. Lestela-Mielonen, M.A., T. Petteri Sokero, M.D., Erkki T. Isometsa, M.D.

Summary:

Objective: New antidepressants emerged and became widely used during the 1990s. The present study investigated quality of care problems in the treatment of depression in a current psychiatric setting.

Method: We investigated the treatment received for depression by all 803 inpatients or outpatients with a clinical diagnosis of ICD-10 depressive episode or recurrent depressive disorder in 1996 in the Peijas Medical Care District, providing psychiatric services for citizens of Vantaa, a city in southern Finland.

Results: Most patients (84%) were found to have received antidepressants, generally in adequate, albeit low doses. Inadequate antidepressant treatment was common only with tricyclic antidepressants. Most patients received a single antidepressant for extended periods; 22% had two or more antidepressant trials. During the treatment period disability pension was granted to 19% of those not already pensioned, two-thirds (67%) of whom had received only one antidepressant trial prior to the pension being granted.

Conclusions: This study supports the perception of improved quality of pharmacotherapy in psychiatric settings, with the exception of treatment with tricyclic antidepressants. Problems of quality of care now are more related to the suboptimal intensity and monitoring of the treatment provided.

NR834 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Acute and Continuation Treatment of Depression in the Elderly

Thomas R. Thompson, M.D., *Department of Psychiatry, Emory University, 1841 Clifton Road, Atlanta, GA 30329*; Leslie E. Smith, B.A., Frederick A. Marsteller, Ph.D., John L. Woodard, Ph.D., Victoria L. Phillips, Ph.D., W. Vaughn McCall, M.D., William M. McDonald, M.D.

Summary:

Electroconvulsive therapy (ECT) and continuation ECT (C-ECT) are being used increasingly in the elderly. However, there have been no recent studies comparing the efficacy of antidepressant medication to an acute course of ECT and no prospective trials of C-ECT in the elderly. This abstract presents data from an ongoing NIMH-sponsored study (MH-156617) of acute and C-ECT in the elderly. Ninety-five subjects with severe major depression (mean age = 76 years, SD = 7; 68% female) were randomly assigned

in a 3:1 ratio to receive either a trial of medication (MED) or an acute course of ECT. 23% of the MED patients failed medication and were given an acute trial of ECT. At the end of 6 months of MED or 6 months after a successful acute course of ECT, subjects in the MED group had significantly higher ($p < 0.05$) scores on the Hamilton Depression Rating Scale (HDRS), Brief Psychiatric Rating Scale (BPRS), and lower scores on the Global Assessment of Function (GAF). 48 of these subjects (mean age = 76 years, SD = 6; 65% female) who received an acute course of ECT were randomly assigned in a 1:1 ratio to either 6 months of C-ECT or medication. Subjects who relapsed were administered an acute course of ECT and C-ECT for 6 months. 14 subjects have completed 6 months of C-ECT without relapse, and three subjects relapsed (18%) and required an acute course of ECT. 11 subjects completed 6 months of maintenance medication, and eight relapsed (40%) and required an acute course of ECT. There were no differences in the two groups at 6 months on the HDRS, GAF, or BPRS.

NR835 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Switching from Previous Antipsychotics to Olanzapine: A Regional Collaborative Multicenter Trial Assessing Two Switching Techniques in Asia Pacific

Bernardo J. Conde, M.D., *Santo Tomas University, Medical Arts Building, Room 2007, Manila, Philippines*; L. Chin-Te, M.D., B. Ho, M.D., S. Mahatme, M.D., M. Marlan, M.D., Nuntika Thavichachart, M.D., T. Vishanuyothin, M.D.

Summary:

Objective: This open-label, multicenter study compared the efficacy and safety of a direct switch (Group I) versus a start-taper switch (Group II) from previous antipsychotics to olanzapine.

Method: 108 outpatients with schizophrenia currently treated with antipsychotics were randomly switched to olanzapine (10 mg/day) for 6 weeks. Group I received only olanzapine while Group II received olanzapine and their usual antipsychotic in decreasing doses over the first 2 weeks. A successful switch was defined as completing 6 weeks of therapy without worsening of symptoms (CGI-S) or extrapyramidal side effects (Simpson Angus Scale). Overall efficacy was assessed by the PANSS, and safety assessments included monitoring of vital signs and adverse events.

Results: Both techniques had comparable successful switching rates (direct 74% versus taper 68%); PANSS total scores ($p < 0.001$) and Simpson Angus scores ($p < 0.01$) were significantly improved at endpoint.

Conclusions: Olanzapine was an effective and safe treatment for this group of patients in Asia and Australia.

Funding provided by Eli Lilly and Company

NR836 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Nizatidine Ameliorates Olanzapine Treatment-Related Weight Gain

Alan F. Breier, M.D., *MC 541, Eli Lilly and Company, Lilly Corporate Center DC 0538, Indianapolis, IN 46285*; Yoko Tanaka, Ph.D., Subaja Roychowdhury, Ph.D.

Summary:

Objectives: All antipsychotic drugs are associated with weight gain. Currently there are relatively few treatment options to mitigate this side effect. Nizatidine is a histamine (H)-2 receptor blocker and has been reported to have appetite-suppressant properties. This double-blind study evaluated the role of nizatidine in ameliorating olanzapine-associated weight gain for 16 weeks in patients with schizophrenia and related disorders.

Methods: After an initial screening period of 2–9 days, patients were randomly assigned to receive olanzapine (5–20 mg)+ placebo, olanzapine (5–20 mg)+ nizatidine (150 mg), or olanzapine (5–20 mg)+ nizatidine (300mg). Seventy-four patients were included in this analysis. Patients were followed for change in weight (primary objective) as well as effects on appetite and primary psychopathology.

Results: Patients treated with olanzapine + nizatidine (300mg) had gained substantially less weight at week 16 than did those treated with olanzapine and placebo ($p < 0.04$). This amelioration was seen as early as 3 weeks. Nizatidine was well-tolerated without significant adverse events, and overall clinical outcomes were not adversely affected.

Conclusions: Nizatidine may ameliorate the weight gain associated with olanzapine treatment.

Funding provided by Eli Lilly and Company

NR837 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Coprescription Patterns with Typical and Atypical Antipsychotics

Mona V. Bijlani, M.D., *Department of Psychiatry, UMDNJ-Extended Trt., 671 Hoes Lane, P O Box 1392, Piscataway, NJ 0885-1392*; Leonid Vorobyev, M.D., Robert G. Stern, M.D.

Summary:

Objective: Patients with schizophrenia and schizoaffective disorder are often treated with both antipsychotic medications and antidepressants or mood stabilizers. The authors reviewed charts of 204 patients with schizophrenia or schizoaffective disorder to study the coprescription patterns of antipsychotics (both typical and atypical) with mood stabilizers and antidepressants.

Method: 204 patient charts were reviewed: 74 with a diagnosis of schizoaffective disorder and 130 with a diagnosis of schizophrenia to study the coprescription patterns. Chi square analyses were conducted to compare the coprescription frequencies.

Results: In the patients with schizoaffective disorder, antidepressants were prescribed at a similar rate with both typical and atypical antipsychotics. Mood stabilizers were also prescribed almost equally with both typical and atypical antipsychotics. In patients with schizophrenia, both antidepressants and mood stabilizers were prescribed more frequently with atypical antipsychotics in comparison to typical antipsychotics. Furthermore, in both disorders there was no significant difference in coprescribing between olanzapine and typical antipsychotics.

Conclusions: Atypical antipsychotics have been studied for their mood stabilizing and antidepressant qualities. This study found no significant differences between the frequency with which antidepressants or mood stabilizers are coprescribed with typical or atypical antipsychotics in schizoaffective disorder. Surprisingly, among schizophrenic patients they were co-prescribed significantly more often with atypical antipsychotics.

NR838 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Preclinical Studies of Weight Gain During Olanzapine Treatment

J. David Leander, Ph.D., *Eli Lilly and Company, Lilly Corporate Center, Indianapolis, IN 46285*; Scott D. Gleason, M.D.

Summary:

Objective: Develop a rodent model of weight gain during olanzapine treatment and assess interventions to reduce weight gain.

Methods: Male rats of various strains and female Sprague Dawley rats were used. Olanzapine was injected once or twice daily, placed in drinking water, or a long-acting depot formulation was injected biweekly. Interventions studied were the appetite sup-

pressants mazindol and sibutramine and the antiparkinson agent amantadine.

Results: Weight gain during olanzapine treatment was not observed in male rats but was observed in female rats treated with olanzapine in drinking water and with the long-acting depot formulation. In female rats maintained on a long-term regimen of olanzapine, sibutramine and amantadine reduced body weight, whereas mazindol did not.

Conclusions: Weight gain in rodents was observed when they were continually exposed to olanzapine. Female Sprague Dawley rats exhibited weight gain during olanzapine treatment more than male rats or other strains. This preclinical model suggests both sibutramine and amantadine may reduce weight gain during olanzapine treatment.

Funding provided by Eli Lilly and Company

NR839 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Transition from Emergency to Routine Dual-Diagnosis Treatment

Andrew P. Ho, M.D., *Department of Psychiatry, Harbor-UCLA, 1000 West Carson Street, Box 498, Torrance, CA 90509*; John W. Tsuang, M.D., Timothy W. Fong, M.D., Carol Giannini, R.N., Christie Finazzo, M.S.W., David Haponski, M.S.W.

Summary:

Objective: Individuals with severe mental illness and comorbid substance disorder are overrepresented in psychiatric emergency rooms and under-represented in outpatient clinics. Successful transition from emergency to routine outpatient treatment is critical for many patients who would otherwise receive no treatment.

Method: We identified consecutive dual-diagnosed patients through review of psychiatric emergency room records. Demographics, symptoms, diagnoses, and outpatient referrals were recorded by dual-diagnosis case managers. After two weeks, the case managers conduct a phone interview to assess the success of transition to outpatient treatment. Online data management and analysis were performed using the Open Infrastructure for Outcomes (www.TxOutcome.Org), a free web-based case and outcomes management system.

Results: Of the 1,227 patients identified, 394 (32%) were successfully interviewed. Among those interviewed, 149 (38%) reported at least one visit to a psychiatric clinic and 59 (15%) reported receiving addiction treatment. Nearly half of those with psychiatric follow up also reported ongoing substance use (42%). Gender, acute symptoms, diagnoses, and type of referral did not predict successful transition.

Conclusions: A significant proportion of patients failed to transition from emergency to routine treatment. By systematically identifying patients who are ill and not in routine treatment, delivery of more effective treatment may be possible.

NR840 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Evaluation of a Systematic Treatment Algorithm for Depressive Disorders: How Effective Are the Different Treatment Steps? A Randomized, Controlled Study by the Berlin Algorithm Study Group

Mazda Adli, M.D., *Department of Psychiatry, Fu Berlin, Eschenallee 3, Berlin 14050, Germany*; Ursula Kiesslinggr, M.A., Michael Linden, M.D., Peter Neu, M.D., Michael Smolka, M.D.

Summary:

The use of systematic treatment algorithms has been suggested to enhance outcome of depressed patients and decrease the development of refractoriness to antidepressants. In a randomized controlled trial comparing the outcomes of 148 inpatients randomly assigned to either treatment according to a standardized stepwise drug treatment regimen (SSTR; N = 74) or to standard treatment as usual (STU; N = 74) we investigated in which step of the SSTR remission was achieved. Response to treatment was assessed at 2-week intervals using the Bech-Rafaelsen-Melancholia Scale (BRMS). 40 of the 41 study completers achieved remission (BRMS $\leq$ 7) in one of the following steps of the SSTR: three (7%) patients remitted after the initial withdrawal/sleep deprivation-phase, 12 (30%) after medium-dose antidepressant monotherapy, six (15%) after high-dose antidepressant monotherapy, 15 (37%) after lithium augmentation, one (2%) after subsequent antidepressant wash-out, and three (7%) after a MAO-inhibitor-lithium combination. The mean time on medication to remission or to discharge was significantly shorter in the SSTR group (42.7 days) than in the STU group (60.0 days) ($t = 2.185$, $p = 0.031$). The majority of patients adhering to an SSTR achieved remission after a trial of antidepressive monotherapy and subsequent lithium augmentation. An algorithm-guided treatment may enhance the efficiency of sequential treatment steps and decrease the variance of treatment execution.

Supported in part by grants from Janssen-Cilag, Lilly Deutschland and Wyeth Pharma, Germany

NR841 Thursday, May 10, 12:00 p.m.-2:00 p.m.

Sleep Disruption in Medication-Free Psychiatric Inpatients

Alan J. Drucker, M.D., *Department of Family Practice, UCSF at Fresno, 445 South Cedar Avenue, Fresno, CA 93702*; Davin M. Young-Clarke, M.A., Erick Wilkins, M.S.W.

Summary:

Objective: This study was designed to examine sleep disruption differences between psychiatric inpatients with schizophrenia and those with depression. The purpose was to assist practitioners in deciding on pharmacological and behavioral interventions for insomnia.

Method: Sixty-two subjects were sequentially selected from Fresno Community Hospital's psychiatric unit. The patients were medication-free for at least 5 weeks prior to observation with less than a 6-month history of symptoms related to their respective diagnoses. Each subject was observed to be awake or asleep every 30 minutes for one night. Observations were made within the context of routine patient supervision.

Results: Schizophrenic patients were awake more often throughout the night, and that both groups experienced the most disruption in the last third of the night ($F = 9.44$, $df = 1, 60$, $p < 0.01$). No significant differences were found between the groups with respect to sleep latency, although the schizophrenic group showed a trend toward increased latency ($t = 1.31$, $df = 60$, n.s.)

Conclusions: There are clinically important similarities and differences between the sleep/wake cycles of inpatients with schizophrenia versus those with depression. Their respective sleep disruption patterns suggest different medication and milieu-based interventions.

This research was supported in part by an educational grant from Wyeth-Ayerst.

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